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A Prospective, Randomized, Double-blinded Control Study on Comparison of Oral Midazolam and Dexmedetomidine as Premedication in Children

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Abstract

Context: Oral premedication is commonly used in pediatric anesthesia to provide preoperative anxiolytics and to ensure smooth induction. Midazolam is currently the most commonly used premedication, but newer drugs such as dexmedetomidine have emerged as alternatives for premedication in the pediatric population. *Aims:* The aim of the study is to compare the clinical effects of oral dexmedetomidine and oral midazolam on preoperative sedation and postoperative recovery profile in children. *Materials and Methods:* We performed a prospective, randomized, double-blinded controlled study in 106 children, 2–10 years of age undergoing elective surgeries under general anesthesia. Patients were randomly assigned to receive either oral dexmedetomidine 4 mcg/kg (Group D, n = 53) or oral midazolam 0.5 mg/kg (Group D, n = 53) 40 minutes prior to mask induction. Preoperative sedation and anxiolytics, the response of the child during separation from the parent, quality of mask acceptance and recovery profile were compared for the two groups. *Statistical Analysis:* Results were analyzed using an unpaired Student's *t*-test and Chi-squared test. $p < 0.05$ was considered statistically significant. *Results:* The level of preoperative sedation at the end of 40 minutes was significantly higher in the dexmedetomidine group (3.74 ± 0.07) than the midazolam group (3.17 ± 0.10). Response to parental separation and quality of mask acceptance was significantly better in group dexmedetomidine compared to group midazolam ($p > 0.05$). Intraoperative Heart rate and Mean Arterial Pressure (MAP) was lower in the dexmedetomidine group compared to midazolam group. The incidence of postoperative agitation was significantly less in the dexmedetomidine group ($p < 0.05$). *Conclusion:* In this study, we concluded that the premedication with oral dexmedetomidine produced better preoperative sedation and recovery from anesthesia in pediatric population compared to premedication with oral midazolam.

Keywords: Propofol; Dexmedetomidine; Intraoperative Sedation; Procedural Sedation; Spinal Anesthesia.

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Introduction

Premedication in children is an important criterion to determine the smooth induction and recovery from the surgery. Most of the pediatric population coming for surgery shows signs of significant preoperative anxiety and fear. To reduce the psychological and physiological effects of preoperative anxiety and fear, most of the anesthesiologists used sedative premedication, parental presence in anesthesiology (PPIA-allowing parents in the premedication room) and behavioral preparation methods.[1] Of these methods, sedative premedication is routinely followed in many centers. Behavioral preparation methods and PPIA are not commonly practiced in busy hospitals.[2] Recent studies have proven that the presence of parents in the operating room does not produce any benefit to the child but gives them satisfaction. Premedication helps in decreasing this anxiety and fear to facilitate a smooth induction of anesthesia and thereby reducing the risk of adverse reactions such as physiological and pharmacological effects of anesthesia induction in a distressed child.[3,4] There are various disadvantages and undesired effects seen in the child coming for surgery without the administration of premedication which include increased secretions in the oral cavity which may lead to increased risk of laryngospasm at the time of induction and extubation, increased possibilty of heart rate fluctuation during the perioperative periodand increased chance of emergence delirium.[5]

Commonly administered routes of premedication are oral, nasal, sublingual, rectal, Intramuscular (IM) and Intravenous (IV). Each one of these routes has advantages and disadvantages of its own. Due to these issues, in routine clinical practice, the anesthesiologist prefers the use of oral administration of sedative agents for premedication purposes before induction of anesthesia. The Disadvantage of oral administration of premedication is that most of the drugs used for premedication have a bitter taste and the possibility of a child spitting the drug when given orally is high. To avoid this, premedication drugs need to be mixed with sweetening agents before administration.

Commonly used premedication drugs include triclofos sodium, ketamine, Midazolam, Clonidine, Fentanyl and dexmedetomidine. Currently, the routinely used sedative drug for premedication in the pediatric population is oral midazolam.[6] Midazolam is a short-acting benzodiazepine. Use of midazolam has been attributed to several advantages like amnesia, rapid onset and offset of action and anxiolytics.[7-10] The disadvantages include respiratory depression, restlessness[5] and its bitter taste requires a sweetening agent to be mixed to make it acceptable for the child. Recently Dexmedetomidine, a selective alpha 2- agonist, have been emerged as an efficient alternative for the use as pediatric premedication.[11–13] Dexmedetomidine has anxiolytic as well as sedative property and it is not known to cause respiratory depression. Few preliminary studies show that dexmedetomidine can be used as a premedication in children coming for elective surgeries to reduce anxiety and to reduce the occurrence and severity of emergence delirium.[14–16] Since, there are only very few studies on oral dexmedetomidine as pediatric premedication, we conducted a randomized double-blinded study on comparing oral midazolam and oral dexmedetomidine as pediatric premedication.

Materials and Methods

This study was registered in the Clinical Trial Registry-India (CTRI) (Trial Number: CTRI/2017/12/010874). After obtaining approval of the institutional Ethical Committee, this study was performed as a prospective, randomized, double-blinded, controlled study in 106 children, aged 2–10 years undergoing elective surgery under general anesthesia at our institution. An informed and written consent was obtained from the parents or legal guardian during the preanesthetic check-up. Intavenous access with appropriate size IV cannula was obtained in the admitting ward on the morning of surgery. Patients were allocated in a randomized manner by computer-generated random envelope method into Two Groups: Group D-(dexmedetomidine n = 53) and Group M-(midazolam, n = 53). They were assigned to receive either oral midazolam 0.50 mg/kg or oral dexmedetomidine 4 mcg/kg 40 minutes before induction of anesthesia in the preoperative holding area. An injectable preservative-free 5 mg/ml preparation of midazolam was used in Group M and the IV formulation of dexmedetomidine (100 mcg/ml) was used in Group D. Both drugs are mixed with freshly prepared pulp-free apple juice to prepare a final volume of 5 ml. Preoperative sedation, the response of the child at parental separation, the response of the child during mask ventilation and recovery profile was compared between the two groups. Sedation status was assessed before the drug administration and thereafter, every 10 minutes for a maximum of 40 minutes after premedication.

Children aged from 2–10 years of ASA Grade I-II undergoing elective surgeries lasting between 30 minutes and two hours were included in the study. Those Children with developmental delay or mental retardation, with a history of emergence delirium in the previous surgery, with known allergies to the study drugs and child spitting out the premedication drug were excluded from the study.

The first anesthesiologist opened the envelope and prepared the drug according to the group generated. The first anesthesiologist did not take any further part in the study. Once the child comes into the premedication room, Electrocardiogram (ECG), pulse-oximeter (SpO_2) and Noninvasive Blood Pressure (NIBP) monitors are attached and the baseline values are noted. Second anesthesiologist, who was blinded to the group involved, administered the drug to the child. Heart rate, blood pressure, and saturation are continuously monitored and recorded every 15 minutes from the time of administration of the drug. The level of sedation was assessed every 10 minutes and recorded from the time of administration of drug till 40 minutes.

The level of sedation was assessed by using a 4-point scale:[20]

1 = anxious, depressed/agitated/crying;

2 = awake, calm, quiet;

3 = drowsy, responds to verbal commands/ gentle stimulation;

4 = asleep.

The child was transferred to the induction room at the end of 40 minutes. The response of the child at parental separation was recorded. It was graded using a 4-point scale[20] as:

1 = crying, cannot be reassured;

2 = awake, anxious, can be easily reassured;

3 = good separation, awake, calm;

4 = asleep.

Once the child comes into the operating theatre, ECG, pulse-oximeter, and NIBP were attached. The facemask was kept on the child with 100 percent oxygen and sevoflurane. Mask acceptance was assessed using a 5-points scale:[20]

1 = combative, crying;

2 = moderate fear of mask, not easily calmed;

3 = cooperative with reassurance;

4 = calm, cooperative;

5 = asleep, steal induction.

Mask induction Scores of 1 and 2 were considered unsatisfactory while a Score of 3–5 was regarded as a successful response to premedication. Injection glycopyrrolate 10 mcg/kg IV was given. Injection fentanyl 2 mcg/kg IV given for analgesic requirement. Anesthesia was induced with sevoflurane. Anesthesia was maintained with nitrousoxide with oxygen (N_2O:O_2) ratio of 2:1. IV fluids were administered according to the holiday Segar formula. In the intraoperative period, continuous monitoring of heart rate, blood pressure, and saturation was done and recorded every 15 minutes. Atracurium was used as a muscle relaxant in patients who required Endotracheal Tube (ETT) insertion and it was avoided in patients who required a Laryngeal Mask Airway (LMA). Use of endotracheal intubation or use of LMA was decided according to the need for the surgery.

At the end of the procedure, the child was reversed from anesthesia. As soon as the child was able to maintain a patent airway, the child was shifted to the recovery room. ECG, pulse oximeter and NIBP monitors attached. The child was let there to wake up naturally in the recovery room. In the recovery room, recovery profile was assessed using a 3 point scale:[20]

1 = Agitated, crying;

2 = Crying but easily consoled;

3 = Calm, asleep.

The child was kept in the recovery room for two hours, at the end of two hours; the child was shifted to the respective wards. The child was followed up in the ward until 12 hours from the time of administration of the drug. Heart rate, blood pressure, and saturation were recorded every two hours.

Statistical Analysis

All values were reported as mean ± Standard Error of the Mean (SEM). Data analysis for numerical data was performed using unpaired Student's *t*-test and for categorical data was performed by Chi-square. A p - value of < 0.05 was considered statistically significant and a p - value of < 0.001 was considered statistically very significant.

Results

One hundred-six children were enrolled in the study and assigned into Group M (n = 53) and Group D (n = 53). There was no statistical difference

between the groups with respect to demographic characteristics, ASA status, and duration of surgery, Table 1. Hemodynamic parameters including heart rate, MAP and saturation were compared between the two groups, a statistically significant reduction of heart rate was noted in Group D at 75th minute of administration of the drug till 120th minute, but no interventions made since, it does not fall below the 20% of the preoperative values. The remaining values were comparable.

Table 1: Demographics, ASA status and duration of surgery

	Group D	Group M	*p* - value
Age (years)	5.92 + 0.36	5.94 + 0.36	0.970
Sex (%) Male/Female	27/26	26/27	0.500
Weight (kgs)	20.43 = 0.81	20.47 + 0.81	0.974
ASA Status ASA 1/ASA 2	49/4	50/3	0.6942
Duration of Surgery (minutes)	76.60 + 3.25	79.23 + 3.04	0.557

The sedation score was compared between the two groups and it was significantly more at 40 minutes in the dexmedetomidine group (3.74 ± 0.07) compared to the midazolam group (3.17 ± 0.10). *p*- value < 0.001, Table 2. Parental separation was compared between the two groups. *p* - value was found to be < 0.001 which is statistically highly significant, Table 3. Mask acceptance was compared between two groups and *p* - value was found to be < 0.001 which is statistically highly significant, Table 4. The recovery profile was compared between the two groups. *p* - value was found to be 0.0001 which is statistically highly significant, (Table 5).

Table 2: Sedation score

Timing	Dexmedetomidine	Midazolam	*t*-test	*p* - value
0 min	1.00 ± 0.00	1.00 ± 0.00	–	–
10 min	1.06 ± 0.04	1.15 ± 0.05	–1.453	0.149*
20 min	2.09 ± 0.06	1.94 ± 0.06	1.801	0.075*
30 min	2.47 ± 0.08	2.43 ± 0.09	0.320	0.749*
40 min	3.74 ± 0.07	3.17 ± 0.10	4.712	0.0001‡

Table 3: Comparison of parental separation

Group	Parental separation			Chi-square	*p* - value
	2	3	4		
Dexmedetomidine	0	14	39	25.81	0.0001‡
Midazolam	14	23	16		

Table 4: Mask acceptance

Group	Mask acceptance			Chi-square	*p* - value
	3	4	5		
Dexmedetomidine	2	30	21	45.196	0.0001‡
Midazolam	34	7	12		

Table 5: Recovery profile

Group	Recovery profile		Chi-square	*p* - value
	2	3		
Dexmedetomidine	6	47	12.425	0.0001‡
Midazolam	22	31		

Discussion

Premedication is required in pediatric population coming for surgery to decrease the adverse psychological effects of hospitalization, operative procedure, emergence delirium, and parental separation. An ideal premedication should provide adequate anxiolysis and sedation to allow a smooth induction of anesthesia. It should be free from side-effects such as hemodynamic disturbances and emergence delirium and respiratory depression. Oral midazolam is one of the routinely used drugs in pediatric anesthesia as premedication and has shown to be more effective in allaying the child's anxiety and fear than the parental presence. Midazolam has both anxiolytic as well as sedative property which is believed to produce a calming effect. This characteristic feature of midazolam makes the children less anxious when they are separated from their parents and during mask placement during the induction of anesthesia. It facilitates gamma-aminobutyric acid receptor-mediated chloride conductance, which has an inhibitory effect on neurons in the cerebral cortex. The dose of 0.50 mg/kg of injectable midazolam given orally as premedication is acceptable, effective and safe. Recently, α_2-receptor agonists such as clonidine[24] and dexmedetomidine have also been found to be useful for premedication in children. These drugs act on central α_2-receptors located at the locus ceruleus causing inhibition of release of noradrenaline and create electroencephalogram activity similar to normal sleep. This results in anxiolytic effects, analgesia, and sedation without respiratory depression.[17–20]

Heart rate was monitored continuously from the administration of the drug and was recorded every 15 minutes till two hours and then recorded every two hours for 12 hours. It was found that there was a significant difference in the heart rate between the two groups at 75 minutes, 90 minutes, 105 minutes and 2 hours. It is concluded that children under Group D had a statistically significant reduction in heart rate after 75 minutes of administration of drugs till two hours of administration of drug compared to children under Group M. Though there was a decrease in heart rate none of the children required intervention because it was not clinically significant. Pant et al.[23] conducted a study on sublingual midazolam and sublingual dexmedetomidine as pediatric premedication and in the study, he found that the heart rate was significantly lower throughout the perioperative period ($p < 0.001$) in the dexmedetomidine group. Their study result was similar to our result.

Blood pressure was continuously monitored from the administration of the drug and the MAP was recorded every 15 minutes till two hours and then recorded every two hours for 12 hours. It was found that there was a significant difference in the MAP at 60 minutes, 75 minutes, 90 minutes, 105 minutes and two hours between two groups. In the remaining times, the MAP between the two groups were comparable. It is concluded that children under Group D had a statistically significant reduction in MAP after 60 minutes of administration of drugs till two hours of administration of drug compared to children under Group M. Though there was a decrease in MAP none of the children required intervention because it was not clinically significant. Oxygen Saturation was comparable between the two groups and there was no significant difference between the two groups in terms of saturation throughout the study.

The sedation score was analyzed just before administration of the drug and then for every 10 minutes till 40 minutes. The sedation score was compared between the two groups and there were no significant differences between the two groups for the first 30 minutes. However, at the end of 40 minutes, there is a significant difference in the sedation score between the two groups. It was concluded that dexmedetomidine produces better sedation over midazolam at the end of 40 minutes. Yuen et al.[25] conducted a study on comparison of oral midazolam and intranasal dexmedetomidine and found similar results in terms of sedation score. In that study, the median sedation score was assessed by the modified Observer Assessment of Alertness and Sedation Scale (OASS) in 6 patients receiving 0.5 mg/kg midazolam compared to median score of 3 in children who received intranasal dexmedetomidine 0.5 mcg/kg. In that study, they concluded that intranasal dexmedetomidine was better than oral midazolam in preoperative sedation.

Parental separation was compared between the two groups and the p - value was found to be 0.0001 which is statistically highly significant. In Group D, 14 children were assessed to have a parental separation score of three and 39 children were assessed to have a parental separation score of four. In Group M, 14 children were assessed to have a parental separation score of two, 23 children were assessed to have a parental separation score of three and 16 children were assessed to have a parental score of four, (Figure 1). It is concluded that oral dexmedetomidine produced better parental

separation than oral midazolam. This result correlates with Pant et al.[23] study on sublingual midazolam and dexmedetomidine where the median of sedation score at parental separation was 6 in children administered midazolam and the median of sedation score at parental separation was 3.5 in children administered dexmedetomidine. *p* - value was < 0.001, they concluded that sublingual dexmedetomidine provided more effective preoperative sedation as compared to sublingual midazolam.

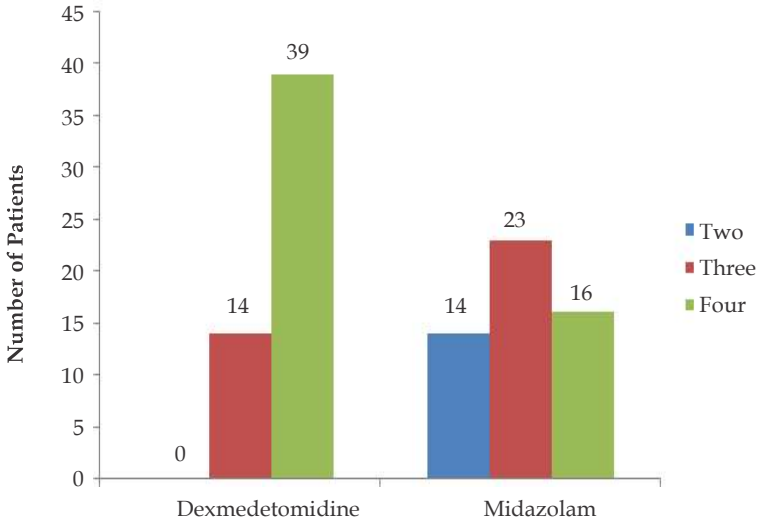

Fig. 1: Comparison of parental separation.

Mask acceptance was compared between two groups. In Group D, two children were assessed under Score 3 for mask acceptance, 30 children were assessed under Score 4 for mask acceptance and 21 children were assessed under Score 5 for mask acceptance. In Group M, 34 children were assessed under Score 3 for mask acceptance, 7 children were assessed under Score 4 for mask acceptance and 12 children were assessed under Score 5 for mask acceptance, (Figure 2). This led to the conclusion that dexmedetomidine is more effective in terms of mask acceptance similar to the results of Pant et al.[23] study on sublingual midazolam and dexmedetomidine. In that study, the median of mask acceptance score was 2 in children administered midazolam and the median of mask acceptance score was 1 in children administered dexmedetomidine. *p* - value was < 0.001, they concluded that sublingual dexmedetomidine provided more effective preoperative sedation for mask acceptance as compared to sublingual midazolam.

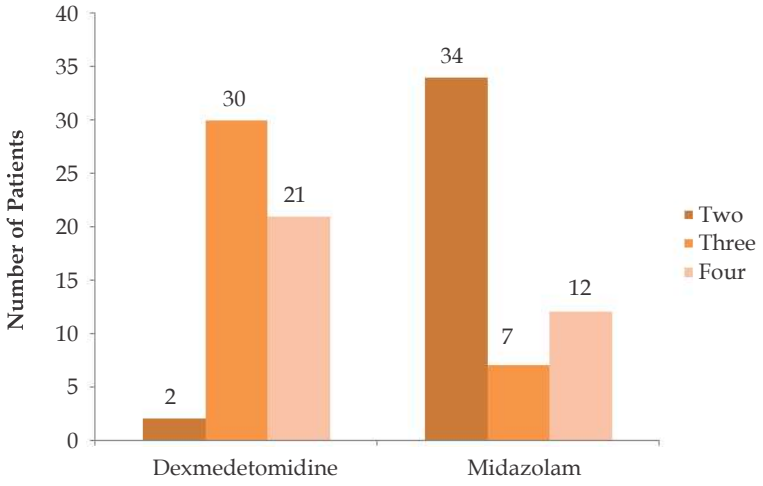

Fig. 2: Comparison of mask acceptance.

Recovery profile was compared between two groups and the *p* - value was found to be 0.0001 which is statistically highly significant. Group D has a better effect on recovery profile when compared with Group M, (Figure 3). Jannu et al.[20] compared oral dexmedetomidine and oral midazolam as pediatric premedication. In that study, they calculated the postoperative agitation score and concluded that children administered oral dexmedetomidine has a better recovery profile compared to oral midazolam. This result is similar to our study result.

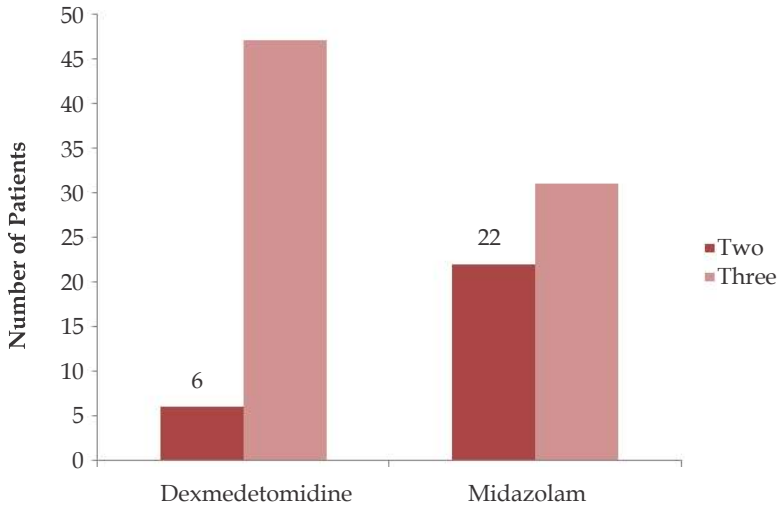

Fig. 3: Comparison of recovery profile.

Conclusion

In this study, we concluded that oral dexmedetomidine as a premedication in children is better than midazolam in achieving sedation, better mask acceptance and better recovery profile from anesthesia.

Support: Nil

Conflicts of interest: Nil

References

1. Kain ZN, Mayes LC, Wang SM, et al. Parental presence during induction of anesthesia *versus* sedative premedication: Which intervention is more effective? Anesthesiology 1998;89:1147–156.
2. Abdallah C, Hannallah R. Premedication of the child undergoing surgery. Middle East J Anesthesiol 2011;21:165–76.
3. Kain ZN, Caldwell-Andrews AA. Preoperative psychological preparation of the child for surgery: An update. Anesthesiol Clin North America 2005;23:597–614.
4. Audenaert SM, Wagner Y, Montgomery CL, et al. Cardiorespiratory effects of premedication for children. Anesth Analg 1995;80:506–510.
5. Vlajkovic GP, Sindjelic RP. Emergence delirium in children: Many questions, few answers. Anesth Analg 2007;104:84–91.
6. Feld LH, Negus JB, White PF. Oral midazolam preanesthetic medication in pediatric outpatients. Anesthesiology 1990;73:831–34.
7. Finley GA, Stewart SH, Buffett-Jerrott S, et al. High levels of impulsivity may contraindicate midazolam premedication in children. Can J Anesth 2006;53:73–78.
8. Sheta SA, Alsarheed M. Oral midazolam premedication for children undergoing general anesthesia for dental care. Int J Pediatr 2009;274380.
9. Heizmann P, Eckert M, Ziegler WH. Pharmacokinetics and bioavailability of midazolam in man. Br J Clin Pharmacol 1983;16(1):43–49.
10. McMillan CO, Spahr-Schopfer IA, Sikich N, et al. Premedication of children with oral midazolam. Can J Anesth 1992;39:545–50.
11. Khan ZP, Ferguson CN, Jones RM. Alpha-2 and imidazoline receptor agonists. Their pharmacology and therapeutic role. Anesthesia 1999;23(7):345–32.
12. Almenrader N, Passariello M, Coccetti B, et al. Premedication in children: A comparison of oral midazolam and oral clonidine. Pediatr Anesth 2007;17:1143–149.
13. Fazi L, Jantzen EC, Rose JB, et al. A comparison of oral clonidine and oral midazolam as preanesthetic medications in the pediatric tonsillectomy patient. Anesth Analg 2001;92:56–61.

14. Shukry M, Clyde MC, Kalarickal PL, et al. Does dexmedetomidine prevent emergence delirium in children after sevoflurane-based general anesthesia? Pediatr Anesth 2005;15:1098–1104.
15. Tobias JD, Berkenbosch JW. Initial experience with dexmedetomidine in pediatric-aged patients. Pediatr Anesth 2002;12:171–75.
16. Ibacache ME, Muñoz HR, Brandes V, et al. Single-dose dexmedetomidine reduces agitation after sevoflurane anesthesia in children. Anesth Analg 2004;98:60–63.
17. Ebert TJ, Hall JE, Barney JA, et al. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology 2000;93:382–94.
18. Anttila M, Penttilä J, Helminen A, et al. Bioavailability of dexmedetomidine after extravascular doses in healthy subjects. Br J Clin Pharmacol 2003;56:691–93.
19. Schmidt AP, Valinetti EA, Bandeira D, et al. Effects of preanesthetic administration of midazolam, clonidine, or dexmedetomidine on postoperative pain and anxiety in children. Pediatr Anesth 2007;17:667–74.
20. Jannu V, Mane RS, Dhorigol MG, et al. A comparison of oral midazolam and oral dexmedetomidine as premedication in pediatric anesthesia. Saudi J Anesth 2016;10: 390–94.
21. Mountain BW, Smithson L, Cramolini M, et al. Dexmedetomidine as a pediatric anesthetic premedication to reduce anxiety and to deter emergence delirium. AANA J 2011;79:219–24.
22. Kurdi MS, Muthukalai SP. A comparison of the effect of two doses of oral melatonin with oral midazolam and placebo on preoperative anxiety, cognition and psychomotor function in children: A randomized double-blind study. Indian J Anesth 2016;60:744–50.
23. Pant D, Sethi N, Sood J. Comparison of sublingual midazolam and dexmedetomidine for premedication in children. Minerva Anestesiol 2014;80(2):167–75.
24. Rad AT, Hassanzad A, Aryaie M et al. Oral clonidine premedication reduces postoperative pain in children. Euro J Exp Bio 2014;4(2):102–105.
25. Yuen VM, Hui TW, Irwin MG, et al. A comparison of intranasal dexmedetomidine and oral midazolam for premedication in pediatric anesthesia: A double-blinded randomized controlled trial. Anesth Analg 2008;106:1715–721.

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Comparitive Evaluation of Crystalloid Preload and Crystalloid Coload on Hemodynamic Parameters in Patients Undergoing Elective Cesarean Section under Spinal Anesthesia

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Abstract

Aims and Objectives: To compare the effects of crystalloid preload and crystalloid coload on hemodynamic parameters in patients undergoing elective cesarean section under spinal anesthesia. *Materials and Methods:* One hundred patients with American Society of Anesthesiologists Physical Status I and II scheduled for elective cesarean section under spinal anesthesia were randomly allocated into two groups with fifty patients each. *Group P*: Received 15 ml/kg of Ringer's lactate solution over 20 minutes prior to spinal anesthesia. *Group C*: Received 15 ml/kg of Ringer's lactate solution over 20 minutes as soon as Cerebrospinal fluid (CSF) was tapped. Patients were assessed for hemodynamic changes, mean and total dose of vasopressor consumption in the intraoperative period. *Results:* The incidence of Hypotension was high in Group P (66%) when compared to Group C (36%) with *p* - value of 0.0027 which is statistically significant. Hypotension appeared early in Group P (6.85 ± 0.83) when compared to Group C (15.83 ± 0.92) minutes with significant *p* - value of < 0.001. Group P also had higher incidence of nausea and vomiting (48% and 34%) when compared to Group C (18% and 12%) respectively with statistically significant difference. (*p* - value 0.0027 and 0.0014 respectively). The incidence of bradycardia and shivering was also high in Group P as compared to Group C though the difference is statistically insignificant. *Conclusion:* Crystalloid coload in the dose of 15 ml/kg is more effective than the crystalloid preload in the same dose for prevention of spinal hypotension in patients undergoing elective cesarean section.

Keywords: Crystalloid preload; Crystalloid coload; Elective cesarean section; Hemodynamic changes; Mean and total vasopressor consumption.

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Introduction

Regional anesthesia, especially Spinal Anesthesia (SA) is commonly used in patients undergoing cesarean section due to its beneficial effects on both mother and fetus.[1] Spinal anesthesia is preferred over General anesthesia due to its distinct advantages such as avoidance of airway related complications, aspiration and neonatal depression.[2,3]

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Spinal anesthesia is usually accompanied with hypotension (Spinal Hypotension) which is often defined as a Systolic blood pressure less than 100 mm Hg or a 20% drop in the baseline level.[4] Spinal hypotension is a common physiological complication with an incidence rate of 25–75% among general population and a little higher incidence rate of 82% in parturients undergoing cesarean section.[5,6] Higher rate of spinal hypotension in parturients is due to aortocaval compression as well as the higher level of block (T_4) required for cesarean section.[7]

Spinal hypotension is mainly due to sympathetic blockade leading to peripheral vasodilation and venous pooling of blood which in-turn leads to decreased venous return and cardiac output.[8] Other maternal side effects associated with spinal anesthesia include nausea, vomiting, aspiration, altered sensorium, bradycardia and cardiac arrhythmias.[2,3] Sustained maternal hypotension is associated with fetal hypoxia and acidosis as a result of placental hypoperfusion.[9] Thus, prevention of spinal hypotension is of paramount importance to the attending anesthetist as both mother and fetus life is at risk.

Several prophylactic measures were investigated to offset the hypotensive effect of spinal anesthesia such as leg wrapping, elastic stockings, optimizing patient's position, intravenous fluids and vasopressors. Of all the methods, most commonly used technique was intravenous volume expansion with intravenous fluids before the initiation of spinal anesthesia, a technique commonly called ˝preload" which was first described by Wollman and Marx.[10,11]

However, the efficacy of preload in preventing spinal hypotension was questioned by some studies and advised the rapid bolus infusion of intravenous fluids in the period just following the spinal injection, a technique commonly called "coload".[12–15]

Mercier et al. suggested fluid coload may be a more physiological and rational approach for prevention of Spinal hypotension because the increase in intravascular volume brought about by co-loading coincides with the time of maximal vasodilation. Crystalloids do not remain in the intravascular space but distribute rapidly into the extracellular space (75%) and hence, the timing of infusion may be the keynote to prevent spinal hypotension.[16]

However, a systematic review and meta-analysis involving eight studies on 518 patients for the effects of preloading and coloading on spinal hypotesion observed a similar incidence of hypotension and nausea/vomiting between the two groups.[17]

Some studies showed that colloids may be more effective than crystalloids for preventing spinal hypotension. However, there are several disadvantages associated with colloids, such as cost, allergic reactions and their effects on coagulation system.[8] Hence, crystalloids are still preferred over colloids by many anesthesiologists.

Based on the above studies, we hypothesized to conduct this study to evaluate the effect of crystalloid preload and crystalloid coload on hemodynamic parameters in patients undergoing elective cesarean section under spinal anesthesia. The rationale of this study was to identify safe fluid loading techniques to prevent spinal hypotension in patients undergoing elective cesarean section under spinal anesthesia.

Materials and Methods

Randomized, prospective, double blind study was conducted on 100 patients scheduled to undergo elective cesarean section at Major operation theatre MIMS, Mandya, Karnataka, India after obtaining approval from Institutional Ethical Committee and informed consent from patients.

Inclusion Criteria

1. ASA I & II patients undergoing elective cesarean section;
2. Age: 18–35 years;
3. Weight: 50–100 kgs;
4. Height: > 150 cm;
5. BMI < 30
6. Singleton pregnancy at term;
7. Uncomplicated pregnancy.

Exclusion Criteria

1. Spinal deformities;
2. Coagulation abnormalities;
3. Medical comorbidities such as Pregnancy Induced Hypertension (PIH), chronic hypertension, Gestational Diabetes Mellitus (GDM), cardiovascular diseases, severe anemia etc;
4. Patients posted for emergency cesarean section;

5. Infection at lumbar puncture site;
6. Allergic to local anesthetics;
7. Any other contraindications for regional anesthesia.

Preoperative assessment of patients including routine blood investigations and Electrocardiogram (ECG) were done a day prior to surgery. Patients were briefed about details of the study and informed consent was taken. Using computer generated random numbers patients were randomized into Group P (Preload Group) and Group C (Coload Group) each having 50 patients. The patients were kept nil per oral as per American Society of Anesthesiologists (ASA) guidelines.[18]

All patients received Tab. Ranitidine 150 mg orally on the night before surgery. On the day of surgery 50 mg Inj. Ranitidine and 10 mg Inj. Metoclopramide were given 2 hours prior to surgery.

For the study, all patients had two 18 G intravenous cannula, one for the administration of intravenous fluid and the other for administering intravenous drugs. On arrival to the major operation theatre, patient was connected to multiparameter monitor to record pulse rate, noninvasive blood pressure, ECG, and oxygen saturation (SpO_2). Under aseptic precautions, all study patients received spinal anesthesia in left lateral position at L3-L4/L4-L5 intervertebral space using 10 mg (2 cc) 0.5% Inj. Bupivacaine heavy with 25 G Quincke's spinal needle.

The patients in Group P received 15 ml/kg of Ringers lactate solution over 20 minutes prior to spinal block. The patients in Group C were given 15 ml/kg of Ringers lactate solution over 20 minutes as soon as Cerebrospinal fluid (CSF) was tapped. After the spinal injection, the patients were put into supine position with a 15 degrees wedge under the right hip. The sensory level was assessed using pin prick to 25 G needle every 5 minutes till the level stabilized for at least three consecutive readings. After achieving a block height of T5, surgeon was asked to start the surgery.

After infusion of predefined fluid in respective study group, Ringers lactate was started at maintenance rate of 10 $ml/kg^{-1}/hr^{-1}$ for the intraoperative period.

A two-operator technique was employed to prevent the observer bias. Randomization was performed by an Anesthetist intended to deliver the studied fluid and to initiate spinal anesthesia while interventions and monitoring were performed by a second Anesthetist blinded to the group allocation.

All patients were continuously monitored for heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, SpO_2 by an investigator every 2 minutes for the first 10 minutes and every 5 minutes till 30 minutes and every 10 minutes till the end of surgery.

Maternal hypotension was defined as a fall in Systolic Blood Pressure (SBP) to less than 100 mm of Hg or Mean Arterial Pressure (MAP) less than 80% of the baseline value. Any episode of maternal hypotension was treated with a bolus dose of crystalloid fluid and Inj. Phenylephrine 25 μg IV repeated every 3 minutes until the blood pressure recovers to normal. The number of doses and the total dose of Phenylephrine required to treat hypotension was recorded.

Bradycardia was defined as a Heart rate less than 50 beats per minute and was treated with intravenous Inj. Atropine 0.6 mg. Any episode of nausea or vomiting was treated with a bolus dose of Inj. Ondansetron 4 mg IV. Continuous monitoring of oxygen saturation was done and supplemental oxygen was delivered through a facemask if SpO_2 falls below 94%. Inj. Oxytocin 20 IU intravenous infusion was administered to the mother once the baby was delivered. APGAR scores were determined at 1 and 5 minutes interval by the attending neonatologist who was unaware of the study group allocation. Fetal blood gas analysis was performed with ABL 90 FLEX analyzer (Radiometer, Copenhagen, Denmark) on blood samples collected from umbilical artery and umbilical vein.

The total blood loss and total intravenous fluid administered were also noted.

Statistical Analysis

Descriptive statistical analysis was done using SPSS® computer software-IBM SPSS Statistics version 26. Results on continuous measurements were presented as Mean ± SD and results on categorical measurements were presented in number and percentage. Student's *t*-test/*Z*-test was used to find the significance of study parameters on continuous scale while Chi-square test/Fishers exact test was used to find the significance of study parameters on categorical scale. Upper sensory level attained was compared with Mann–Whitney *U*-test. Significance was assessed at 5% level. Any *p* - value less than 0.05 ($p < 0.05$) was considered as statistically significant.

Results

The demographic data was comparable among the study groups and the difference was not statistically significant, as shown in (Table 1).

There was no statistically significant difference between the two groups as regards to baseline heart rate, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP), (Table 2).

Table 1: Demographic variables among study groups

Parameters	Mean ± SD		*t*-test statistic value	*p* - value
	Group P (*n* = 50)	Group C (*n* = 50)		
Age (yrs)	25.22 ± 2.65	24.80 ± 2.75	0.777	0.439
Weight (kgs)	69.92 ± 4.70	68.56 ± 3.87	1.578	0.118
Height (cms)	165.40 ± 4.48	165.94 ± 3.18	–0.695	0.489
Body Mass Index	25.61 ± 2.18	24.93 ± 1.79	1.694	0.093
Gestational Age (wks)	38.59 ± 0.43	38.44 ± 0.36	1.841	0.069

Table 2: Comparison of preoperative characteristics among study groups

Parameters	Mean ± SD		*t*- test statistic value	*p* - value
	Group P (*n* = 50)	Group C (*n* = 50)		
Baseline HR (bpm)	72.52 ± 7.44	74.08 ± 5.76	–1.173	0.244
Baseline SBP (mm Hg)	122.60 ± 6.89	121.28 ± 6.84	0.961	0.339
Baseline DBP (mm Hg)	74.96 ± 5.60	74.32 ± 6.53	0.524	0.602
Baseline MAP (mm Hg)	90.90 ± 4.55	89.98 ± 5.09	0.952	0.343

In Group P, the incidence rate of Hypotension was high (66%) when compared to Group C (36%) with *p* - value of 0.0027 which is statistically significant.

No significant difference was observed in mean arterial pressure between the two groups at different times studied, except at 6 and 15 minutes, which showed a significant difference between the two groups (*p*-value < 0.001 and *p*-value < 0.001) respectively. Hypotension appeared early in Group P (6.85 ± 0.83) when compared to Group C (15.83 ± 0.92) minutes with *p* - value of < 0.001, Fig. 1. Similarly, the study of Heart rate also showed no significant difference among the study groups at different times except at 6 and 15 minutes which showed a statistically significant difference with *p* - value of 0.003 and *p* - value of 0.001 respectively, (Fig. 2).

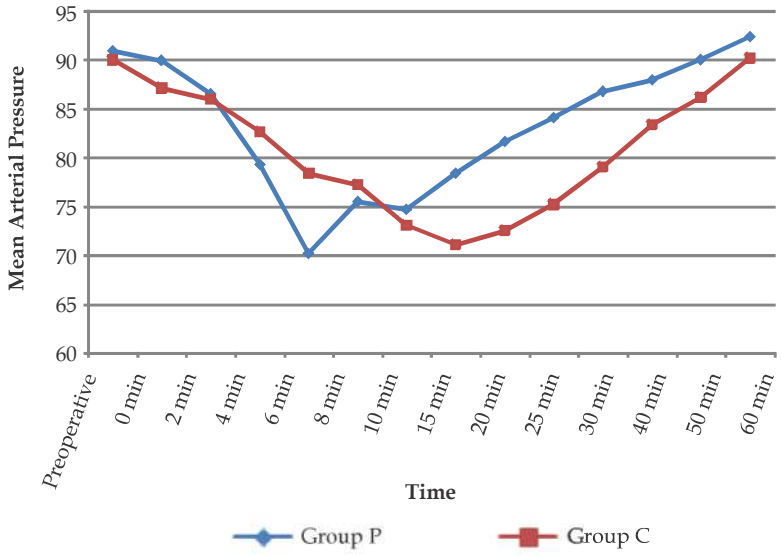

Fig. 1: Trends of Mean arterial pressure among study groups.

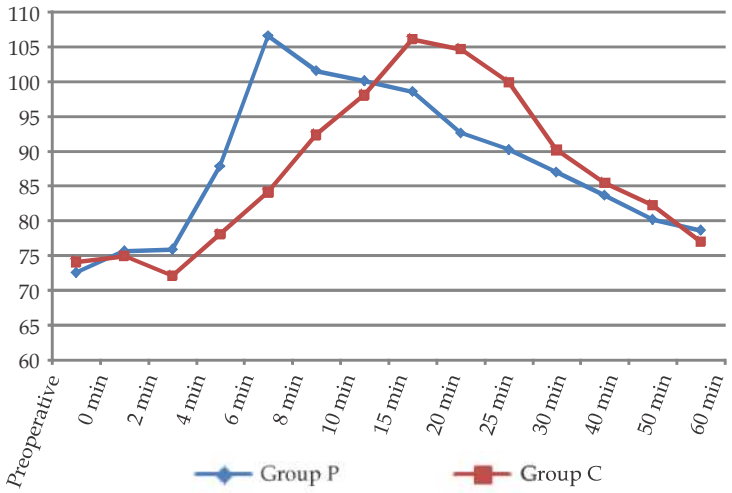

Fig. 2: Trends of Heart rate among study groups.

Group P had higher incidence of Nausea and vomiting (48% and 34%) when compared to Group C (18% and 12%) respectively with statistically significant difference. (*p* - value 0.0027 and 0.0014 respectively). The incidence rate of Bradycardia was also high in Group P (26%) when compared to Group C (16%) though the difference was statistically insignificant (*p* - value 0.2187). Patients complaining of shivering was also more in Group P (42%) when compared to Group C (30%) though the difference was statistically insignificant (*p* - value 0.2113).

Mean number of dose of Phenylephrine used to correct hypotension in Group P was 1.14 ± 1.74 when compared to Group C 0.51 ± 1.72 with *p* - value of < 0.001 which is statistically significant. Patients requiring single as well as double rescue dose of vasopressor to correct hypotension was more in Group P when compared to Group C though the difference was statistically insignificant. The triple rescue dose requirement was also high in Group P as compared to Group C and the difference was statistically significant. (*p* – value = 0.0026**)**

The mean total cumulative dose of vasopressor to correct hypotension was high in Group P (41.67 + 20.41) as compared to Group C (34.72 ± 12.54) mcg though the difference was statistically insignificant (*p* – value = 0.196). The total intravenous fluids used to correct intraoperative hypotension was more in Group P (1780 ± 236) as compared to Group C (1395 ± 215) with statistically significant *p* - value of < 0.001, (Table 3, Figs. 3 and 4).

No adverse neonatal outcome was observed in the study groups in terms of Apgar score and acid-base status, (Table 4).

Table 3: Comparison of intraoperative characteristics among study groups

Parameters	Group P (*n* = 50)	Group C (*n* =50)	*t*-test statistic value/Z-test statistic value	*p* - value
Highest sensory block level	T5 (T3-T6)	T5 (T2-T6)	–0.20	0.8414
Total fluids (ml)	1780 ± 236	1395 ± 215	8.52	< 0.001
Blood loss (ml)	654 ± 186	690 ± 118	–0.115	0.25
Time to first hypotension (min)	6.85 ± 0.83	15.83 ± 0.92	–35.411	< 0.001
Hypotension (%)	33 (66.0)	18 (36.0)	3.01	0.0027
Nausea (%)	24 (48.0)	09 (18.0)	3.19	0.0014
Vomitting (%)	17 (34.0)	06 (12.0)	2.61	0.0096
Bradycardia (%)	13 (26.0)	08 (16.0)	1.23	0.2187
Shivering (%)	21 (42.0)	15 (30.0)	1.25	0.2113
Mean dose of Phenylephrine (No)	1.14 ± 1.74	0.51 ± 1.72	7.5	< 0.001
Single rescue dose of Phenylephrine	18	11	1.542	0.1235
Double rescue dose of Phenylephrine	08	07	0.28	0.7794
Triple rescue dose of Phenylephrine	07	0	3.06	0.0026
Total dose of Phenylephrine (mcg)	41.67 ± 20.41	34.72 ± 12.54	1.311	0.196

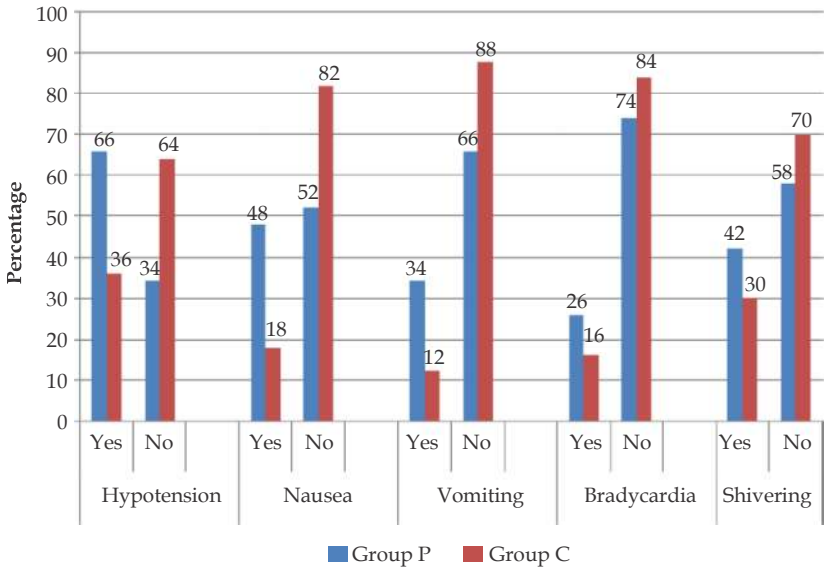

Fig. 3: Comparison of intraoperative characteristics among study groups.

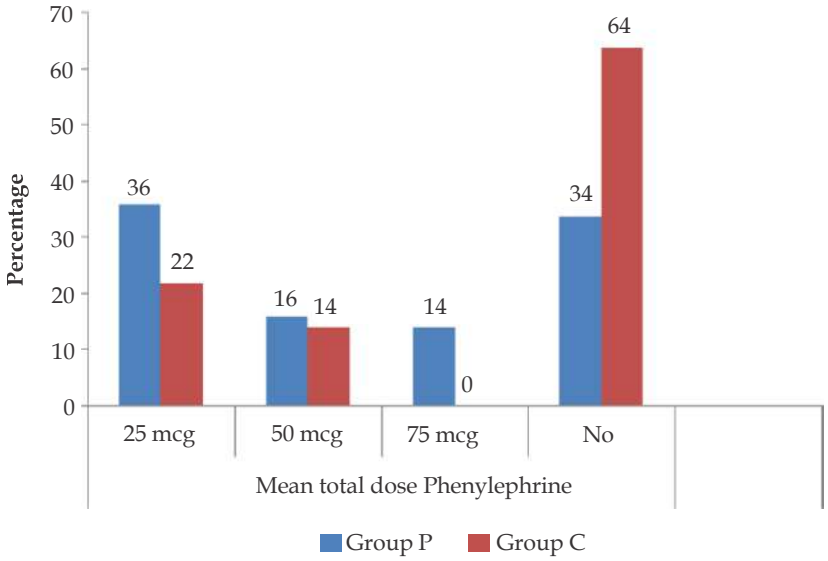

Fig. 4: Comparison of mean total cumulative dose of Phenylephrine use among study groups.

Table 4: Neonatal outcome among study groups

Parameter	Group P (n = 50)	Group C (n = 50)	t-test statistic value	p - value
APGAR score				
At 1 min	8.17 ± 0.73	8.20 ± 0.69	7.336	0.985
At 5 min	9.67 ± 0.47	9.65 ± 0.48	7.758	0.717
Umbilical Vein				
pH	7.34 ± 0.4	7.31 ± 0.2	0.474	0.636
pO_2 (mm Hg)	30.6 ± 7.6	29.9 ± 7.7	0.457	0.648
pCO_2 (mm Hg)	41.5 ± 5.4	41.8 ± 6.2	0.258	0.796
BE (Meq/ml)	–2.5 ± 1.7	–2.7 ± 2.0	0.538	0.591
Umbilical Artery				
pH	7.35 ± 0.4	7.37 ± 0.7	0.367	0.377
pO_2 (mm Hg)	16.9 ± 4.7	17.2 ± 5.1	0.305	0.760
pCO_2 (mm Hg)	52.5 ± 8.2	53.2 ± 7.9	0.434	0.664
BE (Meq/ml)	–2.5 ± 1.3	–2.4 ± 1.7	0.330	0.741

Discussion

Subarachnoid Block (SAB), a form of regional anesthesia is most commonly practiced for cesarean delivery. It has distinct advantages such as rapid onset of action, dense sensory and motor block as compared to epidural anesthesia, preservation of consciousness and airway reflexes of patients thus avoiding aspiration and failed intubation as well as better postoperative pain relief and neonatal outcome as compared to general anesthesia.[1,2]

Spinal Hypotension remains a common and potentially very serious complication due to its detrimental effects on both mother and foetal outcomes. The fall in blood pressure is attributed mainly to the sympathetic blockade resulting in vasodilation of capacitance vessels and peripheral pooling of blood. This in-turn leads to decreased venous return and cardiac output.[2,8] Preventive measures commonly practiced to avoid spinal hypotension in parturients include leg wrapping, elastic stockings, trendlenburg position, left lateral tilt, manual displacement of uterus, intravenous fluids and vasopressors. Inspite of all these prophylactic measures the incidence of spinal hypotension in parturients can be as high as 53% to 82%.[2,5]

Earlier studies conducted by Wollman SB, Marx GF et al. suggested the use of intravenous crystalloid fluids before the initiation of spinal anesthesia, a technique commonly referred as "Preload" for allievating the hypotensive effects of spinal anesthesia.[10,11] This fluid bolus was aimed at restoration of relative hypovolemia secondary to sympathetic blockade following spinal anesthesia thereby increasing the venous return to the heart and cardiac output. However, some studies reported an actual increase in cardiac output in obstretic population following spinal anesthesia thereby, questioned the rationale of infusing the crystalloid fluids before the administration of spinal anesthesia.[12,19,20] Possible reasons proposed for the failure of preload technique in prevention of spinal hypotension include:

a. Crystalloid preload infusion rapidly increases the capillary hydrostatic pressure thereby gets redistributed (75%) into the interstitial space without causing much increase in the central venous pressure;[21–23]
b. Crystalloid preload may induce atrial natriuretic peptide secretion, resulting in peripheral vasodilation and also increased rate of fluid excretion;[24]
c. Crystalloid preload infusion does not increase the intravascular volume at the actual time of maximum vasodilation;[25]
d. Cyrstalloid preload infusion in parturients has been reported to disrupt Glycocalyx which is a carbohydrate rich layer lining the endothelium which plays a major role in maintaining the integrity of endothelial layer of the vessel leading to the diffusion of fluid into the interstitial space.[26]

Park GE, Hauch MA et al. studied the effects of three different doses of preload fluid volume prior to spinal anesthesia who compared 10, 20 and 30 ml/kg crystalloid preload and concluded there was no significant difference in the incidence of hypotension among three study groups.[27] Thus crystalloid preload infusion may not only fail to maintain hemodynamic stability after spinal anesthesia, but also may have a detrimental effect by decreasing the colloidal osmotic pressure leading to pulmonary edema in compromized patients.[28,29]

Moreover American Society of Anesthesiologists (ASA) clinical practice guidelines recommendation concerning spinal anesthesia for cesarean delivery states:

"Although fluid preloading reduces the frequency of maternal hypotension, initiation of spinal anesthesia should not be delayed to administer fixed volume of intravenous fluid."[30]

Dyer RA, Farina Z et al. conducted a study on fifty patients undergoing elective cesarean section for hypotension after spinal anesthesia. Patients were randomly allocated into two groups to receive either 20 ml/kg of crystalloid solution over 20 minutes prior to spinal anesthesia (preload) or an equivalent volume by rapid infusion immediately after spinal anesthesia (coload). Hypotension was observed more in the preload than coload group. Vasopressor requirement was also significantly high in the preload than coload group (p = 0.047). The median number of vasopressor dose used to correct hypotension was significantly high in preload than coload group (p = 0.04). Our study also observed, significantly higher incidence of hypotension in preload group (66%) than coload group (36%) with p – value = 0.0027. The mean number of dose of vaopressor used to correct hypotension was also significantly high in preload group as compared to coload group, (p – value = < 0.001).[20]

Oh A-Y, Hwang J-W, Song I-A et al. conducted a similar study on sixty pregnant women posted for elective cesarean section for hypotension and

vasopressor requirement. Patients were allocated randomly into two groups to receive 15 ml/kg crystalloid fluid either prior to spinal block or after its administration. The incidence of hypotension was significantly higher in the preload group (83.3%) compared to the coload group (53.3%). (p – value = 0.026). The mean total cumulative dose of vasopressor consumption was significantly high in preload group (15.2 ± 11.9 mg) as compared to coload group (7.5 ± 8.6 mg), (p - value = 0.015). Even our study observed, similar results with higher incidence of hypotension in preload group (66%) as compared to coload group (36%) with p – value = 0.0027. The total cumulative dose of vasopressor consumption was also high in preload group (41.67 ± 20.41 mcg) as compared to coload group (34.72 ± 12.54 mcg) though the difference was statistically not significant, (p – value = 0.196).[31] Similar results were also found in other studies.[32]

Mercier FJ, Augè M et al. found that the infusion of crystalloid fluids at the actual time of intravascular volume deficit is more efficient in preventing spinal hypotension than prophylactic administration. They proposed not to use crystalloid preload as it was clinically ineffective. They concluded that the incidence and severity of hypotension can be decreased by combining a prophylactic vasopressor regimen with hydroxyethyl starch preloading, hydroxyethyl starch coloading or crystalloid coloading.[15]

However, contrarary results were found in a study conducted by Bouchnak M, Ben Cheikh N, et al. where they reported a higher incidence of hypotension in the coload group (96.6%) than in the preload group (86.6%). They had compared the infusion of 20 ml/kg crystalloid given over 15 minutes as coload or preload in the obstetric population.[33] However, in our study we compared the infusion of 15 ml/kg of crystalloid fluid given over 20 minutes as coload or preload and observed completely contrarary results as compared to this study. The wide variations in the incidence of hypotension in these studies may be due to the differences in the definitions of hypotension with different volumes and different rate of infusion of crystalloid fluids used in these studies.

A meta-analysis conducted by Banerjee A, Stocche RM comprising eight studies with five hundred and eighteen patients for hypotension in cesarean section found the incidence of hypotension to be 59.3% in coload group as compared to 62.4% in the preload group. They concluded that there is no significant inter group difference and hence, should not delay surgery in order to deliver preload volume of fluid.[17] Similar results were also observed in a study conducted by Jacob JJ, Williams AJ which concluded both preloading and coloading strategy alone are ineffective in the prevention of hypotension in the obstetric population receiving spinal anesthesia and should be supplemented with vasopressor therapy for maintaining normal blood pressure.[34]

The incidence of maternal nausea and vomiting has a direct correlation with the severity and duration of maternal hypotension during spinal anesthesia as observed by earlier studies.[35,36] Our study observed a higher incidence of maternal nausea and vomiting in preload group (48% and 34%) which also experienced higher incidence of hypotension as compared to coload group (18% and 12%) respectively. This may be due to the stimulation of chemoreceptor trigger zone as a consequence of maternal hypotension.[37]

Some studies also compared the hemodynamic changes in pregnant women after using colloid for either preload or for both preload and coload group. Though the hemodynamic changes are less with the use of colloid, one should be very carefull for allergic reactions and its effects on coagulation system.[8,38–40]

There was no evidence of any significant foetal acidosis as all the neonates had an umbilical arterial pH > 7.3. This may be due to the prompt treatment of hypotension with crystalloid fluid and vasopressors which maintained normal fetal perfusion.

The main limitation of this study is absence of a control group. Hence, the efficacy of preload in prevention of spinal hypotension in patients undergoing cesarean section cannot be assessed. In fact, the results of our study proposes the need for conducting more studies with larger sample size and a control group to establish safe fluid loading techniques to prevent spinal hypotension in patients undergoing elective cesarean section under spinal anesthesia.

Conclusion

We conclude that the crystalloid coload in the dose of 15 ml/kg is more effective than the crystalloid preload in the same dose for prevention of spinal hypotension in patients undergoing elective cesarean section. Surgery should not be delayed in view of preloading the patient as preloading alone is not effective in prevention of spinal hypotension and should be supplemented with vasopressors.

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References

1. Mitra JK. Prevention of hypotension following spinal anaesthesia in cesarean section-then and now. Kathmandu Univ Med J (KUMJ) 2010;9:415–19.
2. Birnbach DJ, Browne IM. Anesthesia for obstetrics. In: Miller RD, editor. Miller's Anesthesia. 7th edition. New York: Churchill Livingstone Inc; 2007.pp. 2220–21.
3. Chestnut DH. Obestretic Anesthesia: Principles and Practice. 4th edition. Philadelphia: Elsevier Mosby; 2009.
4. Klohr S, Roth R, Hofmann T, et al. Definitions of hypotension after spinal anesthesia for cesarean section: Literature search and application to parturients. Acta Anesthesiol Scand 2010;54:909–921.
5. Bajwa SJ, Bajwa SK, Kaur J, et al. Prevention of hypotension and prolongation of postoperative analgesia in emergency cesarean sections: A randomized study with intrathecal clonidine. Int J Crit Illn Inj Sci 2012;2:63–69.
6. Shnider SM, Lorimier AA, Asling JH, et al. Vasopressors in obstetrics II: Fetal hazards of methoxamine administration during obstetric spinal anesthesia. Am J Obstet Gynecol 1970;106:680–86.
7. NganKee WD. Prevention of maternal hypotension after regional anesthesia for cesarean section. Curr Opin Anesthesiol 2010;23:304–09.
8. Tamilselvan P, Fernando R, Bray J, et al. The effects of crystalloid and colloid preload on cardiac output in the parturient undergoing planned cesarean delivery under spinal anesthesia: A randomized trial. Anesth Analg 2009;109:1916–921.
9. Mueller MD, Bruhwiler H, Schupfer GK, et al. Higher rate of fetal acidemia after regional anesthesia for elective cesarean delivery. Obstet Gynecol 1997;90:131–34.
10. Wollman S, Marx C. Acute hydration for prevention of hypotension of spinal anesthesia in parturients. Anesthesiology 1968;29:374–80.
11. Marx GF, Cosmi EV, Wollman SB. Biochemical status and clinical condition of mother and infant at Cesarean section. Anesth Analg 1969;48:986–94.
12. Jackson R, Reid JA, Thorburn J. Volume preloading is not essential to prevent spinal-induced hypotension at cesarean section. Br J Anesth 1995;75:262–65.
13. Rout CC, Rocke DA, Levin J, et al. A reevaluation of the role of crystalloid preload in the prevention of hypotension associated with spinal anesthesia for elective Cesarean section. Anesthesiology 1993;79: 262–69.
14. Kamenik M, Paver-Erzen V. The effects of lactated Ringer's solution infusion on cardiac output changes after spinal anesthesia. Anesth Analg 2001;92:710–14.
15. Mercier FJ, Augè M, Hoffmann C, et al. Maternal hypotension during spinal anesthesia for cesarean delivery. Minerva Anestesiol 2013;79(1):62–73.
16. Mercier FJ, Roger-Christoph S, des Mesnard-Smaja V, et al. Crystalloid preloading *vs* postloading for the prevention of hypotension with spinal anesthesia for cesarean delivery (abstract). Anesthesiology 2004;100:A18.
17. Banerjee A, Stocche RM, Angle P, et al. Preload or coload for spinal anesthesia for elective Cesarean delivery: A meta-analysis. Can J Anesth 2010;57:24–31.
18. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: Application to Healthy Patients Undergoing Elective Procedures: A Report by the American Society of Anesthesiologists Task Force on preoperative fasting. Anesthesiology 1999;90:896–905.
19. Langesaeter E, Rosseland LA, Stubhaug A. Continuous invasive blood pressure and cardiac output monitoring during cesarean delivery: A randomized, double-blind comparison of low-dose *versus* high-dose spinal anesthesia with intravenous phenylephrine or placebo infusion. Anesthesiology 2008;109(5):856–63.
20. Dyer RA, Reed AR, van Dyk D, et al. Hemodynamic effects of ephedrine, phenylephrine, and the coadministration of phenylephrine with oxytocin during spinal anesthesia for elective cesarean delivery. Anesthesiology 2009;111(4):753–65.
21. Tølløfsrud S, Elgjo GI, Prough DS, et al. The dynamics of vascular volume and fluid shifts of lactated Ringer's solution and hypertonic-saline dextran solutions infused in normovolemic sheep. Anesthesia & Analgesia 2001;93(4):823–31.
22. Mercier FJ. Cesarean delivery fluid management. Curr Opin Anesthesiol 2012;25(3):286–91.
23. Carey JS, Scharsmidt BF, Culliford AT, et al. Hemodynamic effectiveness of colloid and electrolyte solutions for replacement of simulated operative blood loss. Surg Gynecol Obstet 1970;131:679–86.
24. Pouta AM, Karinen J, Vuolteenaho OJ, et al. Effect of intravenous fluid preload on vasoactive peptide secretion during Cesarean section under spinal anesthesia. Anesthesia 1996;51(2):128–32.
25. Hahn RG and Svens´en C. Plasma dilution and the rate of infusion of Ringer's solution. British Journal of Anesthesia 1997;79(1):4–67.

26. Powell M, Mathru M, Brandon A, et al. Assessment of endothelial glycocalyx disruption in term parturients receiving a fluid bolus before spinal anesthesia: A prospective observational study. Int J Obstet Anesth 2014 Nov;23(4):330–34.
27. Park GE, Hauch MA, Curlin F, et al. The effects of varying volumes of crystalloid administration before cesarean delivery on maternal hemodynamics and colloid osmotic pressure. Anesth Analg 1996;83: 292–303.
28. Ronald Miller D, Lars Erikson I, Lee A. et al. Anesthesia, 7*th* edition, Churchill Livingstone; Elsvier Publication Private Limited: Chapter 88-Postoperative Intravascular Fluid Therapy. pp. 3783–803.
29. Mac Lennan FM, Mac Donald AF, Campbell DM. Lung water during the puerperium. Anesthesia 1987;42:141–47.
30. American Society of Anesthesiologists Task Force on obstetric anesthesia: Practice guidelines for obstetric anesthesia: An updated report by the American Society of Anesthesiologists Task Force on obstetric anesthesia. Anesthesiology 2007;106(4):843–63.
31. Oh A-Y, Hwang J-W, Song I-A, et al. Influence of the timing of administration of crystalloid on maternal hypotension during spinal anesthesia for cesarean delivery: Preload *versus* coload. BMC Anesthesiol 2014;14(1):36.
32. Rao AR, Vijaya G, Mahendra BVVN. Comparison of effects of preloading and coloading with Ringer's Lactate in Elective Cesarean section cases under Spinal Anesthesia. 2015;14(10):57–64.
33. Bouchnak M, Ben Cheikh N, Skhiri A, et al. Relevance of rapid crystalloid administration after spinal anesthesia (coload) in prevention of hypotension during elective cesarean section: A685. Eur J Anesthesiol 2006;23:178.
34. Jacob JJ, Williams A, Verghese M, et al. Crystalloid preload *versus* crystalloid coload for parturients undergoing cesarean section under spinal anesthesia. J Obstet Anesth Crit Care 2012;2:10–15.
35. Hall PA, Bennett A, Wilkes MP, et al. Spinal anesthesia for cesarean section: Comparison of infusions of phenylephrine and ephedrine. Br J Anesth 1994;73:471–74.
36. Turkoz A, Togal T, Gokdeniz R, et al. Effectiveness of intravenous ephedrine infusion during spinal anesthesia for cesarean section based on maternal hypotension, neonatal acid-base status and lactate levels. Anesth Intensive Care 2002;30:316–20.
37. Ratra CK, Badola RP, Bhargava KP. A study of factors concerned in emesis during spinal anesthesia. Br J Anesth 1972;44:1208–211.
38. Tawfik MM, Hayes SM, Jacoub FY, et al. Comparison between colloid preload and crystalloid coload in cesarean section under spinal anesthesia: A randomized controlled trial. Int J Obstet Anesth 2014;23(4):317–23.
39. Nishikawa K, Yokoyama N, Saito S, et al. Comparison of effects of rapidcolloid loading before and after spinal anesthesia on maternal hemodynamics and neonatal outcomes in cesarean section. J Clin Monit Comput 2007;21(2):125–29.
40. Siddik-Sayyid SM, Nasr VG, Taha SK, et al. A randomized trial comparing colloid preload to coload during spinal anesthesia for elective cesarean delivery. Anesth Analg 2009;109(4):1219–24.

Original Research Article

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Comparative Study of Transdermal Patch of Fentanyl with that of Buprenorphine for Postoperative Pain Management in Postthoracotomy Surgery Patients

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Abstract

Background: Pain after thoracotomy is probably the most severe pain experienced by the patient and opioid are one of the most commonly used analgesics for postoperative pain. Hence, the present study was undertaken to compare the efficacy and safety of 25 mcg/hour of fentanyl patch with 20 mcg/hour of buprenorphine patch for postoperative pain management in postthoracotomy patients. *Methods:* Total sixty patients of ASA Grade I, II and III, age between 20 and 60 years, who have undergone thoracotomy surgeries were enrolled in the study and randomly divided into two groups of 30 patients each. Group A received 25 mcg/hour of fentanyl patch and Group B received 20 mcg/ hour of buprenorphine patch immediately after patient was received in critical care unit postsurgery. Patients were followed for three days. *Results:* Demographic profile and baseline characteristics were comparable between two groups. Group A had significantly higher level of mean VAS score as compared to Group B at Day 2 and 3. In the same follow up period, both the groups were comparable in regards to mean level of sedation score and hemodynamic variables (HR, SBP and DBP). In Group A 11 (36.66%) patients and in Group B, 8 (26.66%) patients required single dose of rescue analgesic, (p - value > 0.05). The incidence of nausea and vomiting were 13.33% in Group A and 23.33% in Group B. *Conclusion:* Both the fentanyl and buprenorphine patch are effective and safe in controlling postoperative pain but buprenorphine is better than fentanyl in this respects, as it have longer duration of action and require less rescue analgesic for pain relief.

Keywords: Opioids; Analgesics; Transdermal; Patch; Fentanyl; Buprenorphine; Thoracotomy.

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Introduction

Cardiovascular thoracic surgeries will include thoracotomy or thoracoscopy procedures. Thoracotomy incision will cause impaired pulmonary function and chest pain postoperatively with restricted arm and shoulder movement. This pain originates from pleural and muscular damage, costovertebral joint disruption, intercostal nerve injury during surgery.[1] Thus, postoperative

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pain relief is an essential aspect of critical care management in these patients as it affects the quality of patient recovery and resulting postoperative morbidities. Adequate pain management leads to early mobilization, improves respiratory function and reduces postoperative complications.[2]

At present, various analgesic modalities are available for postthoracotomy pain management including thoracic neuraxial blocks and in dwelling catheters, intercostal nerve blocks, patient controlled analgesia, oral, parenteral and transdermal NSAIDs and parenteral or transdermal opioids. Among these modalities transdermal opioid delivery is advantageous as it avoids the peaks and troughs of intermittent dosage which may lead to various side effects like sedation, nausea, vomiting and respiratory depression.[3]

The fentanyl patch is one of the great commercial successes in transdermal drug delivery. The suitability of this molecule for delivery through skin had been identified in the 1970s, and subsequently, a number of transdermal formulations became available on the market.[4] Buprenorphine is a synthetic opioid analgesic with over twenty-five years of international clinical experience indicating it to be safe and effective in a variety of therapeutic situations for the relief of moderate to severe pain.[5] Hence, the present study was carried out to compare transdermal fentanyl and transdermal buprenorphine for postoperative pain relief.

Materials and Methods

After obtaining approval from Institutional Ethics Committee and informed consent from patients, this prospective randomized study was conducted in 60 patients of ASA Grade I, II and III, having age between 20 and 60 years, weight 40–80 kg and who have undergone thoracotomy surgeries. Patients were divided based on computerized randomization into two groups of 30 patients each. Group A received 25 mcg/hr of fentanyl patch and Group B received 20 mcg/hour of buprenorphine patch immediately after patient received in critical care unit postsurgery. Patients with ASA Grade 4, age < 20 years and > 60 years, known opioid allergy or dependence in the past, skin infection and sensitive skin, patients with impaired pulmonary functions, weight less than 40 kg and more than 80 kg and patients own refusal for participation were excluded from the study. A detailed preanesthetic check-up was done. Patients were taken up for surgery after adequate starvation of 8 hrs. In the operation theatre, intravenous access was established. All noninvasive monitoring was attached including pulse oxymeter, cardioscope; sphygmomanometer. Patients were premedicated with glycopyrrolate 4 μg/kg ondansetron 0.1 mg/kg IV and sedated with midazolam 0.03 mg/kg IV and fentanyl 2 μg/kg IV. After preoxygenation for 5 mins general anesthesia was induced with propofol 2 mg/kg and after ensuring adequate mask ventilation patient was paralyzed with 0.9–1 mg/kg rocuronium and trachea was intubated with portex endotracheal tube of 7.5 mm ID for females and 8.5 mm ID for males. After ensuring correct placement with end tidal CO_2 and proper positioning of the tube positive pressure ventilation was initiated. Anesthesia was maintained with a mixture of 50% O_2 and nitrous oxide mixture and sevoflurane (MAC 1 to 1.2) with 0.3 mg/kg/hr rocuronium infusion. An arterial line was then be secured for invasive arterial blood pressure and heart rate monitoring.

After completion of procedure patient was shifted to critical care unit sedated and paralyzed with assisted ventilation and continuous infusions of the relaxant and other intraoperative drugs required. Patient was put on ventilator, all monitors attached including pulse oximeter, ECG, arterial blood pressure and temperature. After confirming the vital parameters to be normal transdermal opioid patch was applied on clear hair free area of upper arm or chest or back. Along with their routine drugs Inj. Paracetamol TDS and Inj. Tramadol bd was continued for 24 hours postsurgery. As the peak levels of transdermal opioids were attained after 12–24 hours, the analgesia was covered with parenteral NSAIDs and opioids. Patient was gradually weaned over 12 hours and extubated after serial arterial blood gas monitoring and patients response in terms of sensory and motor activity.

After extubation, pain was assessed using visual analog scale whereas sedation scoring was done according to Ramsey Sedation Scale. Continuous hemodynamic monitoring was done. The requirement of rescue analgesics after 24 hours was noted. In case of any side-effects related to the patch, the patch was removed and discontinued. All monitoring and findings were noted for three days postoperatively. In case of any complications were noted and managed accordingly. If not fulfilling the criteria for study, patient was excluded from study.

Statistical Analysis:

The data from both the groups was collected and compared statistically using student *t*-test / Fischer-exact test. Statistically significant differences

between two groups detected by keeping α = 0.05 and power of study 95%.

Observations and Results

Total 60 patients were enrolled in the study, among them 39 (65%) were males and 21 (35%) were females. The demographic profile of the patients and baseline characteristics were comparable between two groups and found no statistically significant difference (p > 0.05) as shown in (Table 1).

Table 1: Demographic profile of the patients and baseline characteristics

Characteristics		Group A	Group B	p - value
Age in years		43.5 ± 10.52	42.73 ± 13.49	0.807
Sex, No. (%)	Male	21 (70%)	18 (60%)	–
	Female	09 (30%)	12 (40%)	–
ASA Grade, No. (%)	I	18 (60%)	17 (56.6%)	–
	II	12 (40%)	13 (43.3%)	–
Heart Rate		87.13 ± 7.46	88.73 ± 8.32	0.436
SBP		126.56 ± 4.87	126.76 ± 8.31	0.909
DBP		82.4 ± 7.07	81.1 ± 7.60	0.495
sPO_2 (%)		98.96 ± 0.96	99 ± 0.98	0.894
VAS		4.4 ± 0.81	4.4 ± 0.81	1
Sedation Score (RSS)		1.96 ± 0.31	1.93 ± 0.25	0.656

Table 2 shows, the mean values of VAS from Day 2 and Day 3 in both groups. Group A had significantly higher level of mean VAS score as compared to Group B during the follow up period. At day 2 and day 3 the difference was highly significant. In Group A, 11 (36.66%) patients and in Group B, 8 (26.66%) patients required single dose of rescue analgesic, The difference in rescue analgesic requirement was not statistically significant (p - value > 0.05).

Table 2: Variation in VAS from day 1 to day 3

Follow-up day	Group A	Group B	p - value
Day 2	1.86 ± 1.16	0.2 ± 0.61	< 0.0001
Day 3	2.2 ± 0.96	0.2 ± .61	< 0.0001

At day 1, 2 and 3, both the groups were comparable in regards to mean level of sedation score, Table 3 and hemodynamic variables (HR, SBP and DBP), Fig. 1. There was no statistically significant difference found between two groups.

The incidence of nausea and vomiting were 13.33% in Group A and 23.33% in Group B. One patient in Group A had itching, (Fig. 2).

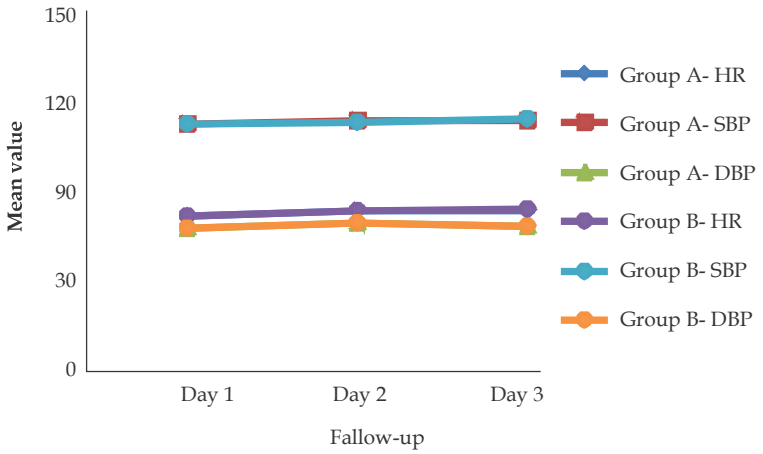

Fig. 1: Comparison of Hemodynamic Parameters between two groups at day 1 to day 3.

Table 3: Variation in Sedation score from day 1 to day 3

Follow-up day	Group A	Group B	*p* - value
Day 1	1.96 ± 0.18	1.96 ± 0.18	1
Day 2	1.96 ± 0.18	2.00 ± 0.00	0.32
Day 3	2.00 ± 0.26	2.00 ± 0.00	1

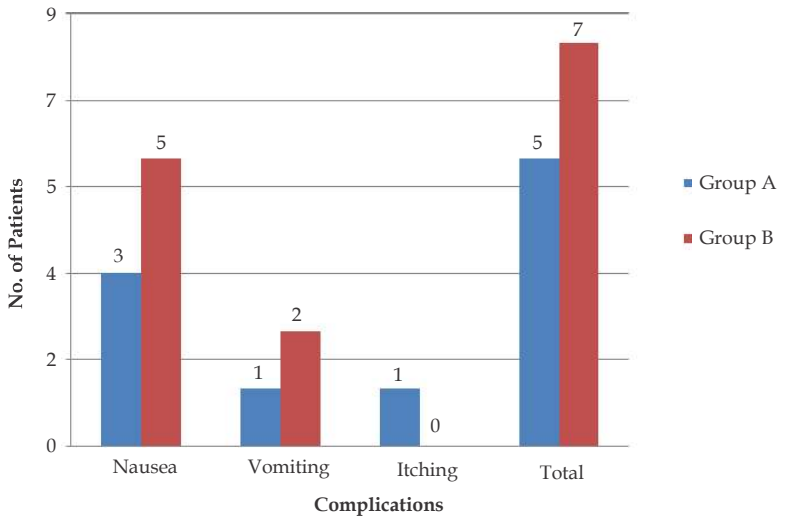

Fig. 2: Complications in both the groups.

Discussion

Thoracotomy is considered the most painful of surgical procedures and providing effective analgesia is the onus for all anesthetists. In postthoracotomy patients analgesia can be administered as boluses or continuous infusion with pharmacokinetic and patient-controlled systems like PCA (Patient Controlled Analgesia),[6] Target Control Infusion (TCI) and a new approach of PMA (Patient Maintained Analgesia). The use of adhesive skin patches (Transdermal Drug Delivery Systems-TDDS) to deliver drugs systemically for postoperative analgesia is a relatively new phenomenon and for that opioids (morphine, fentanyl, pethidine, buprenorphine and tramadol) have been the mainstay of postoperative analgesia.[7]

The first report of fentanyl permeation in human skin samples in the scientific literature appears in the seminal paper by Michaels et al.[8] The suitability of the transdermal route for fentanyl delivery was examined further by Roy and Flynn.[9-11] The first transdermal fentanyl patch was approved by the FDA in the 1990s. Fentanyl patches are designed to deliver fentanyl at four constant rates as 25, 50, 75, and 100 µg/ h^{-1} for a period of 72 h. After initial application, a depot of fentanyl forms in the upper skin layers and serum fentanyl concentrations increase gradually, generally leveling off between 12 and 24 h. The steady-state serum concentration is reached after 24 h and maintained as long as the patch is renewed. However, variations have been found in serum fentanyl concentration during the 72 h period; concentrations tend to be higher in the first 24 h and decrease on the second and third day due to the decreasing concentration gradient between patch and skin. Fentanyl delivery is not affected by local blood supply, but an increase in body temperature up to 40°C can increase absorption rate by about 30%.[7,13]

Similarly, transdermal application of buprenorphine meets all the requirements for successful treatment of chronic pain. Buprenorphine is a partial agonist at the µ receptor and its analgesic efficacy is comparable with the usual doses of other opioids such as pentazocine, morphine and pethidine.[13,14] In India, buprenorphine patches are available in three different strengths as 5, 10, 20 μg/h.[15] Each transdermal patch usually contains 5 mg of buprenorphine in 6.25 cm^2 area releasing 5 µg of buprenorphine per hour over a period of 7 days. Patches with higher strengths have proportionately larger areas. After application, these are usually kept for 7 days. More than one patch may be applied depending on the need, but the total dosage should not exceed 20 μg/h as prescribed by FDA.[16]

In the present study, we compared 25 mcg/hour of fentanyl patch with 20 mcg/hour transdermal buprenorphine patch for postoperative pain relief in postthoracotomy patients. There was no statistically significant difference found between two groups in regards to demographic profile and baseline characteristics as similar to the study done by Arshad et al. [jcdr-9-UC01].

In Group B the VAS score was significantly lowerthan Group A on day 2 and 3. The potency of fentanyl in form of transdermal patch is very good and able to maintain VAS score around 2. As mentioned in previous studies it is comparable. But when compared to the VAS score of buprenorpine patch which is mostly 0, buprenorphine patch 20 mcg/hr seems to be far better. Thus, the result of VAS score in this study suggested that both the patches were effective in controlling postoperative pain but buprenorphine was better in this regard. Fentanyl patch had duration of action of 3 days while buprenorphine patch had duration of action of 7 days. Therefore, buprenorphine provides longer pain relief as compared to fentanyl but the latter is more effective analgesic. In Group A, 11 patients and in Group B, 8 patients were required single dose of rescue analgesic. Further, this finding resolved that buprenorphine patch is better analgesic than fentanyl patch. Arshad et al.[17] reported that fentanyl is better in controlling postoperative pain than buprenorphine, in contrast, it has been observed that in present study the buprenorphine superior than fentanyl, it may be because of double dose of buprenorphine i.e. 20 mcg/hour rather than 10 mcg/hour used in Arshad et al. study.[17]

Sedation scores and hemodynamic variables in both groups were comparable. None of the patient in our study showed excessive sedation or respiratory depression. All patients were calm, comfortable and easily aruosable throughout the study period. The sedation scores were slightly increased in Group B as compared to baseline but in Group A, sedation score were same at day 1, 2, and slightly increased at day three as compared to baseline. Thus, buprenorphine patch provides more sedation than fentanyl patch but this difference was not statistically significant. There are isolated case reports of bradycardia with the use of fentanyl TDS[18] but in current study, we did not found any adverse hemodynamic events in either group.

Nausea and vomiting were main side-effects of the opioid drugs. The incidence of nausea and vomiting were 13.33% in Group A and 23.33% in Group B, this is significantly lower than observed in previous studies.[19,20]

Conclusion

The transdermal fentanyl 25 mcg/h and transdermal buprenorphine 20 mcg/h are safe and effective for postoperative pain relief in postthoracotomy patients but the buprenorphine is better than fentanyl in this respect and can be used for 7 days. However, Fentanyl is more cost-effective and is preferred for postoperative pain management more often but with this study we would like to use buprenorphine patch often however, hope to make it more cost-effective for further studies and clinical use.

References

1. Alzahrani T. Pain relief following thoracic surgical procedures: A literature review of the uncommon techniques. Saudi J Anesth 2017;11:327–31.
2. Dinic VD, Stojanovic MD, Markovic D, et al. Enhanced recovery in Thoracic Surgery: A Review. Front Med 2018;5:14.
3. Cook TM, Riley RH. Analgesia following thoracotomy: A survey of Australian practice. Anesth Intensive Care 1997;25(5):520–24.
4. Lane ME. The transdermal delivery of fentanyl, Eur J Pharm Biopharm 2013. http://dx.doi.org/10.1016/j.ejpb.2013.01.018
5. Ripa SR, McCarberg BH, Munera C, et al. A randomized, 14-day, double-blind study evaluating conversion from hydrocodone/acetaminophen (Vicodin) to buprenorphine transdermal system 10 µg/h or 20 µg/h in patients with osteoarthritis pain. Expert Opin Pharmacother 2012;13(9):1229–241.
6. Lehmann KA. Patient-controlled analgesia for postoperative pain. In: Benedetti C, Chapman CR, Gibson G, editors. Advances in Pain Research and Therapy. New York: Raven Press Ltd; 1990.pp. 297–324.
7. Lyn Margetts FRCA and Richard Sawyer FRCA FIPP. Transdermal drug delivery: Principles and opioid therapy. Continuing Education in Anesthesia, Critical Care & Pain 2007;7(5):171–76.
8. Michaels AS, Chandrasekaran SK, Shaw JE. Drug permeation through human skin: Theory and *in vitro* experimental measurement, AIChE J 1975;21(5):985–96.
9. Roy SD, Flynn GL. Solubility and related physicochemical properties of narcotic analgesics, Pharm Res 1988;5:580–86.
10. Roy SD, Flynn GL. Solubility behavior of narcotic analgesics in aqueous media: Solubilities and dissociation constants of morphine, fentanyl, and sufentanil, Pharm Res 1989;6:147–51.
11. Roy SD, Flynn GL. Transdermal delivery of narcotic

analgesics: Comparative permeabilities of narcotic analgesics through human cadaver skin, Pharm Res 1989;6:825–32.

12. Muijsers RBR, Wagstaff AJ. Transdermal fentanyl. An updated review of its pharmacological properties and therapeutic efficacy in chronic cancer pain control. Drugs 2001;61:2289–307.
13. Dahan A, Yassen A, Bijl H, et al. Comparison of the respiratory effects of intravenous buprenorphine and fentanyl in humans and rats. Br J Anesth 2005;94:825–34.
14. Dahan A, Yassen A, Romberg R, et al. Buprenorphine induces ceiling in respiratory depression but not in analgesia. Br J Anesth 2006;96:627–32.
15. Gupta H, Babu RJ. Transdermal delivery: Product and patent update. Recent Pat Drug Deliv Formul 2013;7:184–205.
16. Kadapamannil D, Rajan S, Tosh P, et al. Comparison of efficacy and safety of transdermal buprenorphine patch applied 48 *versus* 72 hours preoperatively in providing adequate postoperative analgesia following major abdominal surgeries. Indian J Pain 2018;32:46–50.
17. Arshad Z, Prakash R, Gautam S, Kumar. Comparison between Transdermal Buprenorphine and Transdermal Fentanyl for Postoperative Pain Relief after Major Abdominal Surgeries. Journal of Clinical and Diagnostic Research 2015;9(12):UC01–UC04.
18. Plosker GL, Lyseng-Williamson KA. Buprenorphine 5, 10 and 20 μg/h transdermal patch: A guide to its use in chronic nonmalignant pain. CNS Drugs 2012;26(4):367–73.
19. Grond S, Radbruch L, Lehmann KA. Clinical pharmacokinetics of transdermal opioids: Focus on transdermal fentanyl. Clin Pharmacokinet 2000;38(1):59–89.
20. Miyazaki T, Hanaoka K, Namiki A, et al. Efficacy, safety and pharmacokinetic study of a novel fentanyl-containing matrixtransdermal patch system in Japanese patients with cancer pain. Clin Drug Investig 2008;28(5):313–25.

Original Research Article

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Comparison of Ropivacaine with $MgSO_4$ *versus* Ropivacaine with Dexmeditomidine as Adjuvants in Ultrasound-guided Supraclavicular Brachial Plexus Block in Upper Limb Surgeries

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Abstract

Introduction: Regional anesthesia is particularly indicated for patients undergoing peripheral limb surgery because it provides effective intraoperative anesthesia and postoperative pain control. Supraclavicular approach of brachial plexus block is the most commonly used approach and provides the most complete and reliable anesthesia for upper limb surgery. The concurrent injection of α_2 adrenergic agonist drugs has been suggested to improve the nerve block characteristic of LA solutions. *Objectives:* To assess the time of onset and duration of action of Ropivacaine with $MgSO_4$ and Ropivacaine with dexmeditomidine. *Materials and Methods:* Patients with American Society of Anesthesiologists physical status (ASA) Grade 1 or 2 posted for elective upper limb orthopedic surgeries were included in the study. The study patients were randomly divided into 2 Groups with 25 patients in each group namely Group A (n = 25): 20 ml 0.75% ropivacaine (150 mg) +2.5 ml (250 mg) $MgSO_4$ and Group B (n = 25): 20 ml 0.75% ropivacaine (150 mg) + 2.5 ml dexmedetomidine (1 mcg/ kg + normal saline). Brachial plexus block through supraclavicular approach was performed. The primary outcome measure was the onset of sensory and motor blockade, while secondary was the duration of sensory and motor blockade. The adverse reactions during the perioperative period were recorded. *Results:* Overall, the onset of motor and sensory blockade in Group B was faster than Group A and the duration of motor and sensory blockade in Group B was longer than Group A, which was statistically significant with p - value < 0.001. ***Conclusion:*** Dexmedetomidine as an adjuvant to Ropivacaine in the supraclavicular brachial plexus block for upper limb surgery significantly shortens the onset time for sensory and motor block and prolongs the duration of sensory and motor blocks with the use of ultrasound guidance for the peripheral nerve blocks.

Keywords: Dexmedetomidine; Ropivacaine; Regional anesthesia; Brachial block.

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Introduction

Regional anesthesia is particularly indicated for patients undergoing peripheral limb surgery because it provides effective intraoperative anesthesia and postoperative pain control. Brachial plexus block is a versatile and reliable regional anesthetic technique and a suitable alternative to general anesthesia for upper limb surgical procedures. Supraclavicular approach of brachial

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plexus block is the most commonly used approach and provides the most complete and reliable anesthesia for upper limb surgery.

Ropivacaine is a local anesthetic that inhibits neuronal excitement and conduction by inhibiting neuronal sodium channels. Its effect is long-lasting, which makes it a commonly used anesthetic in nerve block anesthesia.[1]

Local anesthetics alone for supraclavicular brachial plexus block provide good operative conditions but have a shorter duration of postoperative analgesia. Dexmedetomidine has been reported as an effective adjuvant for regional anesthetic agents to shorten the onset time of the block, prolong the duration of the block, and increase the quality of analgesia without neurologic sequelae.[2]

The concurrent injection of α_2 adrenergic agonist drugs has been suggested to improve the nerve block characteristic of LA solutions. Dexmedetomidine is a selective α_2 adrenoceptor agonist, which has higher affinity to α_2 receptors compared to clonidine. With Ropivacaine, it results in a dose-dependent increase in the duration of sensory and motor block.[3–9]

The present study was undertaken to compare the effectiveness regarding onset and duration of complete sensory and motor block of 0.75% Ropivacaine with $MgSO_4$ *versus* 0.75% Ropivacaine with Dexmedetomidine in patients undergoing ultrasound-guided supraclavicular brachial plexus block.

Objectives

- To assess the time of onset and duration of action of Ropivacaine with $MgSO_4$;
- To assess the time of onset and duration of action of Ropivacaine with Dexmedetomidine.

Materials and Methods

With a level IV evidence, a hospital based interventional study was carried out for 2 months duration in the department of Anesthesiology, SS Institute of Medical Sciences and Research Centre, Davanagere, Karnataka.

After obtaining Institutional Ethical Committee approval and written informed consent from the close relatives of the patients, sample patients with American Society of Anesthesiologists physical status (ASA) Grade 1 or 2 posted for elective upper limb surgeries were included in the study. The study patients were randomly divided into 2 Groups with 25 patients in each group namely Group A (n =25): 20 ml 0.75% ropivacaine (150 mg) + 2.5ml (250mg) $MgSO_4$ and Group B (n = 25): 20 ml 0.75% ropivacaine (150 mg) + 2.5 ml dexmedetomidine (1 mcg/kg + normal saline).

Adult patients of either sex, without any comorbidity or with controlled comorbidities, admitted for elective upper limb surgeries, patients with age between 18 to 60 years and patients with ASA Grade 1 or 2 were included in the study. Patients with allergy to study drugs, patients who were contraindication for brachial plexus block (bleeding disorders, local or systemic infections), patients with history of cardiac, hepatic, or renal disease, chronic pain or psychiatry disorders and patients with BMI > 30 kg/m^2 were excluded from the study.

Definition of Study Parameters

1. **Onset of complete sensory block** is defined as the time between the last brachial injection of local anesthetic drug to the total abolition of pin prick response in areas innervated by radial, ulnar, and median nerve. Graded as:

   Grade 0 - Normal sensation to pin prick;

   Grade 1 - Dull response to pin prick (onset);

   Grade 2 - No response to pin prick (peak).

2. **Onset of complete motor block** onset of the complete motor block was the time from the end of injection of study drug to complete paralysis of upper limb.

   Bromage scale for motor block:

   Grade 0 - Normal motor function (no effect);

   Grade 1 - Decrease motor strength compared to contra lateral limb;

   Grade 2 - Complete motor block.

3. **Duration of motor block**: It is the time from the onset of motor block to complete recovery of motor block (able to hand raise above head with a movement of arm and forearm).

4. **Duration of sensory block**: It is the time from onset of sensory block to the first pain requiring rescue analgesic.

The preanesthetic assessment was done on the evening before surgery. A routine examination was done by assessing general condition, nutritional status, weight, airway assessment, complete examination of cardiovascular, respiratory system,

site of block, and investigation in all patients. All patients were kept electively nil per oral 6–8 hours before surgery. Written and informed consent was taken from the study population. Standard monitors such as electrocardiogram, pulse oximeter, blood pressure cuff were applied, and patient's baseline parameter such as pulse rate, blood pressure, respiratory rate, and SpO_2 was recorded.

Brachial plexus blockade: Through supraclavicular approach, the patients were placed in the dorsal recumbent position with the head turned away from the site of brachial block, under all aseptic precautions the transducer is positioned in the transverse plane immediately proximal to the clavicle, slightly posterior to its midpoint. The transducer is tilted caudally, to obtain a cross-sectional view of the subclavian artery. The brachial plexus is seen as a collection of hypoechoic oval structures posterior and superficial to the artery. Using a 23-gauge × 1.5 inch needle, 1–2 ml of local anesthetic is injected into the skin 1 cm lateral to the transducer. The local anesthetic is injected in increments around the brachial plexus under direct vision of the ultrasound.

Immediately after block, patients were evaluated for the assessment of onset of sensory and motor blockade. Sensory blockade was assessed by pin prick test and motor blockade by upper limb movements. If the block was considered to be adequate, surgeons were allowed to apply tourniquet and start the surgery. If the block was considered to be inadequate for surgery, the patient was given general anesthesia. Patients were monitored, as shown in (Table 1).

During the whole procedure, vital signs of the patients were recorded. The time of onset of sensory blockade was defined as the time between injection of the anesthetic and loss of sensation to needle prick, and the time of onset of motor blockade was defined as time between injection of the anesthetic and loss of thumb movement. The adverse reactions during the perioperative period were recorded (Fig. 1).

Data were statistically evaluated with IBM SPSS Statistics for Windows, Version 24.0, IBM Corp, Chicago, IL. The patient characteristics and intraoperative data is presented as Mean with SD. Student's *t*-test is used to compare continuous variables and Chi-square test (χ^2) is used to analyze the categorical variables. p - value < 0.05 is considered to be statistically significant.

Results

Fifty ASA 1 and 2 patients of either sex, aged between 18 and 60 years, posted for upper limb surgeries under ultrasound guided supraclavicular brachial plexus block were randomized and selected for the study. The purpose of this study is to compare the efficacy of Dexmedetomidine and $MgSO_4$ as an adjuvant to Ropivacaine in USG-guided Supraclavicular brachial plexus block for upper limb surgeries.

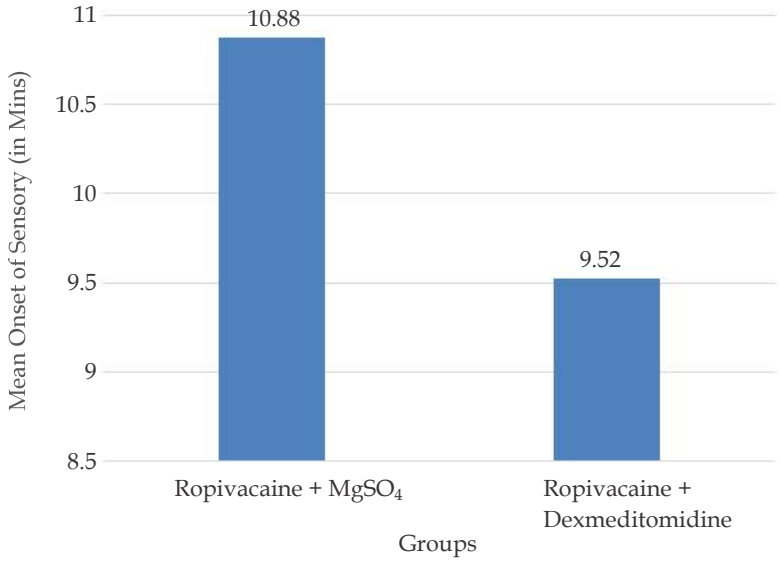

Fig. 1: Mean onset of sensory blockade among both the groups.

Table 1: Comparison of sensory and motor blockade among both the groups

	Ropivacaine + $MgSO_4$		Ropivacaine + Dexmedetomidine		*t*-value	*p* - value
	Mean	SD	Mean	SD		
Onset of Sensory (mins)	10.88	2.05	9.52	1.28	3.397	0.001
Onset of Motor (mins)	13.60	3.12	11.08	1.42	3.615	0.001
Sensory Duration (mins)	488.88	85.03	642.64	108.11	5.589	< 0.001
Motor Duration (mins)	386.48	86.43	508.56	89.89	4.895	< 0.001

The mean onset of sensory blockade in Group A was 10.88 ± 2.05 mins and in Group B was 9.52 ± 1.28 mins.

The mean onset of motor blockade in Group A was 13.60 ± 3.12 mins and in Group B was 11.08 ± 1.42 mins, as shown in Figure 2.

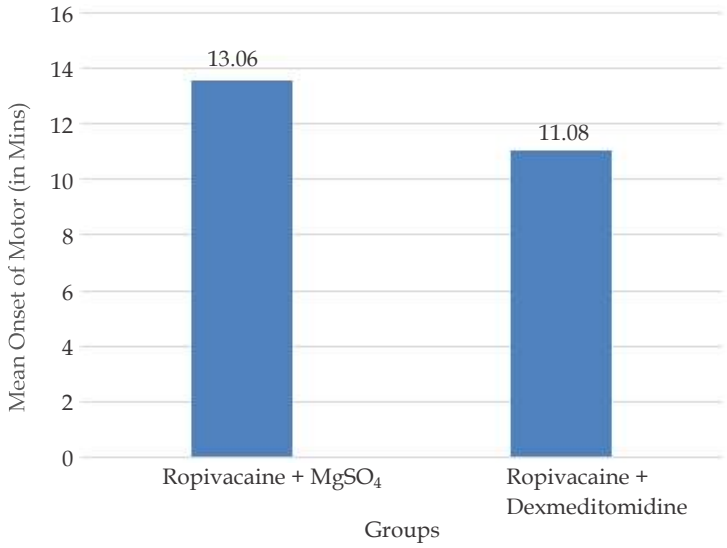

Fig. 2: Mean onset of motor blockade among both the groups.

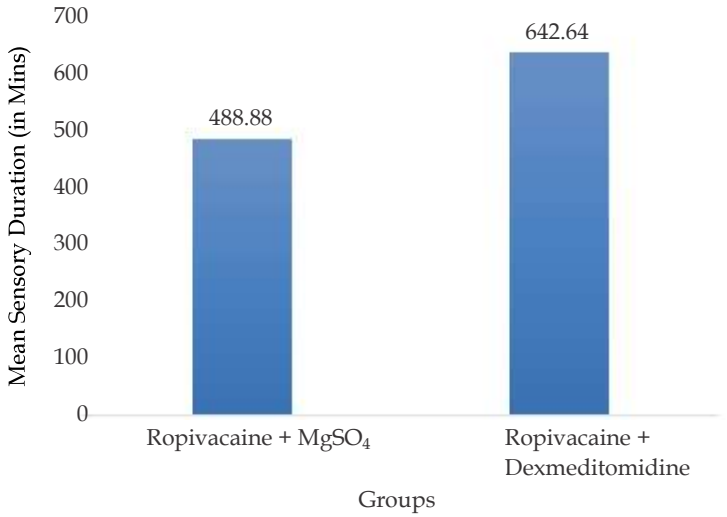

Fig. 3: Mean duration of sensory blockade among both the groups.

The mean duration of sensory blockade in Group A was 488.88 ± 85.03 mins and in Group B was 642.64 ± 108.11 mins, as shown in Figure 3.

The mean duration of motor blockade in Group A was 386.48 ± 86.43 mins and in Group B was 508.56 ± 89.89 mins, as shown in Figure 4.

Overall, the onset of motor and sensory blockade

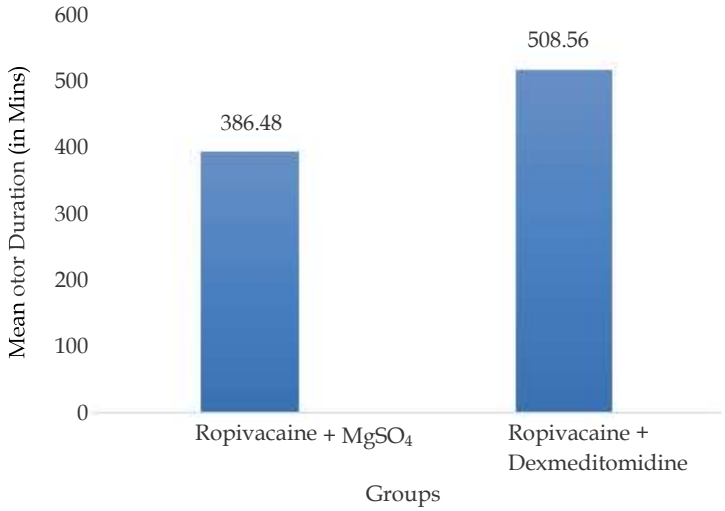

Fig. 4: Mean duration of motor blockade among both the groups.

in Group B was faster than Group A but the duration of motor and sensory blockade in Group B was longer than Group A, which was statistically significant with *p* - value < 0.001.

Discussion

The effective management of postoperative pain, relieve suffering and leads to earlier mobilization, fewer pulmonary and cardiac complications, a reduced risk of deep vein thrombosis, faster recovery with less likelihood of the development of neuropathic pain, reduced cost of care, and increased patient satisfaction.[10]

In modern anesthesia practice, peripheral nerve block has a significant contributory role to avail these benefits. Upper limb surgeries are mostly performed under brachial plexus block. Peripheral nerve blocks not only provide intraoperative anesthesia but also extended analgesia into the postoperative period without any systemic adverse effects using minimal anesthetic drugs. The supraclavicular brachial plexus block is commonly used, as the plexus is most compactly arranged here.[10]

A number of studies have attempted to study various adjuvants as a means of prolonging the duration of analgesia by single injection techniques.[11] α_2 agonists have also been used as adjuvants. However, it has been demonstrated that clonidine, as an adjuvant for peripheral nerve block, prolonged the duration of postoperative analgesia at a cost of an increased risk of sedation, hypotension, and bradycardia, known side-effects of systemic clonidine.[12] This was also observed with the use of dexmedetomidine.[3] Magnesium is known to produce antinociception, to enhance the effect of local anesthetic when given epidurally or intrathecally, by its action on the NMDA receptors found in the peripheral nerve and brachial plexus.[12]

Mukherjee K et al. conducted a prospective, double-blinded randomized controlled study to evaluate magnesium (150 mg) as an adjuvant in ropivacaine-induced supraclavicular brachial plexus block and concluded that it may increase the sensory and motor block duration and time to first analgesic use, and decrease total analgesic needs, with no side effects.[13] Haghighi M et al. randomized 60 patients and conducted a double-blinded study to see the effect of magnesium sulphate (5 mg/kg) on motor and sensory axillary brachial plexus block and concluded that the addition of magnesium sulphate to lidocaine increased the duration of motor and sensory block in the upper extremities during surgeries when compared to the use of lidocaine alone.[14]

Memis D et al.,[15] used the following grades to determine the quality of analgesia for operating condition in a study where dexmetitomedine was added as an adjuvant for lignocaine for intravenous regional anesthesia:

Grade 4 = (Excellent) No complaint from patient;

Grade 3 = (Good) Minor complaint with no need for the supplemental analgesics;

Grade 2 = (Moderate) Complaint that required supplemental analgesia;

Grade 1 = (Unsuccessful) Patient given general anesthesia.

The same grading was adapted by Ali QE et al.[16]

to find out the efficacy of clonidine as an adjuvant to ropivacaine in supraclavicular brachial plexus block.

Patients were also compared for the difference in the heart rate and systolic and diastolic blood pressure after the supraclavicular brachial plexus injection for every 5 mins till 10 mins, then every 10 mins till 30 mins, thereafter every 30 mins till the end of the procedure. Patients oxygen saturation and respiratory rate was also noted at regular intervals, side effects and complications were also noted.

Onset of sensory block

In our study, the time taken for onset of sensory block in Group A was 10.88 ± 2.05 mins and in Group B was 9.52 ± 1.28 mins with *p* - value of 0.001 which was significant. These findings show that there was significant difference in the time of onset of sensory block in both the groups. We observed early onset of sensory blockade in Group B than Group A.

Mukherjee et al. showed that the time of onset of sensory block with 0.5 % ropivacaine alone was 15.91 ± 1.60 mins and 0.5% ropivacaine with $MgSO_4$ is 16.27 ± 3.07 mins.[13] Mangal V et al. also conducted a similar study and the sensory onset time 20 ml 0.75 % ropivacaine alone with ultrasound guided technique was 6.74 ± 1.449 mins,[17] which more or less comes within the standard deviation of our study. In study conducted by Taneja et al. onset of sensory with ropivacaine alone and with $MgSO_4$ was found to be 5.5 ± 0.89 and 6.5 ± 0.65 mins.[18] Therfore, in many studies addition of $MgSO_4$ was found to slightly delay the onset though it was not statistically significant. This shows that Magnesium Sulphate does not have any effect on onset of sensory block when given along with ropivacaine for brachial plexus block.

Liu et al.[19] studied the effect of ropivacaine alone and ropivacaine combined with dexmedetomidine in brachial plexus block and revealed the onset time of 12.4 min in ropivacaine group and 8.9 min in ropivacaine with dexmedetomidine group for sensory blockade. They concluded the shorter onset of action in ropivacaine with dexmedetomidine group as shown in our study and study done by Khemka et al. (Group R was 20.1 ± 1.62 min, in Group R + D was 17.6 ± 1.25 min, with *p* - value of 0.001).[20]

Duration of sensory block

The mean duration of sensory blockade in Group A was 488.88 ± 85.03 mins and in Group B was 642.64 ± 108.11 mins which was statistically significant. Group B cases showed prolonged duration of sensory block than Group A cases.

Mukherjee et al. showed the duration of sensory block for ropivacaine alone was 289.67 ± 62.50 and with $MgSO_4$ was 456.21 ± 97.99 mins.[13] Taneja et al. found that duration for ropivacaine alone was 290 ± 26.95 mins and with $MgSO_4$ was 420 ± 30.25 mins.[18] Ropivacaine causes a greater motor and sensory differentiation with longer sensory blockade compared to other local anesthetics.

Liu et al. proved the duration of sensory blockade was more in ropivacine with dexmeditomidine (482.1 min) than ropivacaine (380.2 min) used alone in brachial plexus block for upper limb surgeries.[19] Khemha et al. showed the mean duration of sensory block in Group R was 561.0 ± 33.87 min and in Group R + D was 790.3 ± 41.23 min, with *p* - value 0.0001.[20] In our study, addition of dexmeditomidine to 0.75% ropivacaine further increased the duration of sensory blockade and hence analgesia.

Onset of motor block

In our study, the mean onset of motor blockade in Group A was 13.60 ± 3.12 mins and in Group B was 11.08 ± 1.42 mins, which was statistically significant with *p* - value < 0.001. Mukherjee et al observed the onset of motor block with ropivacaine alone was 17.80 ± 7.6 mins and with $MgSO_4$ was 19.20 ± 6.2 mins with a *p* - value of 0.30 which is not significant.[13] As Mukherjee et al. study used 0.5 % of ropivacaine they have a longer onset of action compared to our study.

In Taneja et al. study onset of motor blockade with ropivacaine alone and with $MgSO_4$ was found to be 12.4 ± 2.06 and 14.3 ± 2, 64 repectively with *p* - value of < 0.05.[18] In majority of the studies, conduted with ropivacanine there was no significant difference in onset of motor blockade when $MgSO_4$ was added.

In Liu et al. study, they proved that onset of motor blocakde was earlier in group used the combination of ropivacaine with dexmeditomidine (7.5 min) than in group used with ropivacaine alone (12.8 min).[19] Khemka et al. showed the mean onset time for complete motor block in Group R was 24.5 ± 1.48 min, and in Group R + D was 22.5 ± 1.50 min (p = 0.00001) which was statistically significant.[20] Our study showed, significant difference in onset of motor blockade when dexmeditomidine was added to 0.75% ropivacaine.

Duration of Motor block

While the prolongation of the sensory block is a desirable target, prolongation of motor block hampers postoperative recovery, especially if day care surgery is planned, and it is an undesirable outcome. The mean duration of motor blockade in Group A was 386.48 ± 86.43 mins and in Group B was 508.56 ± 89.89 mins, which was statistically significant with p - value < 0.001.

Mukherjee et al. found the duration of motor block with ropivacaine alone to be 242.16 ± 23.86 and with $MgSO_4$ 366.62 ± 24.42 with a p - value of 0.012 which is significant.[13] Taneja et al. also found the duration of motor block with $MgSO_4$ to be significant (motor block without $MgSO_4$ – 236 ± 20.6 and with $MgSO_4$ 350 ± 15.25, with the p - value of < 0.05).[18] Though with addition of $MgSO_4$ the motor duration was longer it was not statistically significant.

Liu et al. proved the duration of motor blockade was more in ropivacine with dexmeditomidine (430.1 min) than ropivacaine (350.1 min) used alone in brachial plexus block for upper limb surgeries,[19] which was similar to our study findings. Khemha et al. showed the mean duration of motor block in Group R was 508.0 ± 17.89 min, and in Group R + D was 680.7 ± 69.38 min which was statistically significant (p = 0.00001).[20]

There was no incidence of headache, nausea, vomiting, hypotension, bradycardia, chest pain, coughing, convulsion and respiratory depression, and procedure related complications. There was no CNS and CVS toxicity seen in either group in our study.

Our study demonstrated that addition of an alpha agonist like Dexmedetomidine to Ropivacaine resulted in early onset and prolonged duration of sensory and motor blockade in patients undergoing upper limb surgeries.

Conclusion

Dexmedetomidine as an adjuvant to Ropivacaine in the supraclavicular brachial block for upper limb surgery significantly shortens the onset time for sensory and motor block and prolongs the duration of sensory and motor blockade with the use of ultrasound guidance for the peripheral nerve block which is one of the latest, precise, and safe method in the present day.

References

1. McClellan KJ, Faulds D. Ropivacaine: An update of its use in regional anesthesia. Drugs 2000;60:1065–1093.
2. Swami SS, Keniya VM, Ladi SD, et al. Comparison of dexmedetomidine and clonidine (α_2 agonist drugs) as an adjuvant to local anesthesia in supraclavicular brachial plexus block: A randomized double-blind prospective study. Indian J Anesth 2012;56:243–49.
3. Abdallah FW, Brull R. Facilitatory effects of perineural dexmedetomidine on neuraxial and peripheral nerve block: A systematic review and meta-analysis. Br J Anesth 2013;110:915–25.
4. Swami SS, Keniya VM, Ladi SD, et al. Comparison of dexmedetomidine and clonidine (α_2 agonist drugs) as an adjuvant to local anesthesia in supraclavicular brachial plexus block: A randomized double-blind prospective study. Indian J Anesth 2012;56:243–49.
5. Chakraborty S, Chakrabarti J, Mandal MC, et al. Effect of clonidine as adjuvant in bupivacaine-induced supraclavicular brachial plexus block: A randomized controlled trial. Indian J Pharmacol 2010;42:74–77.
6. Yoshitomi T, Kohjitani A, Maeda S, et al. Dexmedetomidine enhances the local anesthetic action of lidocaine *via* an alpha-2A adrenoceptor. Anesth Analg 2008;107: 96–101.
7. Saadawy I, Boker A, Elshahawy MA, et al. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in pediatrics. Acta Anesthesiol Scand 2009;53:251–56.
8. Obayah GM, Refaie A, Aboushanab O, et al. Addition of dexmedetomidine to bupivacaine for greater palatine nerve block prolongs postoperative analgesia after cleft palate repair. Eur J Anesthesiol 2010;27:280–84.
9. Esmaoglu A, Yegenoglu F, Akin A, et al. Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block. Anesth Analg 2010;111:1548–551.
10. Gupta D, Mangal V, Sharma G, et al. Efficacy of Magnesium Sulfate as adjuvant to ropivacaine 0.4% for supraclavicular brachial plexus block in patients undergoing upper limb surgeries: A randomized controlled trail. J Recent Adv Pain 2017;3(2):85–89.
11. Kirksey MA, Haskins SC, Cheng J, et al. Local anesthetic peripheral nerve block adjuvants for prolongation of analgesia: A systematic qualitative review. Schwentner C, ed. PLoS ONE 2015;10(9):e0137312.
12. Piplai G, Roy A. Magnesium added to ropivacaine hastens the onset and prolongs the duration of analgesia after supraclavicular approach of brachial plexus block. J Evolution Med Dent Sci 2018;7(09):1087–90.

13. Mukherjee K, Das A, Basunia S, et al. Evaluation of Magnesium as an adjuvant in Ropivacaine-induced supraclavicular brachial plexus block: A prospective, double-blinded randomized controlled study. J Res Pharm Pract 2014;3(9):123–29.
14. Haghighi M, Soleymanha M, Sedighinejad A, et al. The effect of magnesium sulfate on motor and sensory axillary plexus blockade. Anesth Pain Med 2015;5(1):e21943
15. Memis D, Turan A, Karamanlioglu B, et al. Adding dexmedetomidine to lignocaine for IVRA. Anesth Analg 2004;98:835–40.
16. Ali QE, Manjunatha L, Amir HS, et al. Efficacy of clonidine as an adjuvant to ropivacaine in supraclavicular brachial plexus block: A prospective study. Indian J Anesth 2014;58(6):709–13.
17. Mangal V, Mistry T, Sharma G, et al. Effects of dexmedetomidine as an adjuvant to ropivacaine in ultrasound-guided supraclavicular brachial plexus Block: A prospective, randomized, double-blind study. J Anesthesiol Clin Pharmacol 2018;34(3):357–61.
18. Taneja P, Singh M, Singh B, et al. Comparison of 0.5% Ropivacaine with 0.5% Ropivacaine and Magnesium sulphate in supraclavicular brachial plexus block for forelimb and hand surgeries. Int j med res rev 2018;6:03.
19. Zhenqing Liu, Menglu Jiang, Tongsheng Xu et al. Analgesic effect of Ropivacaine combined with Dexmedetomidine on brachial plexus block. BMC Anesthesiology 2018;18:107.
20. Khemka V, Jadeja PD. Comparative study of ropivacaine with dexmedetomidine *versus* ropivacaine alone in supraclavicular brachial plexus block for upper limb surgery. Int J Sci Stud 2017;5(6):74–80.

Original Research Article

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A Comparative Study of the Effects of Intravenous Esmolol and Sublingual Nitroglycerine Spray on Hemodynamic Response Following Tracheal Extubation

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Abstract

Background: Recovery from general anesthesia and tracheal extubation is associated with increased hemodynamic response due to reflex sympathoadrenal activity and can be dangerous in susceptible patients. Many pharmacological methods were used to attenuate hemodynamic response but none were ideal. *Aims:* The aim of this study was to compare the effects of intravenous Esmolol and sublingual Nitroglycerine spray on hemodynamic response following tracheal extubation in patients undergoing general anesthesia for various surgeries. *Methods:* 60 patients of ASA 1 and 2 of either sex undergoing elective surgeries under general anesthesia were placed randomly in either Group A (n = 30) or Group B (n = 30). Group A received intravenous Esmolol 1.5 mg/kg and Group B received Sublingual 0.8 mg NTG spray. Either of the study drug was administered after 1 minute of the reversal agents being given. Hemodynamic variables HR, SBP, DBP and MAP were monitored and noted during tracheal extubation. *Results:* Intravenous Esmolol group had better control over heart rate when compared to Sublingual NTG spray group during tracheal extubation. Sublingual NTG spray group had modest increase in heart rate (Mean of 122 bpm). With respect to Systolic, Diastolic and Mean arterial blood pressure both the groups were found to be statisticaly insignificant and had clinically significant control over hemodynamic response during tracheal extubation. *Conclusion:* Intravenously administered Esmolol in dose of 1.5 mg/kg attenuates tracheal extubation response by having better control on heart rate and blood pressure with minimal complications when compared to sublingual 0.8 mg NTG spray group.

Keywords: Nitroglycerin (NTG); Esmolol; Tracheal Extubation; Hemodynamic response.

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Introduction

Recovery from general anesthesia and extubation is a period of intense physiological stress for patients.[1] This increase in sympathoadrenal activity may result in hypertension, tachycardia and arrhythmias.[1,2]

In order to control hemodynamic changes during tracheal intubation and extubation many pharmacological methods had been devised

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to reduce the extent of hemodynamic events[3] such as beta blockers, calcium channel blockers, opioids, local anesthetics and vasodilating drugs like nitroglycerine (NTG) but none were ideal.[1-4] Hence, the present study was under taken to compare the effect of intravenous Esmolol and sublingual NTG spray to attenuate the hemodynamic response during endotracheal extubation.

Materials and Methods

After obtaining approval from institutional ethical committee, written informed consent from patient belonged to ASA1 and 2 was taken, and routine preanesthetic evaluation was done. Patients were randomly allocated in to one of the two groups using numbers generated from www.random.org. Allocation concealment will be done using sealed envelope method.

Group A: Patients received a single dose of Inj. Esmolol 1.5 mg/kg diluted to 10 ml with Normal saline IV and 2 sprays of Normal saline sublingually;

Group B: Patients received two NTG sprays (2 sprays = 0.8 mg) through sublingual route and 10 ml of Normal saline by IV route.

Inclusion Criteria

1. Patients who have given written informed consent;
2. Patients with American Society of Anesthesiologists (ASA) Grade I & II;
3. Patients aged 20–60 years of either gender;
4. Patients with Body Mass Index (BMI) 19–28;
5. Patients scheduled for elective surgery lasting for 90–120 mins under general anesthesia.

Exclusion Criteria

1. Patients not willing to give written informed consent;
2. Patients with allergic to Esmolol or NTG;
3. Patients with anticipated difficult mask ventilation/Difficult intubation;
4. Patients with uncontrolled hypertension, diabetes mellitus, bronchial asthma, heart block, cerebrovascular disease and hepatic and renal disease;
5. Patients with BP below 90/60 millimeter of mercury (mm of Hg) or above 180/100 mm of Hg;
6. Patients using beta blockers, sympathomimetic agents, calcium channel blockers and vasodilator drugs;
7. Patients with chronic alcohol or drug abuse;
8. Pregnant women/Breastfeeding mothers.

Preanesthetic examination comprised of detailed history, systemic and thorough airway examination was conducted. Preoperative investigations comprised of Complete Blood Count (CBC), urine examination, blood sugar, serum electrolytes, coagulation profile, liver function tests, electrocardiography and echocardiography, Chest *X*-ray as indicated. All the patients were in fasting for 8 hours prior surgery.

Monitoring included Heart Rate (HR), Systolic Arterial Pressure (SBP), Diastolic Arterial Pressure (DBP), Mean Arterial Pressure (MAP), Peripheral Oxygen Saturation (SpO_2), and End-tidal CO_2 ($EtCO_2$).

Anesthetic procedure

Patients were premedicated with Inj. Glycopyrolate 0.005 mg/kg intravenously (IV), Inj. Midazolam 0.02 mg/kg IV and Inj Fentanyl 2 μg/kg IV. Induced with Inj. Propofol 1–2.5 mg/kg IV and Inj. Vecuronium 0.10–0.12 mg/kg IV given to facilitate tracheal intubation, anesthesia was maintained with 40:60 mixture of oxygen and air, and maintained with Isoflurane. Controlled mechanical ventilation was adjusted to maintain $EtCO_2$ pressure between 30 and 35 mm Hg. Hemodynamic parameters HR, SBP, DBP, MAP, $EtCO_2$ and SpO_2 were maintained every 5 minutes intraoperatively.

The BP and HR were maintained between 80% and 120% of the preoperative values by altering the concentration of Isoflurane and giving additional doses of Inj. Fentanyl until completion of surgery. Muscle relaxation was maintained by intermittent boluses of Inj Vecuronium 0.02 mg/kg IV After induction Inj. Paracetamol 1 gm intravenously administered to both the groups. Isoflurane will be stopped after completion of surgery.

Residual muscle relaxation was reversed with Inj Neostigmine 0.05 mg/kg IV and Inj. Glycopyrrolate 0.01 mg/kg IV on appearance of spontaneous ventilation. After 1 minute of the reversal agents being given, either of the study drug was administered.

Group A: Patients was received a single dose of Inj. Esmolol 1.5 mg/kg diluted to 10 ml with normal saline IV and 2 sprays of Normal saline sublingually;

Group B: Patients were received two NTG sprays (2 sprays = 0.8 mg) through sublingual route and 10 ml of Normal saline by IV route.

Study drugs were prepared before hand by an assistant and their identity was unknown to the anesthesiologist who was involved in the study. Thorough oropharyngeal suction was done before extubation. Then tracheal extubation was done once criteria for extubation were met. Return of spontaneous respiration with adequate tidal volume, obeying verbal commands, spontaneous eye opening, and good hand grip were the criteria for extubation. Immediately after tracheal extubation patient were given 100% oxygen by a facemask for 5 minutes.

Parameters like HR, Systolic, Diastolic and Mean arterial Blood Pressures were monitored at the completion of surgery – Baseline, Isoflurane stopped-T0, at the time of giving reversal-T1, 1 min after giving study medication-T2, during extubation-T3, One minute after extubation-T4, Two minute after extubation-T5, Five minutes after extubation-T6, Ten minutes after extubation-T7 and Fifteen minutes after extubation-T8. Events like coughing, bucking and breath holding were monitored. Excessive secretions, bronchospasm, laryngospasm, postoperative nausea and vomiting and any other untoward events were monitored.

Need for Inj. Atropine 0.01 mg/kg IV (HR < 60/min) or Inj. Ephedrine 5mg IV (SBP < 90 mm Hg) or additional dose of Nitroglycerine or Esmolol (SBP > 200 mm Hg, DBP > 120 mm Hg or HR > 150/min) was recorded.

Efficacy parameters

Hemodynamic parameters assessed were HR, SBP, DBP and MAP.

H. Statistical Analysis

Datas were entered in Microsoft excel and exported into SPSS Version 21.0. Datas were analyzed by descriptive Statistics; Student's *t*-test was used to compare the significant difference between two means. ANOVA was used to compare the significant difference between three or more groups. $p < 0.05$ is considered significant.

Results

In Esmolol group, 46.7% were females and 53.3% were males. In nitro-glycerine group, 70% were females and 30% were males. There was no significant difference in gender distribution between two groups, as shown in Table 1 and 2.

Table 1: Gender distribution comparison between two groups

		Groups			
		Group A (Esmolol)		Group B (Nitro-glycerine)	
		Count	%	Count	%
Sex	Female	14	46.7%	21	70.0%
	Male	16	53.3%	9	30.0%

$p = 0.067$.

Table 2: Profile of subjects in the two groups

	Groups				*p* - value
	Group A (Esmolol)		Group B (Nitro-glycerine)		
	Mean	SD	Mean	SD	
Age	37.43	11.11	38.90	11.49	0.617
Height	1.58	0.05	1.60	0.07	0.255
Weight	58.93	4.98	57.93	5.36	0.457
BMI	23.46	1.17	22.54	1.41	0.325

Demographic parameters which were comparable in both the groups.

ASA Grading 1 and 2 which were comparable in both the groups, as shown in Table 3.

Table 3: ASA Grade comparison between two groups

	Groups				
	Group A (Esmolol)		Group B (Nitro-glycerine)		
	Count	%	Count	%	
ASA Grade	Grade 1	22	73.3%	25	83.3%
	Grade 2	8	26.7%	5	16.7%

$p = 0.347$

Baseline HR which are comparable in both the groups. After giving reversal agent, in Nitrglycerine group there was significant increase in HR before and after extubation when compared to Esmolol group and p – value (< 0.001) also showed to be statistically significant between the groups, as shown in Table 4 and Figure 1.

Table 4: Heart rate comparison between two groups at different time intervals

Heart rate	Groups						p - value b/w two groups
	Group A (Esmolol)			Group B (Nitro-glycerine)			
	Mean	SD	p - value	Mean	SD	p - value	
Base line	87.50	12.83		92.50	15.79		0.183
T0	100.33	19.30	< 0.001	96.97	19.75	0.201	0.507
T1	110.67	18.41	< 0.001	115.03	20.88	< 0.001	0.394
T2	99.30	14.99	0.001	122.70	22.72	< 0.001	< 0.001
T3	93.37	12.33	0.056	121.17	21.33	< 0.001	< 0.001
T4	88.77	10.17	0.611	113.47	21.96	< 0.001	< 0.001
T5	85.90	10.25	0.559	103.6	17.83	0.006	< 0.001
T6	81.00	7.50	0.009	94.53	19.13	0.620	0.001
T7	76.40	8.50	< 0.001	84.73	20.40	0.111	0.043
T8	74.60	9.34	< 0.001	80.80	18.04	0.016	0.100

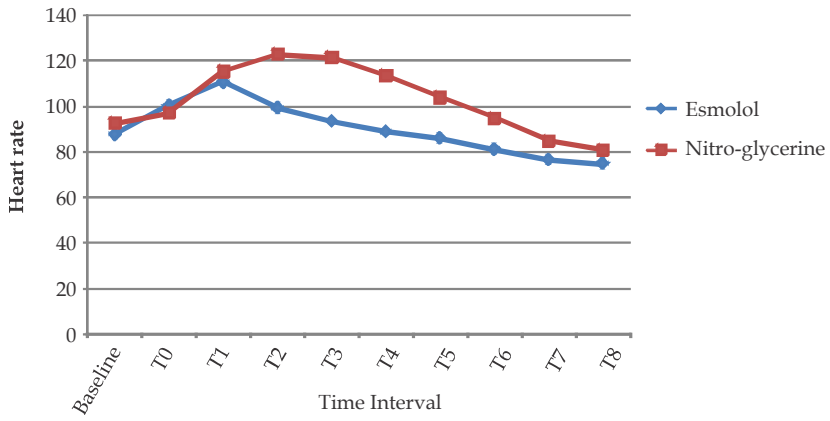

Fig. 1: Heart rate comparison between two groups at different time intervals.

Baseline systolic blood pressure values were comparable in both the groups. After giving reversal agent systolic blood pressure was found to be comparable in both the groups and there was significant decrease in SBP compared to baseline in both the groups. There was no statistical significance between Esmolol group and Nitrglycerine group before and after extubation, as shown in Table 5.

Table 5: SBP comparison between two groups at different time intervals

SBP	Groups						*p* - value b/w two groups
	Group A (Esmolol)			Group B (Nitro-glycerine)			
	Mean	SD	*p* - value	Mean	SD	*p* - value	
Baseline	127.57	10.64		131.60	15.29		0.240
T0	138.07	14.79	0.002	142.43	14.34	< 0.001	0.140
T1	147.67	17.69	< 0.001	153.97	24.93	< 0.001	0.264
T2	140.60	9.98	< 0.001	145.77	27.48	0.004	0.337
T3	135.13	10.56	0.004	140.70	24.11	0.058	0.251
T4	130.67	8.21	0.091	127.57	18.02	0.239	0.395
T5	125.43	8.64	0.252	119.97	27.15	0.033	0.298
T6	121.93	7.10	0.006	119.97	16.01	< 0.001	0.541
T7	118.27	7.55	< 0.001	118.30	14.48	< 0.001	0.991
T8	115.23	7.75	< 0.001	119.10	12.30	< 0.001	0.151

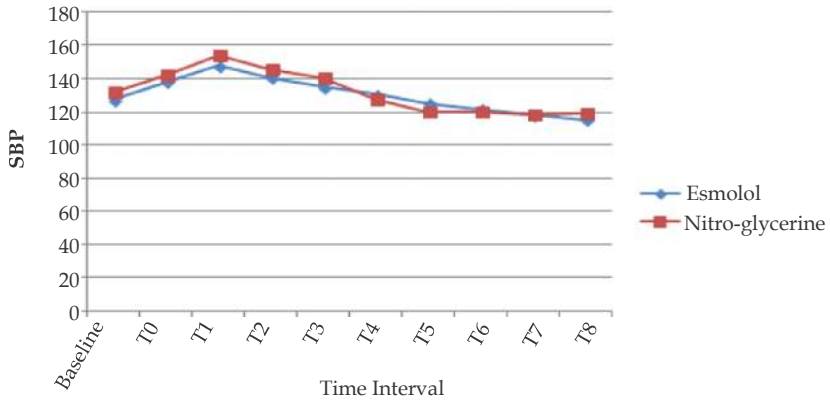

Fig. 2: Line diagram showing SBP comparison between two groups at different time intervals.

Baseline diastolic blood pressure values were comparable in both the groups. After giving reversal agent diastolic blood pressure was found to be comparable in both the groups and there was significant decrease in DBP compared to baseline in both the groups. At T0, T2, T4, T5 intervals DBP were higher in NTG group compared to Esmolol group but at T5 there was statistically significant decrease in DBP values in Esmolol group copmpared to NTG group, as shown in Table 6.

Table 6: DBP comparison between two groups at different time intervals

DBP	Groups						*p* - value b/w two groups
	Group A (Esmolol)			Group B (Nitro-glycerine)			
	Mean	SD	*p* - value	Mean	SD	*p* - value	
Baseline	80.83	11.68		81.27	6.90		0.862
T0	81.57	10.97	0.767	90.57	11.72	< 0.001	0.003
T1	93.77	16.66	<0.001	98.93	14.06	<.001	0.199
T2	83.80	17.30	0.345	91.53	7.46	<.001	0.028
T3	79.57	14.83	0.654	84.47	11.13	0.181	0.153
T4	73.57	14.12	0.011	82.83	9.37	0.418	0.004
T5	69.13	12.82	<.001	79.33	7.21	0.332	<.001
T6	72.60	13.06	0.002	76.70	7.64	0.014	0.143
T7	71.73	11.66	0.001	74.97	6.83	0.001	0.195
T8	72.27	8.71	<.001	73.30	7.32	<.001	0.621

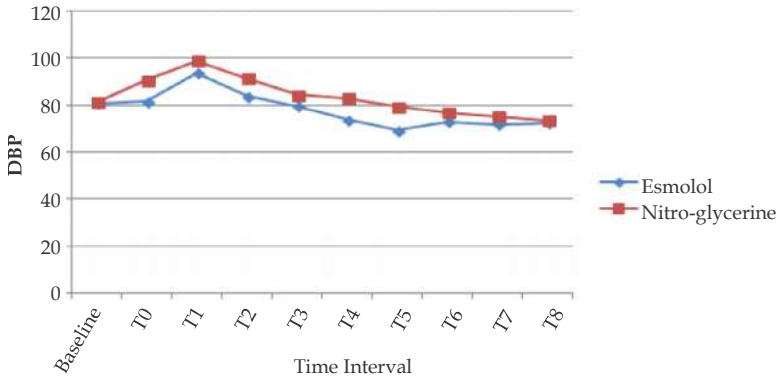

Fig. 3: Line diagram showing DBP comparison between two groups at different time intervals.

Baseline mean arterial pressure values were comparable in both the groups. After giving reversal agent mean arterial blood pressure was found to be comparable in both the groups and there was decrease in mean arterial blood pressure compared to baseline in both the groups. And there was no statistical significance between Esmolol group and Nitrglycerine group before and after extubation, as shown in Table 7.

Table 7: MAP comparison between two groups at different time intervals

MAP	Groups						*p* - value b/w two groups
	Group A (Esmolol)			Group B (Nitro-glycerine)			
	Mean	SD	*p* - value	Mean	SD	*p* - value	
Baseline	96.53	15.31		95.90	8.66		0.844
T0	97.47	12.44	0.734	107.43	12.00	< 0.001	0.003
T1	113.80	21.05	<.001	115.70	14.17	< 0.001	0.683
T2	102.33	20.15	0.073	108.13	6.54	< 0.001	0.139
T3	100.57	18.06	0.172	101.03	9.46	0.035	0.901
T4	91.37	14.03	0.065	98.90	9.23	0.136	0.017
T5	86.70	14.13	0.001	94.27	7.73	0.433	0.013
T6	86.57	12.95	<.001	91.30	7.04	0.017	0.084
T7	85.33	11.52	<.001	89.13	6.52	0.001	0.121
T8	85.83	9.08	<.001	86.53	7.06	<.001	0.740

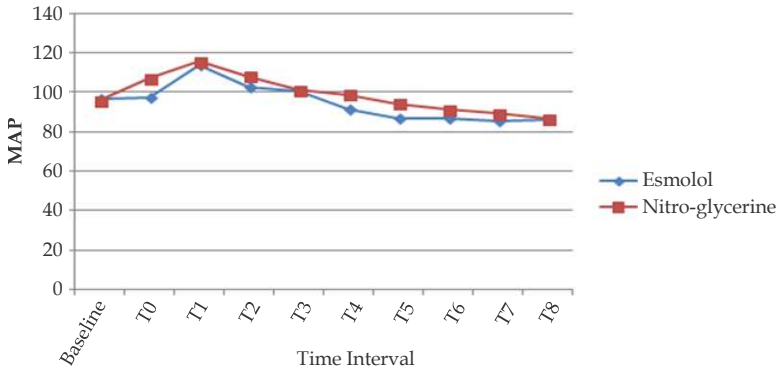

Fig. 4: Line diagram showing MAP comparison between two groups at different time intervals.

In NTG Group 3 patients (10%) had complications like hypotension, laryngospasm, headache and in Esmolol Group 1 patient (3.3%) had complications like hypotension and bradycardia and were treated immediately. There was no significant difference in complications between two groups, as shown in Table 8.

Table 8: Complications

	Groups				
	Group A (Esmolol)		Group B (Nitro-glycerine)		
	Count	%	**Count**	%	
Complications	Absent	29	96.7%	27	90.0%
	Present	**1**	**3.3%**	**3**	**10.0%**

Discussion

Endotracheal intubation and extubation is commonly associated with increase in hemodynamic changes due to reflex sympathetic discharge[1] and stimulation of laryngopharynx[2] which leads to increased plasma catecholamine levels causing tachycardia, increased SVR, hypertension and increased myocardial contractility.[3] These hemodynamic changes leads to serious consequences in patients with hypertension, coronary artery disease, diabetes, preeclampsia, and cerebrovascular disease which may leads to perioperative or postoperative myocardial ischemia and acute heart failure in susceptible patients.[4]

The known factors responsible for such untoward hemodynamic response during extubation are lighter plane of anesthesia, mechanical irritation to airway,[5] pain due to surgery and during emergence from general anesthesia.[6] The study by Miyazaki et al. had shown that extubation increases heart rate and systolic blood pressure by 20 % in more than 70% of patients.[7]

There are various agents which are used to attenuate these hemodynamic changes like intravenous Lignocaine,[8] Topical Lignocaine spray,[9] narcotic opioids like Fentanyl,[10] Alfentanyl,[11] calcium channel blockers like Diltiazem,[3] vasodilators like Nitroglycerine both intravenous[5] and sublingual sprays,[1,2] alpha agonists like Clonidine,[12] Demeditomidine,[13] and Betablockers like Esmolol.[3–5] By controlling the hemodynamic changes that occur during endotracheal extubation which can reduce mortality and morbidiy attributable to anesthesia especially in vulnerable patients.[3]

Attenuating this increased hemodynamic response to extubation is more challenging than that of intubation because we cannot deepen the plane of anesthesia,[15,16] When we use any drug for attenuating the hemodynamic response to tracheal extubation its peak effect should correspond to that of the stimulus, so, there should be two to three minutes time gap between administration of drug and tracheal extubation.[2] Thus, the choice of the drug, route of administration and the timing used in the present study seems to be justified. The study by Dyson A et al.,[17] on Esmolol with doses of 1.5 mg/kg and 2 mg/kg controlled both systolic blood pressure and heart rate but larger dose produced significant decrease in systolic blood pressure. Hence, in our study we have used dose of 1.5 mg/kg of intravenous Esmolol. And the study by Tagalpallewar A et al.,[2] on Nitroglycerine showed satisfactory blood pressure control with 0.8 mg of sublingual dose of NTG spray. Hence, in our study we have used 0.8 mg sublingual NTG spray. But there was no study comparing these drugs, hence this study was undertaken. Because of immediate action, shorter half life and lack of sedative properties of intravenous Esmolol[5] and sublingual NTG spray,[2] we planned to do a prospective randomized controlled double blind study to compare the effects of these drugs on hemodynamic response following tracheal extubation.

In our study, we found intravenous Esmolol significantly attenuated the tachycardia response to extubation when compared to sublinlual NTG group. In intravenous Esmolol group control of heart rate was observed within 1 minute of administration and maintaining upto 15 minutes after extubation, where as in NTG group there was increase in mean heart rate upto 122 beats per minute during and after extubation. Hence, we found intravenous Esmolol has better control over heart rate when compared to sublingual NTG group. Various studies by Acharya N et al.,[3] Vachhani et al.[4] and Kotambkar V et al.[5] on comparison of Intravenous Esmolol and Intravenous NTG showed, Intravenous Esmolol has better control over heart rate during extubation when compared to Intravenous NTG.

Nitroglycerine is known to reduce blood pressure with increase in heart rate.[18] And we found only few studies on sublingual NTG spray to attenuate hemodynamic response to tracheal extubation. The study by Tagalpallewar A et al.[2] found that at the time of extubation there was modest increase in heart rate following sublingual NTG spray which correlates with our study. In present study, the baseline value of systolic, diastolic, mean

arterial pressure were comparable between the groups during intraoperative period. At the time of extubation mean arterial pressure was lower in Esmolol group when compared to NTG group which was found to be statistically significant following extubation and this is in similar to study done by Ersin et al.[19]

However, in a study done by Kotambkar V et al.,[5] systolic, diastolic, mean arterial pressure were significantly lower in NTG group as compared to Esmolol group at the time of extubation this is in contrary to our study. Tagalpallewar A et al.[2] reported that sublingualy administered NTG spray in a dose of 0.8 mg prior to extubation resulted in stable hemodynamics, and allows easy extubation and comfortable recovery.

Complications

In the present study, heart rate less than 60 bpm and blood pressure less than 90/60 mm of hg was considered dangerous and injection Atropine 0.01 mg/kg IV and injection Ephidrine 6mg IV were used as rescue drug for bradycardia and hypotension respectively. In NTG Group 3 patients had complications like hypotension, laryngospasm and headache and in Esmolol group one patient had bradycardia which were treated immediately and there was no significant differences in complications between the two groups.

Limitations

Our study has some limitations like invasive monitoring was not done so evaluation of cardiac output during extubation could not be assessed and effects of these drug in high risk patients needs validation.

Conclusion

We conclude from this study that administration of intravenous Esmolol in a dose of 1.5 mg/kg and sublingual NTG spray in a dose of 0.8 mg prior to extubation in ASA1 and ASA 2 patients are effective and relatively safe method of protecting patients from the complications related to hypertension and tachycardia and allows easy extubation with stable hemodynamics with smooth and comfortable recovery. Increase in Systolic, Diastolic and Mean arterial pressures were controlled by both intravenous Esmolol and sublingual NTG spray but intravenous Esmolol also controlled heart rate during extubation. Hence, we conclude intravenous Esmolol attenuates extubation response by having better control on heart rate and blood pressure with minimal complications when compared to sublingual NTG spray group.

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Conflict of Interest: Nil

References

1. Singh D, Sundrani O, Tagalpallewar A, et al. The effects of Nitroglycerine (NTG) sublingual spray to slunt the hemodynamic response to endotracheal extubation in lumbar disc surgery. Journal of Evolution of Medical and Dental Sciences 2015;4(81):14233–14239.
2. Tagalpallewar A, Ambare B, Agrawal J, et al. Efficacy of sublingual Nitroglycerine spray in attenuation of hemodynamics to tracheal extubation. International Journal of Research in Medical Sciences 2017;5(8):3560–565.
3. Narayan Acharya. Comparative evaluation of esmolol, nitroglycerine and diltiazem on attenuation of cardiovascular responses to tracheal extubation: A prospective randomized study. Sch J App Med Sci Jan 2017;5(1C):188–94.
4. Vachhani R, Gulati Rahul. A comparative study to evaluate the effects of nitroglycerine and esmolol on hemodynamic parameters in controlled hypertensive patients during emergence from anesthesia and extubation. Int J Med Res Prof 2017;3(3):90–93.
5. Kotambkar V, Katdare M. A comparative study of effects of intravenous Nitroglycerine and intravenous Esmolol on hemodynamic response following tracheal extubation. Indian Journal of Basic and Applied Medical Research 2015 June;4(3): 344–56.
6. Shirasaka T, Iwasaki T, Hosokawa N, et al. Effects of landiolol on the cardiovascular response during tracheal extubation. Journal of anesthesia 2008 Aug 1;22(3):322–25.
7. Miyazaki M, Kadoi Y, Saito S. Effects of landiolol, a short-acting beta-1 blocker, on hemodynamic variables during emergence from anesthesia and tracheal extubation in elderly patients with and without hypertension. Journal of Anesthesia 2009 Nov 1; 23(4):483–88.
8. Bidwai AV, Bidwai VA, Rogers CR, et al. Blood-pressure and pulse-rate responses to endotracheal extubation with and without prior injection of lidocaine. Anesthesiology. 1979 Aug;51(2):171–73.
9. Jee D, Park SY. Lidocaine sprayed down the endotracheal tube attenuates the airway-circulatory

reflexes by local anesthesia during emergence and extubation. Anesthesia & Analgesia 2003 Jan 1;96(1):293–97.

10. Nishina K, Mikawa K, Maekawa N, et al. Fentanyl attenuates cardiovascular responses to tracheal extubation. Acta Anesthesiol Scand 1995 Jan 1;39(1):85–89.
11. Fuhrman TM, Ewell CL, Pippin WD, et al. Comparison of the efficacy of esmolol and alfentanil to attenuate the hemodynamic responses to emergence and extubation. Journal of Clinical Anesthesia 1992 Dec 31;4(6):444–47.
12. Zalunardo MP, Zollinger A, Spahn DR, et al. Preoperative clonidine attenuates stress response during emergence from anesthesia. Journal of Clinical Anesthesia 2000 Aug 31;12(5):343–49.
13. Guler G, Akin A, Tosun Z, et al. Single-dose dexmedetomidine attenuates airway and circulatory reflexes during extubation. Acta Anesthesiol Scand 2005 Sep 1;49(8):1088–91.
14. Mikawa K, Nishina K, Takao Y, et al. Attenuation of cardiovascular responses to tracheal extubation: Comparison of verapamil, lidocaine, and verapamil-lidocaine combination. Anesthesia and Analgesia 1997 Nov 1;85(5):1005–10.
15. Heartley M, Vaughan RS. Problem associated with tracheal extubation. Br J Anesth 1993:71:561–68.
16. Bostan H, Eroglu A. Comparison of the clinical efficacies of fentanyl, esmolol and lidocaine in preventing the hemodynamic responses to endotracheal intubation and extubation. Journal of Current Surgery 2012;2(1):24–28.
17. Dyson A, Isaac PA, Pennant JH, et al. Esmolol attenuates cardiovascular responses to extubation. Anesth Analg 1990;71:675–78.
18. James P Rathmell, Shafer Steven. Vasodilators, chapter 20. Pamella Flood, Stoelting's handbook of pharmacology and physiology in anesthetic practice. 5th edition. New Delhi: Wolters Kluwer; 2013.p.309.
19. Ersin Y, Çelik M, Besler M, et al. Comparing the effects of esmolol and diltizem to depressing the hemodynamic response against tracheal extubation. The Medical Journal of SSK Göztepe Educational Hospital. 2005;20(4):193–96.

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Comparison of Postoperative Analgesia by Intraperitoneal Infiltration of Bupivacaine versus Bupivacaine with Dexmedetomidine in Laparoscopic Surgeries

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Abstract

The primary aim is to compare postoperative analgesia by intraperitoneal infiltration of bupivacaine *versus* bupivacaine with dexmedetomidine in laparoscopic surgery. The secondary objective to assess postoperative pain relief, rescue analgesic drug requirement and side-effects in both groups. The study was approved by the University's institutional ethics committee (Reg No. ECR 518/Inst/MH/2014/RR-17) and written informed consent was obtained from all subjects participating in the trial. The study was conducted prior to patient enrollment at Bharati Vidyapeeth Medical College institutional ethics committee (REF: BVDUMC/IEC/62, Principal investigator: Hemadip Tavethiya, Date of registration: 7th September, 2018). This prospective comparative study enrolled a sample of 52 patients, 26 in each group. Group B received only Bupivacaine intraperitoneally and Group BD received Bupivacaine with adjuvant Dexmedetomidine intraperitoneally. VAS score was seen at 1, 2, 4, 6, 12, 24 hours postsurgery and VAS score > 3 was given IV paracetamol or IV diclofenac sodium as rescue drug. *Results:* VAS at different time intervals, overall VAS in 24 h was significantly lower (2.34 ± 0.84, 3.65 ± 0.47), total analgesic consumption was low in Group BD than Group B. *Conclusion:* Intraperitoneal instillation of bupivacaine in combination with dexmedetomidine is superior to bupivacaine alone.

Keywords: Laparoscopic surgery; Bupivacaine hydrochloride; Dexmedetomidine hydrochloride; Intraperitoneal injection; Postoperative pain.

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Introduction

Surgery using minimal laparoscopic approach are now a days common with the benefits of less discomfort, shorter hospitalization and earlier return to normal activity.[7,17] Main disadvantage of such Surgery is post operative pain at incisional site, during coughing and respiratory movement and handling during first hour after surgery.[7] Hence, pain management remains the mainstay for anesthesiologist.

Use of Local anesthetic agents into the intraperitoneal space is one of the effective way of the postoperative pain relief.[8] It suppresses many of the pain mediated stress responses due to stretching of peritoneum, irritation due to residual carbon dioxide after laparoscopic surgery and inflammation of peritoneum.[8,17]

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Intraperitoneal instillation of local anesthetic agents alone or in combination with adjuvant such as α_2 agonists like clonidine and dexmedetomidine has been found to reduce postoperative pain following laparoscopic surgery.[17]

Materials and Methods

This prospective, randomized study was carried out on 52 patients after getting approval from ethical committee and written inform consent. Patients was divided into 2 groups by simple randomization, Group B & Group BD (26 patients each). Study was conducted between October 2018 and September 2019.

Group B received only Bupivacaine intra peritoneally;

Group BD received Bupivacaine with adjuvant Dexmedetomidine intraperitoneally.

Patients of ASA Grade I/II between 18 and 60 years of age posted for all elective laparoscopic abdominal surgery in which Bupivacaine can be used were included. Patients with cardio-pulmonary systemic illness, emergency surgeries or patients on enzyme inducer drugs (Isoniazid, Phenytoin, Rifampicin, etc.), allergic to Bupivacaine or Dexmedetomidine, patient may required postsurgery intraabdominal drain were excluded from the study.

All patients were transported to the operating room without premedication. On arrival to operating room, an 20-gauge intravenous (IV) catheter was inserted and 6 ml/kg/h crystalloid was infused intraoperatively monitoring of electrocardiography, noninvasive blood pressure, oxygen saturation (SpO_2) was started and baseline values were recorded. Preoxygenation with 100% oxygen (O_2) was done for 3 min. General anesthesia was induced with IV Midazolam 1mg, IV Fentanyl 2 μg/kg, IV propofol 2.0–2.5 mg/kg followed by Succinylcholine 2 mg/kg to facilitate orotracheal intubation.

The trachea was intubated with a cuffed orotracheal tube of appropriate size. Anesthesia was maintained with 50% air in oxygen with 0.2–2% sevoflurane. Intermittent boluses of vecuronium bromide were used to achieve muscle relaxation. Minute ventilation was adjusted to maintain normocapnia (end tidal carbon-dioxide [$EtCO_2$] between 34 and 38 mm Hg) and $EtCO_2$ was monitored. Nasogastric tube of appropriate size was inserted.

During laparoscopy, intraabdominal pressure was maintained 12–14 mm Hg. At the end of surgery the CO_2 was removed carefully by manual compression of the abdomen at the end of the procedure with open trocar.

Patients were randomly allocated to one of the groups using table of randomization, Group B (n = 26): Intraperitoneal bupivacaine (2 mg/kg) 0.25% + 5 ml normal saline (NS), Group BD (n = 26): Intraperitoneal bupivacaine (2 mg/kg) 0.25% + dexmedetomidine 1 μg/kg (diluted in 5 ml NS). Drug was given to patient intraperitoneally before trocar removed at the end of surgery.

All patients stayed in PACU for 2 h after the end of surgery. The primary outcome variable was to compare pain (visual analog scale [VAS]) score. The secondary outcome included time to the first request of analgesia in the postoperative period, total dose of rescue analgesic used in 24 h period (postoperative) and any adverse/side-effects.

The intensity of postoperative pain was recorded for all the patients using VAS score at 1, 2, 4, 6, 12, 24 hour after surgery and over all VAS score (mean of all VAS scores).

All the study patients were instructed about the use of the VAS score before induction of anesthesia (VAS score 0 - no pain, VAS score 10 - worst possible pain). Patients who reported VAS > 3 were given Diclofenac 75 mg intravenous or Paracetamol 1 gm intravenous as rescue analgesia. Patients were also observed for postoperative nausea and vomiting. Patients who suffered nausea or vomiting were given ondansetron 4 mg IV. Time to the first request of analgesia (considering the extubation as time 0), total dose of analgesia and adverse or side-effects over 24 h postoperatively were noted.

Statistical analysis was performed using SPSS ver. 20. Results were expressed as mean ± standard deviation, number and percentage (%). Data were analyzed normally distributed data were assessed using independent sample *t*-test (for comparison of parameters among groups). Comparison was carried out using Chi-square (χ^2) fisher exact test with a p - value reported at 95% confidence level. p - value < 0.05 considered as statistically significant.

Results

There was no significant difference with respect to age, sex, weight and ASA physical status, duration of surgery and anesthesia time, (Table 1).

Table 1: Demographic characteristics of patients, operative data in studied groups

Variable	Mean ± SD		p^*	Statistical Significance
	Group B (n = 26)	Group BD (n = 26)		
Age (years)	39.0 ± 14.29	34.08 ± 12.38	0.19	NS
Sex				
Males	7 (58.3)	5 (41.7)	0.510	NS
Females	19 (47.5)	21 (52.5)		
ASA				
I	16 (48.5)	17 (51.5)	0.773	NS
II	10 (52.6)	9 (47.4)		
Duration of surgery (min)	95.58 ± 55.16	123.46 ± 67.92	0.11	NS

ASA: American Society of Anesthesiologists, SD: Standard Deviation, Group B: Bupivacaine only, Group BD: Bupivacaine with dexmedetomidine; p^* < 0.05 considered as statistically significant. p^* value > 0.05 by independent sample t-test.

So, there was no significant difference with respect to age, sex, weight and ASA physical status, duration of surgery. Visual analog scale at different time intervals were statistically significantly lower at all times in Group BD than Group B, (Table 2 and Fig. 1).

Table 2: Postoperative VAS# score (mean ± SD) in studied groups

Time (in hrs)	Group B (n = 26)	Group BD (n =26)	p^*	Statistical Significance
1	3.0 ± 0.00	1.0 ± 0.00	0.99	NS
2	3.12 ± 1.21	1.69 ± 0.47	0.0001	S
4	3.04 ± 1.14	2.15 ± 0.67	0.001	S
6	3.42 ± 1.47	2.92 ± 1.35	0.209	NS
12	3.38 ± 1.35	2.85 ± 1.34	0.158	NS
24	5.42 ± 0.50	4.96 ± 1.18	0.076	NS

p^*: Level of significance between Group B and Group BD; VAS#: Visual Analog Scale; SD: Standard Deviation; p^* < 0.05 Considered as statistically significant.

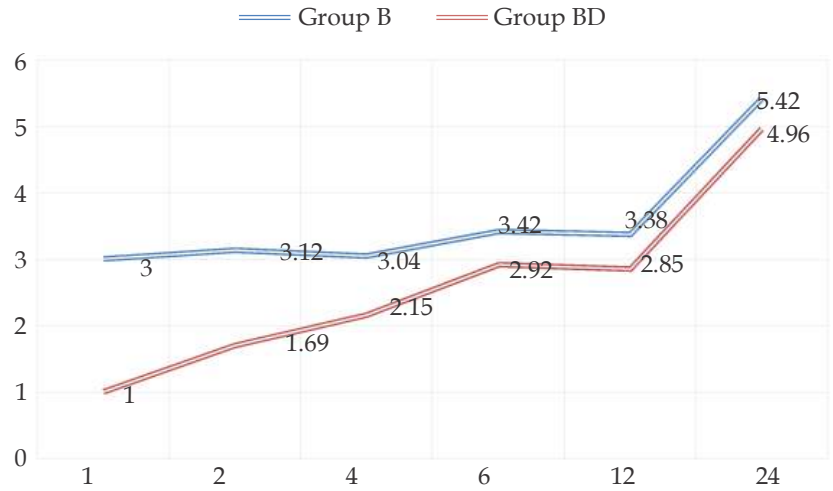

Fig. 1: Postoperative VAS comparision.

Furthermore, overall VAS in 24 h was also significantly lower in Group BD (2.34 ± 0.84) than Group B (3.65 ± 0.47), (Table 3 and Fig. 2).

Table 3: Overall Postoperative VAS# score (mean ± SD) in studied groups

Variable	Group B (n = 26)	Group BD (n = 26)	p*	Statistical Significance
Overall VAS 24 hrs postoperatively	3.65 ± 0.47	2.34 ± 0.84	0.0001	S

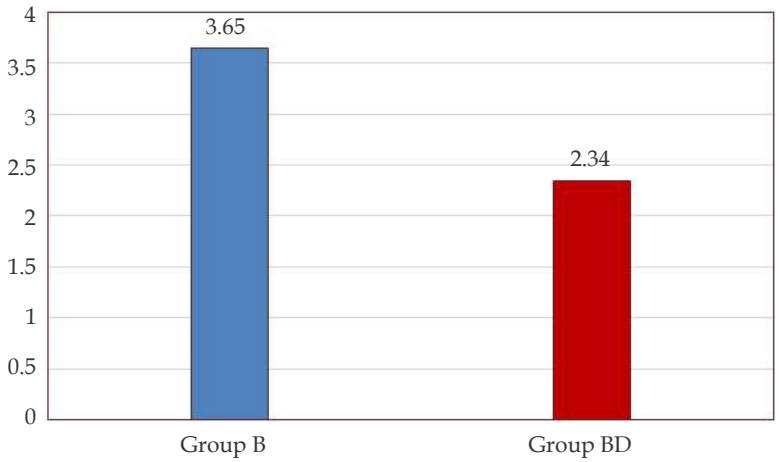

Fig. 2: VAS score comparision in 24 hours.

Table 4: Hourly consumption of rescue analgesic drug is also significantly low

Drug used in 2 hrs	Group		p*	Significance
	B	BD		
Not used	20	26	0.009	S
Diclofenac	4	0		
PCM	2	0		
Total	26	26		
Drug used in 4 hrs				
Not used	18	26		
Diclofenac	3	0	0.014	S
PCM	5	0		
Total	26	26		
Drug used in 6 hrs				
Not used	13	18		
Diclofenac	3	7		
PCM	9	1	0.010	S
PCM + Diclophenac	1	0		
Total	26	26		
Drug used in 12 hrs				
Not used	8	20		
Diclofenac	8	2	0.0001	S
PCM	10	4		
Total	26	26		
Drug used in 24 hrs				
Not used	0	16		
Diclofenac	13	3	0.0001	S
PCM	13	10		
Total	26	26		

p*: Level of significance between Group B and Group BD;

p* value < 0.05 by Fisher Exact test

Discussion

Laparoscopic surgery is the most effective in all the day care surgery. But pain management is also important in laparoscopic surgery. Effects of insufflation during laparoscopic surgery are *via* two mechanism.

1. Mechanical effect due to increase intraperitoneal pressure (e.g., Decrease venous return; Decrease cardiac output; Decrease blood pressure; etc.)
2. Chemical effects due to CO_2 absorption and its inflammatory effect on peritoneum (e.g., Hypoxia; Aacidosis; Cardiac arrythmias; etc.)

Due to inflammation and irritation of peritoneum pain scale is increase which is already present due to surgery. Pain have three component in laparoscopic surgery visceral, parietal and referred pain.[16] The major portion of pain is parietal but may studies showed that in early postoperative time major portion is occupied by visceral pain due to small incision and less tissue trauma to abdominal wall.[16]

For this multi factorial pain stimulus requirement of pain management also multimodal. For this intraperitoneal local anesthetic agent give some additive effect of analgesia. Which is further give more analgesic effect with some adjuvant added with it. But analgesic effects are different according to various study by intraperitoneal instillation of local anesthetic agents.

BMP Rademaker[3] shown that 20 ml of local analgesic agent is not effective for postoperative pain management, it is may because of low amount of agents.

This justification is covered by our study and adequate amount of drug with adequate concentration is used. They also shown some argument about position of patient during instillation, gravity is also a factor to act the drug on specific nerve ending sites.

A Ng, G Smith[1] shown that intraperitoneal instillation of anesthetic appear to demonstrate more effective in elective gynecological laparoscopic surgery because of it is less traumatic surgery than other laparoscopic surgery like laparoscopic cholecystectomy or laparoscopic hernia repair.

Usha Shukla, T Prabhakar[17] assessed effect of dexmedetomidine is *via* dorsal root neuron level, where they release substance *P* and through the action on *G* protein. They also assessed dexmedetomidine is give better analgesia effect with bupivacaine as compared to bupivacaine alone or bupivacaine with tramadol.

Khaled Mohamed Fares, Sahar Abd Elbaky Mohmed[9] give conclusion that for postoperative pain management in laparoscopic colorectal carcinoma surgery 50 ml of 0.25% bupivacaine with dexmedetomidine 1 mcg/kg is effective as compare to 50 ml of 0.25% bupivacaine alone.

Our study results correlates with study done by Usha Shukla[17] and Khaled Mohamed Fares[9] which have shown that intraperitoneal instillation of 50 ml of Bupivacaine with 1 mcg/kg dexmedetomidine was effectively reduce postoperative pain as compare to 50 ml bupivacaine alone in laparoscopic cholecystectomy[17] and laparoscopic colorectal surgery[9] respectively. Our study show no significant difference with respect to Age, Sex, ASA status and Duration of surgery (Table 1).

In our study VAS score was below 3 in both group in first two hour but patient was more comfortable in Group BD as compare to Group B and no rescue analgesic drug used in first hour postoperatively in both group so, in First hour study is not significant statically ($p = 0.99$) but mean VAS was as low as 1.0 ± 0.00 in Group BD as compare to Group B which has mean VAS score 3.0 ± 0.00 (Table 2).

But in second and fourth hour VAS score was increase in both Group BD and B (mean VAS 1.69 ± 0.47 and 3.12 ± 1.21 respectively in second hour and mean VAS 2.15 ± 0.67 and 3.04 ± 1.14 respectively, shown in Table 2 but during this time period rescue drug used only in Group B and significantly analgesia maintain in Group BD ($p < 0.05$), (Table 4).

After fourth hour VAS score was above 3 in both group and rescue analgesia was used in both Group BD and B so, test is not significant statistically after fourth hour postoperative but number of patient required rescue analgesia was significantly low in BD all the time in 24 hour duration, (Table 2 and 4).

Overall low VAS score and patient's comfortability was in Group BD in 24 hour time interval with mean VAS 2.34 ± 0.84 as compare to Group B with mean VAS 3.65 ± 0.47 so, test show significant in overall VAS score in 24 hour with significantly low *p* - value ($p = .0001$), (Table 3).

Limitation

Our study is postoperative VAS which is subjective entity and difficult to quantify.

Conclusion

We conclude that intraperitoneal instillation of 0.25% bupivacaine in adequate volume (2 mg/kg) with adjuvant dexmedetomidine 1 mcg/kg reduce pain and analgesia requirement in postoperatively in elective laparoscopic surgery as compare to 0.25% bupivacaine (2 mg/kg) alone.

References

1. Ng A, Smith G. Editorial 1: Intraperitoneal administation of analgesia: Is this practic of any utility? BJA:British Journal of Anesthesia 2002 October 1;89(4):535–37.
2. Lakshmi Praveena B, Bharathi B. Intraperitoneal ropivacaine with dexmedetomidine or fentanyle for postoperative analgesia following laparoscopic cholecystectectomy: A comparative randomized trial. Anesthesia Essays and Researches 2019 Jan–Mar;13(1):169–73.
3. Rademaker BMP, Kalkman CJ. Intraperitoneal local anaestehetics after laparoscopic cholecystectomy: Effects on postoperative pain, metabolic responses and lung function. British Journal of Anesthesia 1994;72:263–66.
4. Babu R, Jain P. Intraperitoneal instillation: Ropivacaine *vs* bupivacaine for postoperative pain relife in laparoscopic cholecystectomy. Int J Health Sci Res 2013;3:42–47.
5. Beder El Baz MM, TEM Farahat. Intraperitoneal levobupivacaine alone or with dexmedetomidine for postoperative analgesia after laparoscopic cholecystectomy. Anesthesia Essays and Researches, 2018 Apr–Jun;12(2):355–58.
6. Devalkar PS, Sweta Salgaonkar. Intraperitoneal instillation of 0.25% bupivacaine for laparoscopic cholecystectomy: Effect on postoperative pain. IJCMAAS 2016;12(2): 91–95.
7. M El-labban Gouda, N Hokkam Emad. Intraincisional *vs* intraperitonial infiltration of local anesthetic for controlling early postlaparoscopic cholecystectomy pain. Journal of Minimal Access Surgery 2011 Jul–Sep;7. Cochrane Database Syst Rev. 2014 Mar 3;25:CD009060.
8. Gurusamy KS, M Nagendran. Methods of intraperitoneal local anesthetic instillation for laparoscopic cholecystectomy. Cochrane Database of Systematic Reviews 2014 Mar 25;(3):CD009060.
9. Mohamed Fres Khaled. Efficacy and safety of intraperitoneal dexmedetomidine with bupivacaine in laparoscopic colorectal cancer surgery, a randomized trial. Pain Medicine 2015;16:1186–194.
10. Khurana S, Garg Kamakshi. A comparative study on postoperative pain relief in laparoscopic cholecystectomy: Intraperitoneal bupivacaine *versus* combination of bupivacaine and buprenorphine. Anesthesia Essays Res 2016;10:23–28.
11. Malhotra N, Chanana C. To compare the efficacy of two dose of intraperitoneal bupivacaine for pain relief after operative laparoscopy in gynecology. Arch Gynecology Obstet 2007;276: 323–26.
12. RK Meena, K Meena. A comparative study of intraperitoneal ropivacaine and bupivacaine for postoperative analgesia in laparoscopic cholecystectomy: A rendomized contolled trial. Anesth Pain Intensive Care 2016;20:295–300.
13. Pacharla Indira, RR Effects of intraperitonial instillation of local anesthetic agents in laparoscopic cholecystectomy: A clinical comparision between 0.5% lignocaine, 0.2% ropivacaine & 0.125% bupivacaine. Journal of Medical Science and Clinical Research, 2016, Jan;4(1):8919–926.
14. Radhe Sharma, Singh Manjit. Intraperitoeal instilation of bupivacaine and ropivacaine for postoperativeanalgesia in laparoscopic cholecystectomy. Anesthesia Essays and Researches 2018 Apr–Jun;12(2):377–80.
15. Rapolu S, Anil Kumer K. A comparative study on intraperitoneal bupivacaine alone or with dexmedetomidine for postoperative analgesia following laparoscopic cholecystectomy. IAIM 2016;3:33–40.
16. Shivhare P, Dugg P. A prospective randomized trial to study the effect of intraperitoneal instillation of ropivacaine in postoperative pain reduction in laparoscopic cholecystectomy. J Minim Invasive Surg Sci 2014;3:e18009.
17. Shukla Usha, Pravakar T. Intraperitoneal bupivacaine alone or with dexmeditomidine or tramadol for postoperative anlgesia following laparoscopic cholecystectomy: A comparative evaluation. Indian Journal of Anesthesia, 2015 Apr;59(4):234–39.

Original Research Article

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Comparison of the Upper Lip Bite Test (ULBT) with the Ratio of Height to Thyromental Distance (RHTMD) for the Prediction of Difficult Laryngoscopy in Apparently Normal Patients

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Abstract

Background: Various anatomical measurements & noninvasive clinical tests, singly or in various combinations can be performed to predict difficult laryngoscopy & intubation in apparently normal patients. Recently introduced "Upper Lip Bite Test (ULBT)" & "Ratio of Height to Thyromental Distance (RHTMD)" are claimed to have high predictability in comparison to commonly used Mallampatti Grading (MPG). *Materials and Methods:* We conducted a prospective single blinded observational study of 150 adult patients of ASA Grade I & II, assessed them for MPG, ULBT & RHTMD according to standard methods & correlated with the Cormack & Lehane grade. The Data analysis was done using Graphpad Software. *Result:* ULBT & RHTMD had more sensitivity, specificity, positive predictive value & negative predictive value, i.e., 83%, 85%, 69%, 89%, 56%, 78%, 89%, 92% respectively as compared to MPG 28%, 85%, 48%, 73%. P - value for both the tests were < 0.01 in comparison with MPG. *Conclusion:* Amongst the three methods used, RHTMD is best predictive test for difficult laryngoscopy in apparently normal patients, but ULBT can also be used as an acceptable alternative which is less cumbersome than RHTMD.

Keywords: Upper Lip Bite Test (ULBT); Mallampatti Grading (MPG); Ratio of Height to Thyromental Distance (RHTMD).

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Introduction

Airway management can be considered to be the foremost important component, critical to the anesthetic management of a patient. Indeed, almost 85% of all mistakes concerning airway management result in irreversible cerebral damage[1] and upto 30% of all anesthetic deaths can be attributed to the management of difficult airway.[2,3]

Around 1–18% of the general population have a difficult airway which is a significant percentage.[4-9] Hence, many different tests have been developed in order to predict the incidence of a difficult airway and thus reduce the chances of an airway mishap. Several preoperative airway

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assessment test include the Inter-Incisor Gap (IIG), Head and Neck Movement (HNM), modified Mallampati Test (MMT), Sternomastoid Distance (SMD) and Thyromental Distance (TMD). These tests are useful bedside tests but have a low sensitivity and low positive predictive value (33-71%) while false positive results are high.[10–13]

Prediction of a different intubation is important as it can help in preventing airway accidents but which anatomical landmarks and clinical features are the best predictors is still controversial. The recently introduced Upper Lip Bite Test (ULBT) and Ratio of Height to Thyromental Distance (RHTMD) are simple noninvasive bedside tests which have better predictive value of a difficult airway in apparently normal looking patients compared to the commonly used Modified Mallampatti Test (MMT).

We conducted this study to compare sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) for ULBT and RHTMD in comparison to MMT to predict difficult laryngoscopy in apparently normal looking patients.

Aims and Objectives

To compare the efficacy of ULBT and RHTMD with the commonly used MMT in terms of:

(a) Sensitivity

(b) Specificity

(c) Positive Predictive Value (PPV)

(d) Negative Predictive Value (NPV)

Materials and Methods

After obtaining the approval from our institutional ethical committee, this observational, single blinded prospective evaluation was designed on a study group of 150 adult patients, all of whom were above 18 years of age, of either sexes, who belonged to either ASA Grade 1 or 2 category and were undergoing elective procedures under general anesthesia. Patients unable to sit or stand erect, those with obvious facio-maxillary anomalies, ASA 3, 4 and edentulous patients were excluded from the study.

Following routine preanesthetic check up by the attending anesthesiologist, written informed consent was taken from each patient, The airway was assessed preoperatively in the preoperative room on the day of surgery by the same anesthetist in all studied patients to avoid inter observer error. All the patients were assessed using all the 3 tests.

The oropharyngeal view was assessed using a Modified Mallampatti Test (MMT) by asking the patient to open his or her mouth maximally and to protrude the tongue without phonation while being seated. Upper Lip Bite Test (ULBT) was done to assess the range of freedom of the mandibular movement with respect to the architecture of the teeth concurrently. Each patient was asked to bite their upper lip with their lower incisor and were categorized as follows:

Class 1: lower incisor can hide the mucosa of upper lip. (easy laryngoscopy and intubation)

Class 2: lower incisor can partially hide mucosa of upper lip. (difficult laryngoscopy and intubation)

Class 3: lower incisor unable to touch mucosa of upper lip. (difficult laryngoscopy and intubation)

Thyromental distance was measured in the midline from the upper end to thyroid cartilage to the mentum of mandible with the neck fully extended and mouth closed, using a rigid ruler.

Class 1 : > 6.5 cms

Class 2 : 6–6.5 cms

Class 3 : < 6 cms

Patients height (in cms), body weight (kgs) and Body Mass Index (BMI) were also recorded. Ratio of height to thyromental distance was calculated and graded as follows:

RHTMD = Height (in cms)/TMD (in cms)

1. Grade 1 : < 23.5 (easy laryngoscopy and intubation);
2. Grade 2 : > 23.5 (difficult laryngoscopy and intubation).

Standardized anesthetic protocol was followed in all the patients. Patients were kept NBM for 8 hrs. Standard monitoring were applied. Venous access was obtained and premedication was given which included Inj. Glycopyrrolate 0.04 mg/kg, Inj. Ranitidine 1 mg/kg, Inj. Fentanyl 2 μg/kg. All patients were preoxygenated with 100% O_2 *via* facemask. All patients were induced with Inj. Thiopentone 5 mg/kg and Inj. Succinylcholine 1 mg/kg to facilitate endotracheal intubation.

Laryngoscopy was performed after complete relaxation with patient's head in the sniffing position, laryngoscopy was performed with a Macintosh no 3 or 4 laryngoscope blade by anesthesiologist (of atleast 2 year of experience) who was blinded to the results of preoperative airway assessment.

Glottic visualization was assessed using a modified Cormack and Lehane (CL) classification.

Cormack & Lehane Grades 3 & 4 were considered as difficult laryngoscopy and these results were compared with predictions of modified mallampatti test, upper lip bite test and ratio of height to thyromental distance. True Positive (TP), False Positive (FP), True Negative (TN), False Negative (FN) were calculated for individual tests. Sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), likelihood ratio were calculated and results were derived.

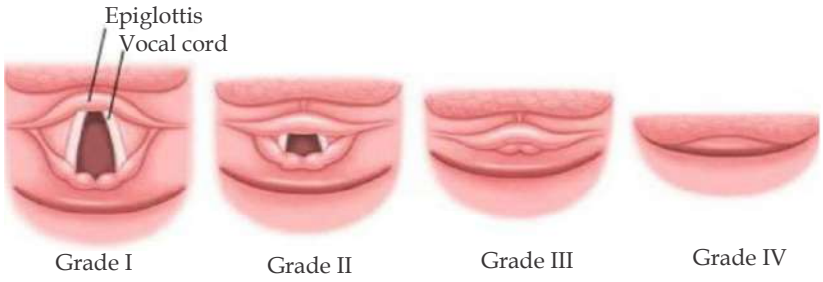

Fig. 1:

Standard formula for different tests for data analysis:

1. Sensitivity = TP/(TP + FN) No. of difficult intubations correctly predicted/No. of difficult intubations;
2. Specificity = TN/(TN + FP) No. of easy intubations correctly predicted/No. of easy intubation;
3. PPV = TP/(TP + FP) No. of difficult intubation correctly predicted/No. of intubation predicted to be difficult;
4. NPV = TN/(TN + FN) No. of easy intubation correctly predicted/No. of intubation predicted to be easy;
5. Likelihood ratio = Sensitivity/1-specificity. It is defined as how much more likely is it that a patient who tests positive has a disease compared with one who tested negative.

Observations and Results

As we can see in Table 1, there was no significant difference in context to age, sex and BMI, ($p \geq 0.001$).

Table 2 shows, the detailed results of the true and false positive and negative results of our study data. As we can see, the true positive and false negative results in our commonly done MMT is quiet different from the results in ULBT and RHTMD methods. According to the results in Table 2, sensitivity and specificity was calculated and is shown in (Table 3).

The data analysis was done using Graph pad

Table 1: Demographic data

Variable	Laryngoscopic Examination		*p* - value
	Easy	Difficult	
	(CL I & II)	(CL III & IV)	
Age (yrs)	44.35 ± 10.04	45.43 ± 9.33	0.6
BMI (kg/cm^2)	20.41 ± 4.10	20.80 ± 3.98	0.4
Sex (M/F)	71/31	31/19	

Table 2: Sensitivity and specificity of test

	MPG Classification	ULBT	RHTMD
True Positive (TP)	13	41	41
True Negative (TN)	90	70	91
False Positive (FP)	15	31	11
False Negative (FN)	32	08	07
Total	150	150	150

Software. ULBT & RHTMD were found to have more sensitivity, specificity, positive predictive value and negative predictive value i.e. 83%, 85%, 69%, 89%, 56%, 78%, 89%, 92% respectively compared to MPG of 28%, 85%, 48%, 73%. *p* - value for both tests were < 0.01 (0.0001, 0.0007) for ULBT & RHTMD respectively in comparison with MPG test.

Table 3: Sensitivity specificity PPV NPV of test

	MPG Classification	ULBT	RHTMD
Sensitivity	28%	83%	85%
Specificity	85%	69%	89%
Positive Predictive Value	48%	56%	78%
Negative Predictive Value	73%	89%	92%

Discussion

The incidence of difficult laryngoscopy and intubation varies from 1.5 to 13%. One of the causes of death and permanent brain damage related to anesthesias is failed intubation.[21] An unexpected difficult intubation is one of the most important contributory factor in cases of anesthesia related mortality and morbidity.[14] Hence, the search for a predictive test which is easy to perform and is very efficient is still continuing.

The RHTMD and ULBT are relatively newer tests with better predictability as compared to MMT. Schmitt et al. showed that the ratio of height to TMD has a better predictive outcome as compared to TMD alone.[15] They showed that RHTMD > 25 cm can be used to predicting difficult laryngoscopy as compared to our study RHMTD ≥ 23.5 cm was determined. Mohammadreza Safavi et al. compared RHTMD, ULBT and MMT in predicting difficult laryngoscopy. They also found that RHTMD has a better sensitivity and specificity as compared to MMT.[20] Our study also showed similar results.

Wilson et al. explained five risk-factors associated with difficult laryngoscopy-weight, jaw movement, head and neck movement, buck teeth and receding mandible.[16] One of our techniques of ULBT, measures the combined effect of jaw movement, protruding teeth and receding jaw - this combining three of the factors of difficult laryngoscopy. So, it gives a better predictive value.

Khan et al.[17] and Hester et al.[18] found out ULBT was superior to MMT in every aspect for predicting a difficult airway. Even in our study, we found the same result. Khan et al. showed sensitivity, specificity, PPV, NPV and accuracy of ULBT were 76.5%, 88.7%, 28.9%. 98.4%, 88.0% respectively. While Hester et al determined sensitivity of 55%, specificity of 97%, PPV of 83%, accuracy of 90% for ULBT.

Merah et al. studied that sensitivity, specificity and PPV of TMD for predicting difficult intubation were 15.4%, 98.1%, 22.2% respectively.[23] Savva reported that TMD had a sensitivity of 64.7% and a specificity of 81.4%.[14] TMD alone has been used to predict difficult airway since many years, but its value as an indicator is questionable as it varies with patients size and body proportions.

Krobbuaban B et al.[19] and Krishna et al.[22] also found the ratio of height to TMD to be a more accurate predictor of difficult laryngoscopy. They assumed RHTMD ≥ 23.5 cm to predicting difficult intubation.

In our study, The incidence of difficult intubation was 8.3% . The validity of MPG to predict a difficult intubation was low. The addition of RHTMD and ULBT to MPG for preoperative assessment improved the accuracy in predicting a difficult airway. Any test used for airway assessment should be easy to perform at the bedside, noninvasive, highly sensitive to predict the maximum number of patients of difficult airway correctly, highly specific to predict easy airway and should be free observer bias as much as possible. It is also highly desirable that the test should have a high PPV (to avoid disastrous consequences of difficult laryngoscopy and intubation) and low NPV (so, that only a few patients are subjected to the protocols for difficult intubation).

Conclusion

Among the 3 methods used in our study, RHMTD was found to be the best in predicting difficult airway in apparently normal looking patients, but ULBT can also be used as an acceptable alternative which is less cumbersome as compared to RHTMD.

References

1. Caplan RA, Posner KL, Ward RJ, et al. Adverse respiratory events in anesthesia: A closed analysis. Anesthesiology 1990;72:828–33.
2. Benumof JL, Scheller Ms. The importance of transtracheal jet ventilation in the management of the difficult airway. Anesthesiology 1989;71:769.
3. Bellhouse CP, Dore C. Criteria for estimating likelihood of difficulty of endotracheal intubation with Macintosh laryngoscope. Anesthesia Intensive Care 1988;16:329.
4. Cormack RS, Lehane J. Difficult tracheal intubation in obstetrics. Anesthesia 1984;39:1105–111.
5. Aro L, Takki S, Aromaa U. Technique for difficult intubation. BR J Anesthesia 1971;43:1081.
6. Mallampatti SR, Gatt SP, Gugino LD, et al. A clinical sign to predict difficult tracheal intubation: A prospective study. Canadian Anesthesia Soc J 1985;32:429–34.
7. Philips OC, DUerksen RL. Endotracheal intubation a new blade for direct laryngoscopy. Anesth Analg 1973;52:691.
8. Finucane BT, Santora AH. Difficult intubation. In: Principles of Airway Manangement. Philadelphia: Davis;1980.
9. Deller A, Schreiber MN, Gramer J, et al. Difficult intubation: Incidence and predictability: A prospective study of 8284 adult patients. Anesthesiology 1990;73:1053.
10. Klock PA, Benumof JL. Definition and incidence of difficult airway. In: Hagberg CA, editor. Benumof's Airway Management: Principle and practice. 2nd edition. Philadelphia: Mosby Elsevier; 2007. pp. 215–33.
11. Merah NA, Wong DT, Ffoulkes-Crabbe DJ, et al. Modified Mallampatti test, thyromental distance and inter-incisor gap are the best predictors of difficult laryngoscopy in West Africans. Can J Anesth 2005;52;291–96.
12. Tse JC, Rimm EB, Hussain A. Predicting difficult endotracheal intubation in surgical patients scheduled for general anesthesia: A prospective blind study. Anesth Anal 1995;81:254–58.
13. Domi R. The best prediction test of difficult intubation. J Anesthesil Clin Pharamacol 2010;26: 193–96.
14. Savva D. Prediction of difficult tracheal intubation. British J of Anesthesia 1994;73:149–53.
15. Schmitt HJ, Kirmse M, Radespiel-Troger M. Ratio of patient's height to thyromental distance improves prediction of difficult laryngoscopy. Anesth Intensive Care 2002;30:763–65.
16. Wilson ME, Spiegelhalter D, Robertson JA, et al. Predicting difficult intubation. Br J Anesth 1988;61:211–16.
17. Khan ZH, Kashfi A, Ebrahimkhani E. A comparison of the upper lip bite test with modified Mallampatti classification in predicting difficulty in endoreacheal intubation a prospective blinded study. Anesth Analg 2003;96:595–59.
18. Hester CE, Dietrich SA, White SW. A comparison of preoperative airway assessment techniques: The modified Mallampatti and the upper lip bite test. AANA J 2007;75:177–82.
19. Krobbuaban B, Diregpoke S, Kumkeaw S. An assessment of the ratio of height to thyromental distance compared to thyromental distance as a predictive test for prediction of difficult tracheal intubation in Thai patients. J Med Assoc Thai 2006;89:638–42.
20. Mohammadreza Safavi, Azim Honarmand, Narges Zare. A comparison of the ratio of patient's height to thyromental distance, modified Mallampatti and the upper lip bite test in predicting difficult laryngoscopy. Soudi Journal of Ansthesia 2011 Jul–Sept;5(3):258–63.
21. Gupta S, Pareek S, Dulara SC. Comparisn of two methods for predicting difficult intubation in obstretic patients. Middle East J Anesthesiol 2003;17:275–85.
22. Krishna HM, Agarwal M, Dali JS, et al. Prediction of difficult laryngoscopy in Indian population: Role of ration of patient's height to thyromental distance. J Anesthesi Clin Pharmacol 2005;21:257–60.
23. Merah NA, Wong DT, Ffoulkes-crabbe DJ, et al. Modified Mallampati test, thyromental distance and inter-incisor gap are the best predictors of difficult laryngoscopy in West Africans. Can J Anesth 2005;52:291–96.

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Single-dose Intravenous Dexmedetomidine as an Adjuvant for Prolongation of Spinal Anesthesia

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Abstract

Context: Dexmetedomidine is α_2 agonist used as adjuvant to spinal anesthesia for prolongation of sensory, motor block, postoperative analgesia. *Aims:* To study the effect of single-dose IV dexmetedomidine on hemodynamic profile, sensory-motor block prolongation, sedation. Methods and Material: 100 adult patients of ASA 1 and 2 posted for elective infraumbilical surgery were included. They were randomly divided into 2 groups. Group D received intravenous dexmtedomidine 0.5 μg/kg over 10 min slowly. Group M - 0.5 mg/kg over 10 mins. Both drugs were administered 15 min after spinal anaesthesia with 15 mg 0.5% intrathecal bupivacaine heavy. Vital data, duration of sensory and motor block, sensory regression, Ramsay Sedation score and side effects were evaluated. *Results:* Duration of sensory block in Group D was 308 ± 20 min prolonged than Group M 200 ± 15 min. Duration of two segment regression time in Group D – 140 ± 8 min more than Group M 120 ± 6 min. Ramsay sedation score was slightly more for Group D without any respiratory depression. Patients of both groups remained hemodynamically stable through out with minimal side-effects. *Conclusions:* Intravenous dexmetedomidine significantly augments the sensory and motor block of intrathecal bupivacaine providing excellent sedation.

Keywords: Dexmetedomidine; Midazolam; Motor and sensory block; Sensory regression, Sedation.

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Introduction

Spinal anesthesia is unique form of regional anesthesia where many drugs as adjuvant agents can be added to suppliment and prolong sensory and motor blockade in large no of patients with less amount of drugs undergoing lower abdominal surgeries, sedation plays an important role as it provides anxiolysis and amnesia.[1–4]

In modern era anesthetists are fortunate to have agents that can be used intrathecally or intraveously to augment the duration and efficacy of block and we call them adjuvants. Epinephrine, magnesium sulphate, fentanyl, midazolam, clonidine were used until now and now-a-days dexmetedomidine is trending.

Dexmetedomidine is a selective alpha-2 agonist, newer congener of clonidine and is 8 times more selective. It was first introduced for short-time intensive care unit sedation in 1999. Since, then it is rapidly emerging drug now-a-days as an adjuvant to regional anesthesia, general anesthesia,

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MAC, premedication, postoperative sedation and analgesia. it induces cooperative sleep, does not disturb the sleep architecture or respiratory drive, thus proves as an excellent drug for sedation in intubated/nonintubated patients in critical care and icu short procedures.[5] Alpha-2 agonists are being increasingly used as adjuvants as they provide sedation, analgesia, hypnosis and sympatholysis without respiratory depression. Midazolam is among the currently available benzodiazapine with fast onset, short recovery time, hence wildely used sedative in spinal anesthesia and produces good sedation to counter act anxiety of patients.[6]

We conducted this randomized, prospective, double blinded clinical study to study the effect of single dose dexmetedomidine by administering it intravenously in association with spinal anesthesia and compared with midazolam

Materials and Methods

We carried out prospective, double blind randomized study after approval of ethical committee. Written and informed consent was obtained from all the participating patients. We studied 100 adult patients of physical status American Society of Anesthesiologists ASA 1 and 2, of either sex aging from 25 to 60 years posted for elective infraumblical surgeries and randomly allocated into two groups. Patients excluded were, those refusing of giving consent, bleeding diathesis, infection at the puncture site, belonging to ASA 3 and 4 Patients on α_2 adrenergic receptors antagonists, calcium channel blockers, or angiotensin-converting enzyme inhibitors, Patients having cardiac rhythm abnormalities, Any drug allergy, pregnancy, lactating mother, obesity, Any major illness involving RS, CVS or CNS. All contraindication to spinal analgesia including, spinal deformity, patient on anticoagulants, preexisting neurological deficits in lower extremities were excluded. Preanesthesia examination was done preoperatively with a detailed history, general and systemic examinations, airway and back and spine were also examined. All routine laboratory investigations were done. Patients received 0.5 mg alprazolam tablet night prior to surgery and were kept nil by mouth on day of surgery. In the preoperative recovery room, peripheral IV line was secured with 18 g cannula and they were preloaded with 10 ml/kg of ringer lactate solution. Patients were then randomly allocated into either of two groups:

Group D: Intrathecal 0.5% bupivacaine heavy 3 ml, followed by infusion of intravenous dexmedetomidine 0.5 mcg/kg over 10 min.

Group M: Intrathecal 0.5% bupivacaine heavy 3 ml followed by infusion of midazolam 0.05 mg/kg over 10 mins.

Above study drugs were administered,15 min after spinal anesthesia with bupivacaine 0.5% 15 mg (n = 50 per group).

Preparation of Infusion

One ml of injection dexmedetomidine, will be diluted in 19 ml of normal saline; hence, the concentration of the drug in the solution is 5 μg/ml. Similarly for Group M: The infusion will be prepared by diluting 3 ml midazolam in 17 ml normal saline. Total infusion volume for each group is 20 ml.

These infusions were prepared by an independent senior resident who was not involved in the subsequent phases of the study. Thus, both the resident conducting the case as well as the patient were unaware of the assigned group in all the cases.

Standard monitoring was done, which includes noninvasive Blood Pressure (BP), electrocardiography, Heart Rate (HR), and Oxygen (O_2) saturation. All patients were supplemented with 4 L/min of O_2 by simple face (NRBM) mask. Subarachnoid block with 3 ml of 0.5% bupivacaine was performed in the L3–L4 interspace using a 25-gauge Quincke's spinal needle with the patient in sitting position.

After performing the spinal block vital signs were recorded at 0, 5 , 10 ,15 min initially, and every 30 min thereafter, 15 minutes after the subarachnoid block, dexmedetomidine group (Group D) received dexmedetomidine infusion 0.5 μg/kg over 10 min, and group (Group M) received midazolam 0.05 mg/kg (not more than 2.5 mg) infusion over 10 min.

Observations

Following variables were assessed:

Onset, height, duration, and regression of sensory block (two segment regression) by the loss of pinprick sensations. Before giving the study drug or placebo, the sensory level was recorded after giving the study drug Sensory block assessed every 2 min for the first 10 min and thereafter, every 5 min during surgery. In the Postanesthesia Care Unit (PACU), recorded every 15 min for the next 4 h or regression to S1 level, after which the patient

was shifted to the ward. The time of giving the intrathecal injection was considered as zero. Motor block was assessed by modified bromage scale:

0 No paralysis, able to flex hips/knees/ankles;

1 Able to move knees, unable to raise extended legs;

2 Able to flex knees, unable to flex knees;

3 Unable to move any part of the lower limb;

The level of sedation was evaluated using six point Ramsay Sedation Scale (RSS):

1. Patient fully awake and oriented;
2. Patient cooperative, drowsy and tranquil;
3. Patient asleep but responds to oral commands;
4. Asleep, but responds to light glabellar tap;
5. Asleep, sluggish response to light glabellar tap;
6. Asleep, no response.

Postoperative pain was assessed using Visual Analog Scale (VAS), every 15 min until the first analgesic given, and 4 hourly for the next 24 h, rescue analgesia will be given in the form of injection diclofenac sodium 75 mg Intramuscular (IM) when VAS score was more than 3.

For the purpose of this study, hypotension was considered Systolic BP of < 90 mm Hg and treated by foot end elevation, and fluid bolus of 300 to 500 ml. If such hypotension did not respond to this fluid administration, then injection mephentermine 5 mg IV was administered. If it did not respond to two repeated doses of mephentermine, then dopamine infusion was started to maintain the BP. Bradycardia for these cases was defined as HR < 50 beats/min (20% decrease from the baseline), and if persist treated with 0.6 mg of intravenous atropine.

Results

There was no statistically significant difference in all subjects in Group D and Group C with respect to demographic profile that included patients age, sex, height, weight, ASA physical status and duration of surgery, (Table 1).

Table 1: Demographic Data

	Group D	Group M	*p* - Value
Age (years)	43 ± 9.4	42 ± 8.5	0.578
Height (cm)	145 ± 5	147 ± 5.2	0.0528
Weight (kg)	55 ± 5.4	53 ± 6.1	0.085
Duration of Surgery (min)	130 ± 15.4	133 ± 22	0.435
ASA Grade (1:2)	35:15	40:10	NS

The two segment regression time in Group D was 148 ± 8 min and Group M was 120 ± 6 min. with *p* - value being (< 0.0001) statistically highly significant, (Table 2). The duration of motor block was 230 ± 15 min in Group D and 160 ± 10 min in Group M with *p* - value being < 0.0001 statistically highly significant, (Table 2). Total duration of sensory block for Group D was prolonged (308 ± 20 min) than Group M (200 ± 15 min) with *p* - value < 0.0001 and difference is statistically highly significant, (Table 2).

Table 2: Spinal anesthesia parameters

	Group D	Group M	*p* - value
Duration of 2 Segment Regression (min)	148 ± 8	120 ± 6	< 0.0001
Duration of Motor block (min)	230 ± 15	160 ± 10	< 0.0001
Duration of Sensory block (Request for 1^{ST} rescue analgesia) (min)	308 ± 20	200 ± 15	< 0.0001

Sedation score was measured using modified Ramsay Sedation Score and was quite similar intraoperatively through out in both groups with dexmetedomidine having slightly higher scores and good sedation without any respiratory depression than Group M, (Table 3).

Table 3: Modified Ramsay sedation score (The time of giving the drug is taken as 0)

Time	Group D	Group M
0	2	2
15	3.64 ± 0.6	3.6 ± 0.3
30	4.3 ± 0.7	3.9 ± 0.7
45	4.6 ± 0.5	4.2 ± 0.5
60	4.6 ± 0.4	4.2 ± 0.4
75	4.56 ± 0.5	4.4 ± 0.2
90	4.4 ± 0.5	4.3 ± 0.2
120	4.2 ± 0.6	4.0 ± 0.4
180	3.2 ± 0.5	3.2 ± 0.2

Six (12%) patients of Group M had postoperative shivering which was managed, no patient in Group D had shivering (p - value 0.0112, not significant). While nausea occurred in 9 (18%) patients in Group D and 2 (4%) patients in Group M, p - value 0.1398. However, only 1 (2%) patient in Group D had vomitting (p - value 0.3197), (Table 4). Patients in both Groups D and M remained hemodynamically stable through out the surgery, (Figs. 1 and 2).

Table 4: Side-effects

	Group D	Group M	p - value
Shivering	0	6 (12%)	0.0112
Nausea	9 (18%)	4 (8%)	0.1398
Vomitting	1 (2%)	0	0.3197

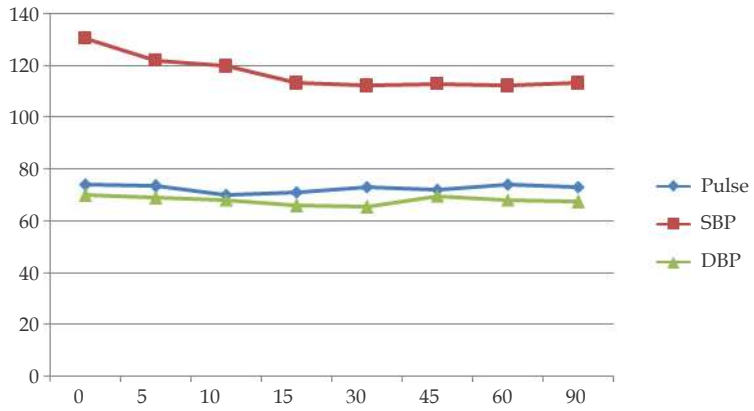

Fig. 1: Group D vitals (pulse, systolic blood pressure, diastolic blood pressure).

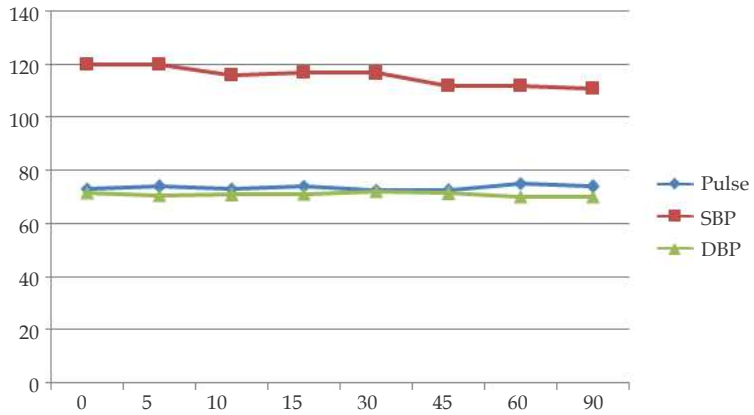

Fig. 2: Group M vitals (pulse, systolic blood pressure, diastolic blood pressure).

Discussion

Subarachnoid block causes sympatholysis whish is hallmark feature of central neuraxial blockade. the hemodynamic stability was attained after 15 mins of giving intrathecal bupivacaine, after which we administered intravenous dexmetedomidine and midazolam slowly over 10 mins.

Jyotsna Kubre et al. in her study entitled "Single dose IV dexmetedomidine prolongs spinal anesthesia with hyperbaric bupivacaine" administered intravenous dexmetedomidine 45 mins after the intrathecal bupivacaine.[7]

In our study, patients of both groups Group D and Group M remained vitally stable through out the surgery. The decrease in heart rate was more evident in Group D as compared to Group M and was not statistically significant. This is due to the postsynaptic activation of α_2 adenoreceptors in CNS, that results in decrease in sympathetic activity and circulatory levels of catecholamines.[8,9] Similar observation was made by Jyotsna et al. and Group D had decrease in heart rate in her study.[7]

Aantaa R, Jaakola ML in their study "A comparison of dexmetedomidine an alpha-2 adenoreceptor agonist and midazolam as a premedication intramuscularly for minor gynecological surgeries" and observed that bradycardia was caused by dexmetedmodine but it was longlasting when given as premedication.[10]

In other studies, continuous infusion was administered throughout the procedure, hypotension and bradycardia remained intraopertively as well as postoperatively which lead to increase consumption of other drugs to treat these effects.[11–13]

Henceforth, when peak hemodynamic effects of intrathecal subarachnoid block were settled, in our study, single-dose intravenous dexmetedomidine was given slowly to overcome these complications. In both groups of our study there was decrease in BP which was clinically and stastically not significant, normally dexmetedomidine does not have any direct effect on heart rate. Although it causes a dose dependent increase in coronary vascular resistance and O_2 extraction but the demand/supply ratio is unaltered. It shows biphasic response occurs after administration of bolus 1 microgram/kg causing transient rise in BP and reflex decrease in heart rate. This initial response is due to effect of B adenoreceptor stimulation of vascular smooth muscle[14] in our study as we administered the drug slowly over 10 mins there was stabilization of Heart Rate and BP 10–15% below the baseline value.

This result was very-well supported by Mamta Mahobia et al. as they had similar timing and conclusion.[7] However, Tekin M, in his research "effect of dexmetedomidine IV on duration of spinal anesthesia with prilocine "found no significant diffrence in MAP in dexmetedomidine group.[11]

In our research, the duration of 2 segment regression in Group D pt. was 148 ± 8 min and Group M was 120 ± 6 min, p - value < 0.0001 being statistically highly significant. The total duration of sensory block was prolonged in Group D 308 ± 20 min than Group M 200 ± 18 min. The total duration of motor block in Group D was 230 ± 15 mins and group M 160 ± 10 mins. These prolonged effects in patients of Group D can be explained by the fact that the site of action of dexmetedomidine is locus cerulus and is mediated by hyperpolarization of nonadrenergic neurons and inhibits noradrenaline release and thus inhibits activity of descending medullospinal noradrenergic pathways.[15]

Jyotsna et al., study also concluded that the duration of sensory blockade was prolonged in dexmetedomidine group 341.7 ± 20.8 min as compared to control group 329 ± 22.1. The 2 dermatomal regression time was also prolonged 115.5 ± 8.8 as compared to control group 95.8 ± 14 min. The motor block was also augmented in Group D 278 ± 11 min as compared to control group - 250 ± 14.8 min.[7]

Bajwa S et al. who reviewed "Dexmetedomidine: An adjuvant making large roads into clinical practice," had similar observations that dexmetedomidine as an adjuvant in neuraxial anesthesia prolongs the sensory and motor blockade with more intense and good postoperative analgesia.[15,16]

Honge et al.[13] who admisintered intravenous dexmetedomidine as an adjuvant to regional anesthesia with hyperbaric bupivacaine observed that complete resolution of motor and sensory blockade was significantly prolonged in Dexmetdomidine group and the findings of our present study corroborate the result.

We assessed sedation by modified ramsay sedation score which was quite similar intraoperatively through out in both groups, Group D has slightly higher scores and good sedation without any respiratory depression than Group M. Evidences suggests that of the 3 major receptor subtypes α_2A, α_2B and α_2C in CNS, α_2A and α_2C predominate in CNS and are responsible for

sedative, analgesic and sympatholytic components of agonist action.[17]

Dexmetedomidine induced sedation is called "Cooperative sedation" as it does not cause much respiratory depression with wide safety margins, sleep induced with it has rapid eye movement and is easily arousable.[18] However, the sedation induced by drugs acting on GABA system such as midazolam or propofol that produce clouding of Conciousness.[7] Rekha Kumaru, Ani Kumar concluded that Ramsay Sedation Score was significantly higher in dexmetedomidine group as compared to control group. Mustafa et al. l noted that the median sedation score was 4 in dexmetedomidine gorup in their study.[13]

In our study, none of the patients of Group D had shivering as compared to Group M patients where 6 (12%) had postoperative shivering (*p* - value 0.0112). The incidense of nausea was in 9 (18%) patients in Group D and 4 (8%) patients in Group M and vomitting was observed in only 1 patient in Group D.

Venn RM et al. in their study "Pharmacokinetics of dexmetedomidine infusions for sedation of postoperative patients requiring intensive care" had similar observations.[20] Elvan EG et al. carried out a study to observe the incidence of postoperative shivering in patients undergoing elective abdominal hysterectomy. His study results proved that intraoperative infusion of dexmtedomidine prevented postoperative shivering.[21]

A study entitled "A balanced anesthesia with dexmtedomidine decreases postoperative nausea and vomitting after laprosocopic surgery" was done by Massad IM et el. He concluded that on combining dexmetedomidine to other anesthetic agents for patients posted for general anesthesia, there was significant decrease in insidence of postoperative nausea and vomiting.[22] All these findings are similar to our study and thus strengthen our results.

Conclusion

We concluded that dexmetedomidine is superior to midazolam as it provides arousable sedation, analgesia, hypnosis and sympatholysis without causing respiratory depression. Single-dose IV dexmetedomidine 0.5 microgram/kg given slowly prolongs the durations of sensory and motor blockade.

Midazolam is a nearly ideal supplement providing sedation with effective anxiolysis, fast onset, short recovery time, predictable depth of anesthesia, with minimal side-effects and no evidence of accumulation.

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Conflict of Interest: Nil.

References

1. Kamibayashi T, Maze M. Clinical uses of alpha2 -adrenergic agonists. Anesthesiology 2000;93:1345–359.
2. Saxena H, Singh S, Ghildiyal S. Low-dose intrathecal clonidine with bupivicaine improves onset and duration of block with hemodynamic stability. Internet J Anesthesiol 2009;23:1.
3. Thakur A, Bhardwaj M, Kaur K, et al. Intrathecal clonidine as an adjuvant to hyperbaric bupivacaine in patients undergoing inguinal herniorrhaphy: A randomized double-blinded study. J Anesthesiol Clin Pharmacol 2013;29:66–70.
4. Sethi BS, Samuel M, Sreevastava D. Efficacy of analgesic effects of low-dose intrathecal clonidine as adjuvant to bupivacaine. Indian J Anesth. 2007;51:415–19.
5. Eren G, Cukurova Z, Demir G, et al. Comparison of dexmedetomidine and three different doses of midazolam in preoperative sedation. J Anesthesiol Clin Pharmacol 2011;27:367–72.
6. Midazolam in Spinal Anesthesia—Intrathecal or Intravenous? By Beyazit Zencirci Submitted: September 13th 2013 (Reviewed: June 12th 2014 Published: September 3rd 2014); DOI: 10.5772/58750.
7. Kubre Jyotsna, Sethi Ashish. Single-dose intravenous dexmedetomidine prolongs spinal anesthesia with hyperbaric bupivacaine, Anesth Essays Res 2016 May–Aug;10(2):273–77. doi: 10.4103/0259-1162.174465 PMCID: PMC4864683PMID: 27212760
8. Yazbek-Karam VG, Aouad MM. Perioperative uses of dexmedetomidine. Middle East J Anaesthesiol. 2006;18:1043–58. [PubMed] [Google Scholar]
9. Arain SR, Ebert TJ. The efficacy, side effects, and recovery characteristics of dexmedetomidine versus propofol when used for intraoperative sedation. AnesthAnalg. 2002;95:461–6. [PubMed] [Google Scholar]
10. Aantaa R, Jaakola ML, Kallio A, et al. A comparison of dexmedetomidine, and alpha 2-adrenoceptor agonist, and midazolam as IM premedication for minor gynecological surgery. Br J Anesth 1991;67:402–09.
11. Tekin M, Kati I, Tomak Y, et al. Effect of dexmedetomidine IV on the duration of spinal anesthesia with prilocaine: A double-blind, prospective study in adult surgical patients. Curr Ther Res 2007;68:313–24.

12. Hong JY, Kim WO, Yoon Y, et al. Effects of intravenous dexmedetomidine on low-dose bupivacaine spinal anesthesia in elderly patients. Acta Anesthesiol Scand 2012;56:382–87.
13. Al-Mustafa MM, Badran IZ, Abu-Ali HM, et al. Intravenous dexmedetomidine prolongs bupivacaine spinal analgesia. Middle East J Anesthesiol 2009;20:225–31.
14. Patel CR, Engineer SR, Shah BJ, et al. Effect of intravenous infusion of dexmedetomidine on perioperative hemodynamic changes and postoperative recovery: A study with entropy analysis. Indian J Anesth 2012;56:542–46.
15. Bajwa S, Kulshrestha A. Dexmedetomidine: An adjuvant making large inroads into clinical practice. Ann Med Health Sci Res 2013;3:475–83.
16. Mannion S. Sedation, spinal anesthesia and older patients. J Postgrad Med 2007;53:155.
17. Nelson LE, Lu J, Guo T, et al. The alpha 2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. Anesthesiology 2003 Feb;98(2):428–36.
18. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care 2000;4:302–308.
19. Kumari Rekha, Kumar Anil. Intravenous dexmedetomidine as an adjunct to subarachnoid block: A simple effective method of better perioperative efficacy. J Anesthesiol Clin Pharmacol 2017 Apr–Jun;33(2):203–208. doi: 10.4103/joacp.JOACP_367_15 PMCID: PMC5520593.PMID: 28781446
20. Venn RM, Karol MD, Grounds RM. Pharmacokinetics of dexmedetomidine infusions for sedation of postoperative patients requiring intensive caret. Br J Anesth 2002;88:669–75.
21. Elvan EG, Oç B, Uzun S, et al. Dexmedetomidine and postoperative shivering in patients undergoing elective abdominal hysterectomy. Eur J Anesthesiol 2008;25:357–64.
22. Massad IM, Mohsen WA, Basha AS, et al. A balanced anesthesia with dexmedetomidine decreases postoperative nausea and vomiting after laparoscopic surgery. Saudi Med J 2009;30:153741.

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Comparison of Ramosetron and Dexamethasone for Prophylaxis of Postoperative Nausea and Vomiting in Patients Undergoing Middle Ear Surgeries

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Abstract

Background: Nausea and vomiting are common complications of anesthesia and surgery. Patients undergoing middle ear surgeries are exposed to a higher-risk of Postoperative Nausea Vomiting (PONV). These complications may alter the results of reconstruction and anatomical alignments. Numerous antiemetics have been studied to prevent and treat PONV in patients undergoing middle ear surgeries. The aim of this study is to compare the effect of ramosetron and dexamethasone for prophylaxis of postoperative nausea and vomiting in patients undergoing middle ear surgeries. *Methods:* In a randomized controlled clinical trial, 60 patients were divided into two groups, one receiving ramosetron, one receiving dexamethazone, all patients were subjected to middle ear surgeries. The patients in the Group R received ramosetron (0.3 mg IV) and the patients in Group D received dexamethasone (8 mg IV), Using Bellivelle's scoring system, the incidence of PONV and its severity during the 24-hour period after surgery were measured and compared. *Result:* The incidence rates of PONV in dexamethasone group is 89.9%, and with ramosetron group is 29.9%, which showed statistically significance (p - value < 0.0001). The incidence rate of postoperative nausea and vomiting in dexamethasone group is significantly higher than that of ramosetron group. *Conclusion:* Ramosetron 0.3 mg IV given before induction of anesthesia is an effective means of reducing PONV in middle ear surgeries. Compaed to dexamethasone 8 mg IV ramosetron 0.3 mg IV significantly reduces PONV in the immediate postoperative period. Ramosetron is suitable alternative to dexamethasone in controlling PONV

Keywords: Postoperative nausea and vomiting; Dexamethasone; Ramosetron; Middle ear surgeries.

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Introduction

Patients complain of nausea and vomiting after surgical operations, starting from recovery room to the early hours of transferring the patient to the ward, without hypotension and other complications is defined as Postoperative Nausea and Vomiting (PONV).[1] Tympanoplasty and mastoidectomy are two of the most common procedures performed in the middle ear and accessory structures.[2] In middle ear surgeries due to stimulation of the labarynth, incidence and severity of postoperative nausea and vomiting is very high.[2] Following general anesthesia with

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inhaled anesthetics, the rate of postoperative nausea and vomiting has been reported to vary (20% to 30%) and, is the second most common complaint reported following various surgical operations and in different methods of anesthesia.[3]

Ramosetron is a serotonin 5-HT_3 receptor antagonist used mainly as an antiemetic following chemotherapy.

Its effects are thought to be on both peripheral and central nerves. Ramosetron reduces the activity of the vagus nerve, which deactivates the vomiting center in the medulla oblongata, and blocks serotonin receptors in the chemoreceptor trigger zone. However, it is expensive and has some dangerous side-effects such as headaches and high blood pressure that can lead to serious complications, especially in susceptible and hypertensive patients.[1] Dexamethasone, which is used frequently in the patients undergoing ear, throat and nose surgical operations, is cheap and has no serious side-effects. If dexamethasone is given, orally or parenterally, over a period of more than a few-days, side-effects common to systemic glucocorticoids may occur. PONV has multiple causes and is influenced by a number of factors including anesthetics, surgery and individual risk-factors like smoking, anxiety and age. After the age of 50 years, the incidence of PONV decreases to about 13% in every 10 years.[5]

Ramosetron is a selective serotonin 5-hydroxytryptamine Type 3 (5-HT_3) receptor antagonist, has better inhibitory activities than other available antagonists such as ondansetron, granisetron, tropisetron.[6] Because of higher binding affinity and a slower rate of dissociation from the target receptor ramosetron is more potent and has longer-lasting antiemetic effects than older agents.[7] This class of selective 5-HT_3 receptor antagonists prevents serotonin binding to 5-HT_3 receptors at the ends of the vagal afferent branches, which directly signals the vomiting center in the medulla oblongata and in the chemoreceptor trigger zone of the brain.[7,8]

Dexamethasone has been useful in preventing and treating nausea in the patients undergoing chemotherapy, it is widely used in preventing PONV. It has been shown that given intravenously one dose (8–10 mg) of this drug is effective in preventing PONV.[9] However, postoperative nausea and vomiting remain a significant problem. This problem prompted us to compare the efficacy of ramosetron and dexamethasone in the prevention of postmiddle ear surgery nausea and vomiting.

Materials and Methods

The study is a randomized controlled clinical trial performed at Kempegowda Institute of Medical Science and Hospital, Bangalore, Karnataka, over a period of 8 months. Sixty patients with physical conditions of ASA (American Society of Anesthesiologists) I or II undergoing middle ear surgeries were divided into two groups of 30 patients each to receive ramosetron, dexamethasone, preoperatively. Simple randomized sampling procedure was carried out. Patients with digestive problems, a history of treatment with antiemetics and nausea in the preceding 24 hours, perioperative steroids as anti edema therapy or obesity (BMI > 40) were excluded from the study. A written consent was obtained from all the patients. The study was approved by the Ethics Committee. Before the induction of anesthesia, 0.3 mg of ramosetron or 8 mg of dexamethasone administered intravenously to respective groups.

The volume of the administered drug was 2 ml in the two groups. In each group, premedication was given using Midazolam at 0.15 mg/kg, Glycopyrrolate (.01 mg/kg) and Fentanyl at 1–2 μg/kg. Induction was carried out with Propofol (1–2.5 mg/kg) and Atracurium (0.5 mg/kg). Anesthesia maintained with volatile anesthetic agent with isoflurane 1–1.5% with nitrous oxide 60% in oxygen.

All patient received intravenous paracetamol 1 g infusion during surgery. End tidal CO_2 was maintained between 30 and 35 mm Hg. The patient heart rate, systolic and diastolic blood pressure were noted every 15 min.

At the end of the surgery neuromuscular block was reversed with neostigmine and glycopyrrolate. After the clinical assessment of adequacy of reversal of neuromuscular block, trachea was extubated. After the end of surgery all patient received 75 mg diclofenac infusion for postoperative analgesia.

Patients were randomly allocated to receive ramosetron 0.3 mg (given at the beginning of surgery)) (Group R, n = 30), dexamethasone 8 mg (given at the beginning of surgery) (Group D, n = 30). Using a questionnaire, all instances of nausea and vomiting were recorded carefully every few hours for 24 hours until the patient was discharged to the ward. The intensity of vomiting was evaluated through the Bellville scoring scale (lack of nausea and vomiting = 0, nausea = 1, nausea with belching = 2, and vomiting = 3).

Data were collected on the type of the surgical operation, age, ASA category, duration of anesthesia, duration of the operation, blood pressure before and after the operation, saturation of peripheral oxygen (SpO_2), heart rate during the surgery. Presence and the intensity of nausea or vomiting at 0–2, 2–8, 16–24 hours after the operation were recorded.

Time of usage of rescue antiemetic following surgery were analyzed.

Results

There is no differences in patient demographic amoung treatment group. There is no statistically significant differences between the two groups in terms of systolic and diastolic blood pressure, SpO_2. The average systolic or diastolic blood pressure measured before induction in two group were not significantly different.

Table 1: Baseline parameters

Variables	Group D	Group R	Total	*p* - value
Age in yrs	39.57 ± 14.80	37.87 ± 14.62	38.72 ± 14.61	0.656
ASA				
1	20 (66.7%)	20 (66.7%)	40 (66.7%)	1.000
2	10 (33.3%)	10 (33.3%)	20 (33.3%)	
Gender				
Female	13 (43.3%)	12 (40%)	25 (41.7%)	0.793
Male	17 (56.7%)	18 (60%)	35 (58.3%)	

Student *t*-test/Chi-square test.

Table 2: Blood pressure, saturation of peripheral oxygen, duration of operation, duration of recovery

Variables	Group D	Group R	Total	*p* - value
HR (Per Min)	72.31 ± 2.47	71.83 ± 2.21	72.02 ± 2.34	0.432
SBP (mm Hg)	116.41 ± 20.52	113.73 ± 20.35	115.08 ± 20.31	0.618
DBP (mm Hg)	70.82 ± 4.99	71.40 ± 3.88	71.11 ± 4.44	0.616
SpO_2%	99.99 ± 0.2	99.99 ± 0.02	99.99 ± 0.02	1.000

Student *t*–test.

There was no significant difference among PONV in the first two hours of postoperative period. However, in 2 to 8 hours after surgery the PONV in Group D is significantly higher than that in the Group R.

Table 3: Nausea, vomiting, nausea and belching

	Group D (*n* = 30)	Group R (*n* = 30)	Total (*n* = 60)	*p* - value
Belleville's score 0 to 2 hours postop				
Lack of nausea and vomiting (0)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea (1)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea and belching (2)	0 (0%)	0 (0%)	0 (0%)	1.000
Vomiting (3)	4 (13.3%)	0 (0%)	4 (6.7%)	0.112
Belleville's score 2 to 8 hours				
Lack of nausea and vomiting (0)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea (1)	1 (3.3%)	0 (0%)	1 (1.7%)	1.000
Nausea and belching (2)	9 (30%)	0 (0%)	9 (15%)	0.002**
Vomiting (3)	9 (30%)	0 (0%)	9 (15%)	0.002**
Belleville's score 8 to 16 hours				
Lack of nausea and vomiting (0)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea (1)	0 (0%)	1 (3.3%)	1 (1.7%)	1.000

	Group D (n = 30)	Group R (n = 30)	Total (n = 60)	p - value
Nausea and belching (2)	4 (13.3%)	4 (13.3%)	8 (26.6%)	1.000
Vomiting (3)	0 (0%)	0 (0%)	0 (0%)	1.000
Belleville's score 16 to 24 hours				
Lack of nausea and vomiting (0)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea (1)	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea and belching (2)	0 (0%)	4 (13.3%)	4 (6.65%)	1.000
Vomiting (3)	0 (0%)	0 (0%)	0 (0%)	1.000

Chi-square/Fisher Exact Test.

Table 4: Rescue antiemetic distribution in two groups of patients studied

Time for rescue antiemetic (Hours)	Group D	Group R	Total	p - value
NR (not received)	3 (10.0%)	21 (70%)	24 (40%)	0.0000021*
0–2	4 (13.3%)	(0)	4 (6.67%)	0.03842747*
2–8	19 (63.3%)	(0)	19 (31.6%)	< 0.001*
8–16	4 (13.3%)	5 (16.6%)	9 (15%)	0.71739745
16–24	0 (0.0%)	4 (13.3%)	4 (6.67%)	0.03842747*
Total	30 (100%)	30 (100%)	60 (100%)	

- Rescue antiemetic was required significantly in first 2 hours and 2 to 8 hours in Group D with a p - value of < 0.001 where as rescue antiemetic was not required during this time in Group R after surgery.
- 2 to 8 hours postoperatively was the time when maximum patients required antiemetic in Group D compared to Group R.
- The p - value < 0.0001 proves that lesser number of Group R patients required rescue antiemetic in the study period.

Table 5: Comparison of total number of patients requiring rescue antiemetic in both groups

Duration in hours for rescue antiemetic	Group D (n = 30)	Group R (n = 30)	p - value
0 – 24 hours	27	9	0.00001*
Not received	3	21	

The Chi-square test: The p - value is < .00001. The result is significant at p < .05

Discussion

The efficiency of administration of ramosetron (0.3 mg IV) and dexamethasone (8 mg IV) before anesthetic induction on postoperative nausea and vomiting was evaluated in middle ear surgical operations. The postoperative nausea and vomiting incidence rate after middle ear surgical operations has been reported to be significant.[10] The incidence of nausea and vomiting after middle ear surgery is high might be attributed to the complex innervation of this area by the cranial nerves V, VII, VIII and X, and cervical nerves II and III.[11,12] The proximity of cranial surgical field to the semilunar ducts and vestibular system, and heat and vibration transmission at excision of the surgical field through stimulation of the ampulla can lead to postoperative nausea, dizziness, and vomiting. Therefore, postoperative nausea and vomiting are more common in these patients.[9]

Ramosetron is a newer 5-HT_3 receptor antagonist which is more potent and has a longer duration of antiemetic action than the older agents. This has been attributed to the higher binding affinity and slower rate of dissociation from the target receptor of ramosetron compared to ondansetron. The elimination half-life of ramosetron is also longer than that of ondansetron (9 h *vs* 3.5 h). Many of the recent studies have shown that ramosetron is more effective than ondansetron in preventing PONV for the patients undergoing various other surgeries.[13–15] The benefits of administering dexamethasone as

a more costeffective antiemetic and efficacious analgesic drug[35] should be weighed against the potential side-effects.[16]

In the this study, the incidence rates of PONV in dexamethasone group is 89.9%, and with ramosetron group is 29.9%, which showed statistically significance (p value < 0.0001). The incidence rate of postoperative nausea and vomiting in dexamethasone group is significantly higher than that of ramosetron group. Limited studies have compared the effects of dexamethasone and ramosetron on PONV. Further in the immediate period with 0–8 hours, 76.6% in Group D had nausea and vomiting, compared to none in Group R which is statistically significant p (< 0.001). Yoon-Kang Song et al., conducted a study on effects of ramosetron and dexamethasone on postoperative nausea, vomiting, pain, and shivering in female patients undergoing thyroid surgery and conclude that two antiemetic drugs, ramosetron and dexamethasone, significantly reduced the incidence and severity of postoperative nausea and the need for administration of rescue antiemetic drugs.[17] Lopez-Olaondo et al. reported that dexamethasone was as effective as ondansetron in reducing nausea and vomiting induced by chemotherapy.[18] Another study showed that dexamethasone was a little more effective than ondansetron in preventing posttonsillectomy PONV.[19] Also, a study of 60 patients undergoing laparoscopic cholecystectomy showed that the incidence rate of PONV in the dexamethasone group was significantly lower (20% *versus* 43.3%).[20] The difference in the findings of the above studies might be related to wide range of differences in sample sizes, patients qualities, type of surgical operations and anesthetic techniques, the way that PONV was defined and studied.

The present study, showed that ramosetron was more effective than dexamethasone in preventing PONV; therefore, it may be more suitable to be administered in such a situation where we can reduce the amount of recue antiemetic and complications arising out of PONV.

Conclusion

- Ramosetron 0.3 mg IV given before induction of anesthesia is an effective means of reducing PONV in middle ear surgeries;
- Compaed to dexamethasone 8 mg IV ramosetron 0.3 mg IV significantly reduces PONV in the immediate postoperative period;
- Ramosetron is suitable alternative to dexamethasone in controlling PONV.

References

1. Miller RD, Eriksson LI, Fleisher LA, et al. Miller's Anesthesia, 6th edition. USA: Churchill Livingstone; 2009.pp.2317–333.
2. Fujii Y. Clinical strategies for preventing postoperative nausea and vomitting after middle ear surgery in adult patients. Curr Drug Saf 2008;3:230–39.
3. Jabalameli M, Rouholamin S, Gourtanian F. A comparison of the effects of fentanyl and remifentanil on nausea, vomiting, and pain after cesarean section. Iran J Med Sci 2011;36:183–87.
4. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anesthesiology 1992;77:162–84.
5. Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? Anesthesiology. 1999;91:109–118. doi: 10.1097/00000542-199907000-00018. PubMed PMID: 10422935.
6. Kim WO, Koo BN, Kim YK, et al. Ramosetron for the prevention of postoperative nausea and vomiting (PONV): A meta-analysis. Korean J Anesthesiol 2011;61: 405–412.
7. Rabasseda X. Ramosetron, a 5-HT_3 receptor antagonist for the control of nausea and vomiting. Drugs Today (Barc) 2002;38:75–89.
8. Hesketh PJ, Gandara DR. Serotonin antagonists: A new class of antiemetic agents. J Natl Cancer Inst 1991;83:613–20.
9. Liu Y H, Li M J, Wang P C, et al. Use of dexamethasone on the prophylaxis of nausea and vomiting after tympanomastoid surgery. Laryngoscope 2001;111(7):1271–274. doi: 10.1097/00005537-200107000-00024
10. Isik B, Cekmen N, Arslan M, et al. Comparison of the antiemetic effects of ondansetron and dexamethasone on middle ear surgery. Saudi Med J 2006;27: 646–51. doi:10.1097/00003643-200606001-00042.
11. van den Berg AA. A comparison of ondansetron and prochlorperazine for the prevention of nausea and vomiting after tympanoplasty. Can J Anesth 1996;43: 939–45.
12. Honkavaara P. Effect of transdermal hyoscine on nausea and vomiting during and after middle ear surgery under local anesthesia. Br J Anesth 1996;76:49–53. doi: 10.1093/bja/76.1.49.
13. Gan TJ. Selective serotonin 5-HT_3 receptor antagonists for postoperative nausea and vomiting: Are they all the same? CNS Drugs 2005;19:225–38.
14. Hahm TS, Ko JS, Choi SJ, et al. Comparison of the

prophylactic antiemetic efficacy of ramosetron and ondansetron in patients at high-risk for postoperative nausea and vomiting after total knee replacement. Anesthesia 2010;65:500–504.

15. Kim SI, Kim SC, Baek YH, et al. Comparison of ramosetron with ondansetron for prevention of postoperative nausea and vomiting in patients undergoing gynecological surgery. Br J Anesth 2009;103:549–53.
16. White PF, Watcha MF. Are new drugs costeffective for patients undergoing ambulatory surgery? Anesthesiology 1993;78(1):2–5.
17. Song, YK. and Lee. Effects of ramosetron and dexamethasone on postoperative nausea, vomiting, pain, and shivering in female patients undergoing thyroid surgery. Can J Anesth 2013;27:29.
18. López-Olaondo L, Carrascosa F, Pueyo FJ, et al. Combination of ondansetron and dexamethasone in the prophylaxis of postoperative nausea and vomiting. Br J Anesth. 1996;76:835–40. doi: 10.1093/bja/76.6.835.
19. Bolton CM, Myles PS, Nolan T, et al. Prophylaxis of postoperative vomiting in children undergoing tonsillectomy: A systematic review and meta-analysis. Br J Anesth 2006;97:593–604. doi: 10.1093/bja/ael256

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A Comparative Study on Efficacy of Intravenous Fentanyl *Vs* Ultrasonography (USG) Guided Fascia Iliaca Compartment Block Prior to Subarachnoid Block in Patients Undergoing Fracture Femur Surgeries

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Abstract

Background: Pain arising from fracture of femur is of severe nature, and any degree of movement can worsen the pain. Surgery for fixation of femoral fractures may be done under spinal anesthesia. Fascia Iliaca Compartment Block (FICB) produces a simultaneous block of the femoral and of the lateral femoral cutaneous nerves, provides good pain relief for patients with fracture femur and even intravenous fentanyl can also be used to relieve the pain. *Aims:* We conducted this study to compare the analgesic efficacy of Intravenous Fentanyl (IVF) and Ultrasonography (USG) Fascia Iliaca Compartment Block (FICB) for preoperative pain relief and while positioning for subarachnoid blockand also to assess the duration and quality of postoperative analgesia in the first 12 hrs. *Materials and Methods:* Sixty patients aged 18 to 65 years, with American Society of Anesthesiologists status I to II, undergoing surgery for femur fracture were chosen for the study and randomized into 2 groups. Group A (n = 30) received 1 mcg/kg fentanyl Intravenously and Group B (n = 30) underwent ultrasonography (USG) guided FICB with 0.5% Bupivacaine of 20 ml volume, 20 minutes prior to positioning for subarachnoid block. Preprocedural and postprocedural parameters such as hemodynamic parameters, visual analog scale (VAS) scores for 12 hours and quality of positioning and request of first rescue analgesia were recorded. *Results:* Preprocedural VAS scores were similar in both groups. Postprocedure VAS score in Group B was significantly less compared to Group A. Patients in Group B had better quality of positioning for subarachnoid block. Requirement of first rescue analgesia was prolonged in Group B compared to Group A. *Conclusion:* FICB group patients had better quality of positioning subarachnoid block and prolonged postoperative analgesia. This suggests USG guided FICB is an effective way to reduce patient discomfort during positioning for subarachnoid block in femoral fractures and prolong postoperative analgesia.

Keywords: Fascia iliac compartment block; Intravenous fentanyl; Subarachnoid block; Femoral fractures.

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Introduction

Fracture femur, a common injury, is associated with significant pain and is generally treated with internal fixation with an implant.[1] These surgeries are usually conducted under central neuraxial blocks, but patients experience pain on attempted flexion at hip joint during positioning for neuraxial blockade[2] and need analgesia.

A Fascia Iliaca Compartment Block (FICB), which produces a simultaneous block of the femoral and of the lateral femoral cutaneous nerves,[3] provides good pain relief for patients with femoral shaft fracture.[4] Patients experience pain in the postoperative period and analgesics are required in frequent doses causing undesirable side-effects, i.e. Opioids cause respiratory depression, hypotension, confusion and impractical for ward administration, instead, a single local anesthetic dose as peripheral nerve block provides adequate and prolonged analgesia.[5] Amongst the procedures, ultrasound guided FICB is superior in terms of efficacy, safety and easy administration[6] providing unilateral analgesia, reducing side-effects, without motor blockade and fewer neurological complications.[7,8]

Materials and Methods

Institutional Ethical Committee approval and informed consent from the patient were taken prior to study. Patients of both sexes posted for elective fracture femur surgeries who were unable to sit due to pain, age between 18 and 65 years, American Society of Anesthesiologists (ASA) physical status Grade 1 & 2, were included in the study. Patients who refused to give consent, who could sit comfortably and contraindication for spinal anesthesia were excluded from study.

The sample size was computed based on previous studies, keeping reduction in Visual analog scale scores by 15% after Fascia iliac compartment block as the primary outcome variable. Power - 80% and confidence interval of 95%, required sample size in each group was 28, approximated to 30.

Patients were divided into two groups 30 in each: IV Fentanyl (Group A) and USG guided FICB (Group B). Group A (n = 30) – received 1 mcg/kg Fentanyl IV Group B (n = 30) – underwent USG guided FICB with 0.5 % Bupivacaine of 20 ml volume. All patients were subjected to preanesthetic evaluation one day before surgery and advised tablet alprazolam 0.5 mg night before surgery. In the preoperative waiting room, patients was connected to standard monitoring like noninvasive blood pressure, pulse oximetry, electrocardiogram and baseline readings noted. Baseline Visual Analog Scale (VAS) score was noted.

Patients were randomized in a 1:1 allocation ratio by simple randomization using randomization. com, a web based tool, into two groups of 30 each, i.e. Group A and Group B. Patients were in Group A will receive 1 mcg/kg Fentanyl IV 20 minutes prior to surgery and patient will be shifted into the operating room. While positioning for Subarachnoid block, additional 0.5 mcg/kg dose will be added if VAS score > 4.

Patients who were in Group B will underwent Ultrasound guided Fascia Iliaca Compartment Block 20 min prior to shifting into OT. Under aseptic precautions, Sonosite ultrasound machine with linear probe was placed transversely, just inferior to the inguinal ligament, one-thirds of the distance from Anterior Superior Iliac Spine to Pubic Tubercle. Fascia Lata and Fascia Iliaca was visualized as 2 hyperechoic lines. A short beveled, 23G Quincke's spinal needle was introduced through the skin in a lateral to medial orientation and directed in plane to the probe to allow visualization of the full needle throughout the procedure. Needle tip was visualized penetrating the Fascia Lata and Fascia Iliaca. After puncturing Fascia Iliaca and negative aspiration, 20 ml of 0.5% Bupivacaine was injected in 10 ml aliquots over 2–3 minutes.

An expanding anechoic collection just below fascia iliaca was the visual confirmation of correct placement of drug. 20 minutes after administering the block, patient was be shifted into the operating room. Patient was placed in sitting position and subarachnoid block was done using Inj. Bupivacaine 0.5% (H) 3 ml.

All vital parameters, VAS score (0 = no pain and 10 = worst pain), patient positioning (satisfactory or nonsatisfactory) and time taken to perform subarachnoid block was noted. Post operatively we monitored time for first rescue analgesia and VAS score on every 3 hours upto 12 hrs.

Statistical Analysis

Results obtained will be analyzed using descriptive statistics. Parametric variables will be analyzed using paired "t" test, unpaired "t" test and ANOVA. Parameter variables described as mean ± SD; qualitative variables were described as numbers (percentage) and as median and range. p - value of < 0.05 was considered as significant.

Results

Demographic parameters were not significantly different between the groups, (Table 1). Baseline values for Heart Rate (HR), systolic blood pressure, diastolic blood pressure, SpO_2 and respiratory rate were comparable in both the groups and not significant. It was noted that HR was significantly reduced in both groups p = 0.05 (before and after procedure), (Table 2).

Table 1: Demographic data

Parameters	FICB (n = 30)	IV Fentanyl (n = 30)	p -value
Age (mean ± SD)	42.03 ± 14.37	38.66 ± 14.79	0.377
Weight (mean ± SD)	58.1 ± 8.2	57.93 ± 8.6	0.96
Male	19	22	0.577
Female	11	8	
ASA 1	10	17	0.11
ASA 2	20	13	

Table 2: Vital clinical parameters before and after procedure

FICB	Before FICB (mean ± SD)	20 min After (mean ± SD)	p - value
PR (b/min)	78.2 ± 8.26	70.23 ± 7.07	< 0.05
SBP (mm Hg)	129.33 ± 12.39	123.66 ± 14.17	0.32
DBP(mm Hg)	81.33 ± 6.41	83.96 ± 6.39	0.48
SpO_2 (%)	99.16 ± 0.87	99.3 ± 0.95	0.88
RR (min)	20.43 ± 2.98	18.36 ± 2.45	0.12
IV Fentanyl	**Before IV Fentanyl (mean ± SD)**	**20 min After (mean ± SD)**	**p - value**
PR (b/min)	78.6 ± 9.21	71.28 ± 8.8	< 0.05
SBP (mm Hg)	131.14 ± 28.5	127.16 ± 12.07	0.41
DBP (mm Hg)	83.77 ± 6.05	84.36 ± 5.62	0.24
SpO_2 (%)	99.22 ± 0.78	99.14 ± 0.96	0.52
RR (min)	19.78 ± 2.8	19.66 ± 2.38	0.72

VAS score after 20 mins of procedure was reduced in both groups, however, Group B (FICB) patients had lower VAS score compared to Group A (IVF) and it was statistically significant p = 0.05, (Fig. 1).

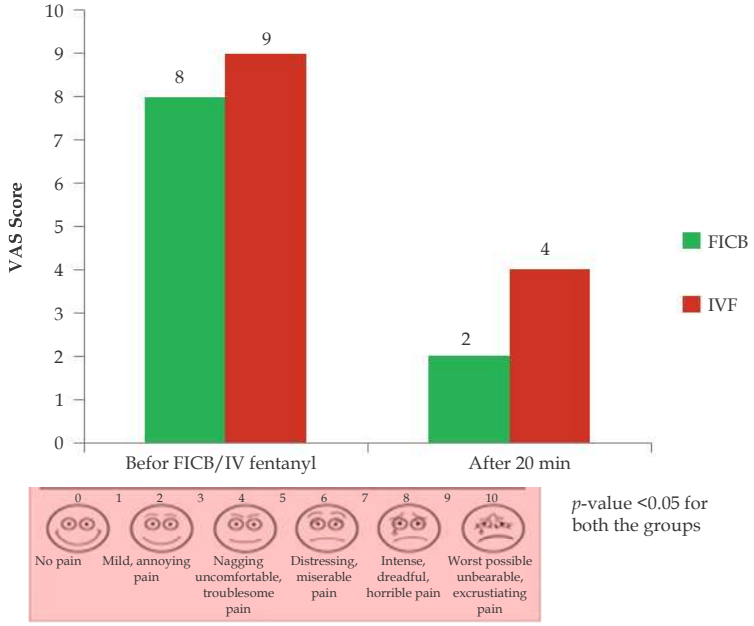

Fig. 1: VAS Score before and after procedure.

Quality of patient positioning for spinal anesthesia was most satisfactory in Group B (FICB) compared to group A (IVF) and it was statistically significant p = 0.05, (Table 4). This was further assed by time taken to perform subarachnoid block which was lesser in FICB group compared to IVF Group, (Table 3 and 4).

Table 3: Patient positioning for Subarachnoid block

Parameters	FICB (n = 30)	IV Fentanyl (n = 30)
Satisfactory	26	11
Not-satisfactory	4	19

*p - value < 0.05.

Table 4: Time to perform subarachnoid block

Parameters	FICB (n = 30)	IV Fentanyl (n = 30)
Time (min)	6.9 ± 2.5	10.8 ± 5.4

Postoperative assessment showed time for first rescue analgesia was higher in Group B (FICB) i.e. 7.46 ± 1.64 when compared to Group A (IVF) i.e. 3.86 ± 1.59 and significant p = 0.05, (Table 5). Postoperative VAS score was significantly less in Group B compared to Group A, (Fig. 2).

Table 5: Rescue analgesic requirement

Parameters	FICB (mean ± SD)	IV Fentanyl (mean ± SD)
Time to 1st rescue therapy	7.46 ± 1.64	3.86 ± 1.59*

*p - value < 0.05.

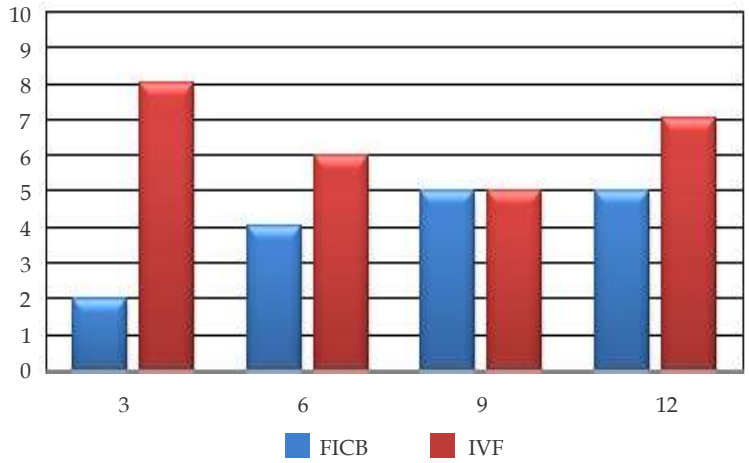

Fig. 2: Postoperative VAS Score.

Discussion

In present era of trauma, the number of patients encountered with fracture femur is routinely observed. It has noted such patients suffer from severe pain and anxiety. Any degree of movement can increase the pain and causes more discomfort to the patients. Spinal anesthesia is universally accepted and preferred technique of anesthesia for surgical repair of fracture femur. This is due to many advantages of spinal anesthesia over general anesthesia like better analgesia, early mobility, less deep vein thrombosis and less of postop pulmonary complications in elderly patients.

For the technique of spinal anesthesia proper positioning of the patient is at most important. Pain itself can lead to improper position and difficulty in performing subarachnoid block

and more so, very distressing for patients and stressful situation for performing anesthetist. So, to reduce the pain for proper position during subarachnoid block, various agents like midazolam, ketamine, fentanyl, alfentalyl etc. are used which have their own limitations because of their adverse effects. To overcome this, nerve block are frequently used. Ultrasound guided FICB which block femoral nerve and lateral cutaneous nerve of thigh provides better analgesia and aids in satisfactory positioning of patients during subarachnoid block.

In our study, both USG guided FICB and IV fentanyl provided reduction in VAS scores. However, in contrast, FICB was found to provide superior analgesia over IV fentanyl Madabushi R et al.[3], Mosaffa et al.[4] showed similar results.

Although we followed attainment of VAS score of < 4 before attempting patient positioning, patients invariably reported a higher VAS at the end of positioning from the time of initiation of sitting in IV fentanyl group. A study by Ranjit S et al.[5] and Yun et al.[2] found similar results that the FICB offers better hip flexion and ability to sit upright. In IV fentanyl group, 3 hour after surgery VAS score was significantly higher compared to FICB group and requires early rescue therapy compared to FICB group. Study done by Madabushi R et al., used ropivacaine 0.3%[3] and Mosaffa et al., used lignocaine 1%[4] have shown FICB superior over IV fentanyl but there was an early requirement of rescue therapy in FICB group compared to our study. This may be because of use of bupivacaine which is long acting local anesthetic drug.

Conclusion

FICB offers superior analgesia, satisfactory positioning for central neuraxial block than IV fentanyl in patients undergoing surgery for fracture femur and reduces rescue analgesic requirement by providing prolonged postoperative analgesia.

Limitation: We have not measured sitting angle.

Conflict of Interest: None.

References

1. Zywiel MG, Prabhu A, Perruccio AV, et al. The influence of anesthesia and pain management on cognitive dysfunction after joint arthroplasty. Clin Orthop Relat Res 2014;472:1453–66.
2. Yun MJ, Kim YH, Han MK, et al. Analgesia before a spinal block for femoral neck fracture: Fascia iliaca compartment block. Acta Anesthesiol Scand 2009;53(10):1282–87.
3. Madabushi R, Rajappa GC, Thammanna PP, et al. Fascia iliaca block *vs* intravenous fentanyl as an analgesic technique before positioning for spinal anesthesia in patients undergoing surgery for femur fractures: A randomized trial. J Clin Anes 2016;35:398–403.
4. Mosaffa F, Esmaelijah A, Khoshnevis H. Analgesia before performing a spinal block in the lateral decubitus position in patients with femoral neck fracture: A comparison between fascia iliaca block and IV fentanyl. Reg Anesth Pain Med 2005;30(Suppl. 1):61.
5. Ranjit S, Pradhan BB. Ultrasound guided femoral nerve block to provide analgesia for positioning patients with femur fracture before subarachnoid block: Comparison with intravenous fentanyl. Kathmandu Univ Med J (KUMJ) 2016 Apr–Jun;14(54):125–29.
6. Lopez S, Gros T, Bernard N. Fascia iliaca compartment block for femoral bone fractures in prehospital care. Reg Anesth Pain Med 2003;28:203–207.
7. Foss N, Kristensen B, Bundgaard M, et al. Fascia iliaca compartment blockade for acute pain control in hip fracture patients. Anesthesiology 2007;106(4):773–78.
8. Terese T Horlocker, Sandra L Kopp, Denise J Wedel. Peripheral nerve blocks in Ronald D Miller, Neal H Cohen. Miller's Anesthesia, 8th edition. Vol 2. Philadelphia: Elsevier; 2015.pp.3179–80.

Original Research Article

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A Descriptive Study to Assess the Awareness and Acceptance of Labor Analgesia in Pregnant Women Admitted for Safe Confinement

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Abstract

Background: Labor pain is very painful. Parturients struggle with agony of pain due to lack of awareness and knowledge. These is significant decrease in acceptance also. *Aims:* Aims to evaluate awareness & to educate for acceptance of labor analgesia in pregnant women. *Methods:* A sample size of 240 pregnant women were included in our study. Each parturient will be counselled and after obtaining a written informed consent the questionnaires will be given which contains questions related to awareness, acceptance, utilization of most common pain relief methods available in the hospital. Results obtained are analyzed by descriptive statistics. Chi-square, Fisher exact test, student *t*-test. SPSS version 21.0 used for calculation. $p < 0.05$ is considered significant. *Results:* Most of the parturients (81%) were not aware of labor pain relief techniques and only 18% were aware. Around 45% did not utlise labor analgesia because of lack of knowledg. Now, after awareness 69% were ready to accept labor analagesia and 39% were not ready to accept. Postcounseling we saw around 13% increase in acceptance. Hence, we found that by creating awareness, there was increase in acceptance for labor analgesia and utilization of labor analgesia techniques. *Conclusion:* Awareness among parturients attending our hospital is found to be less. By providing education and counseling, awareness and acceptance can be increased. Obstetricians and anesthesiologist should work as a team and should ensure utilization of labor analgesia services.

Keywords: Labor pain; Awareness; Acceptance; Labor analgesia.

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Introduction

Labor is intensely painful, however, the time course of pain intensity is highly variable, dynamic and unpredictable.[1] Studies have found that Asian women reported more pain in labor. Most of the Indian parturients still suffer from agony of labor pains due to lack of awareness, unfound fears and lack of availability of labor analgesia service.[2]

Labor pain affects both mother and foetus. Uterine contraction pain evokes a generalized neuroendocrine stress response producing widespread physiological effects during the first stage of labor. They include increased oxygen consumption, hyperventilation and respiratory alkalosis; increased cardiac output, systemic resistance and blood pressure; delayed gastric emptying; impaired uterine contractility and

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diminished uterine perfusion; and metabolic acidemia.[3]

In our hospital 9465 normal deliveries were conducted in the previous year, out of which only 44 (0.46%) utilized labor analgesia services, which is much lower than the published statistics (11%) in India. The reason for such low acceptance inspite of availablility of services in our hospital was not clear. Hence, the present study was designed to know the attitudes of women towards labor pain awareness of labor analgesia and possible benefit of counseling on acceptance of it.

Methods

The study was a descriptive survey conducted between January 2019 and June 2019 in Vani Vilas Hospital attached to Bangalore Medical College and Research Institute, Bangalore. Assuming number of deliveries to be 10000 in current year, that there would be an increase in utilization rate of 6% for labor analgesia after counseling, and an absolute difference 3% a total of 236 parturients were required, to attain a confidence interval of 95%. We included 240 parturients in the survey. Questionnaire used for study was adapted from Shidhaye et al.,[4] and is prepared based on our needs in English language, will be explained in kannada/hindi by researcher. It was validated by sending it to 2 subject experts and 2 language experts. Each questions was scored on a scale of 1 to 5, questions carrying score of 4 or more is included in the questionnaire. It was send to 10 volunteers and their response was assessed. Each pregnant woman will be counseled about the study, after obtaining a written informed consent questionnaire will be given, which contains questions related to awareness, acceptance, utilization of most common pain relief methods available in the hospital. Pain experience will be assessed with Visual Analog Score. Socio economic classification will be done based on BG Prasad classification[5]. Women will then be counseled about the labor analgesia through-Handouts, Short video, discussion with beneficiary, postcounseling acceptance level was assessed and will be asked to answer questions about whether they are willing to use any of the labor analgesia methods during delivery. The researcher was present to answer any doubts. Confidentiality of the patients was maintained. Pain experience was graded with VAS score.

Various knowledge and attitude-related parameters such as perceived severity, nature of labor pain, methods of labor analgesia and perceptions regarding labor analgesia were taken as primary outcome parameters. Practise-related parameters including availing of labor analgesia services in the previous pregnancies and their perceptions about the same were also assessed. All the parameters were presented as frequency and percentages.

The data were also presented in appropriate graphs such as box and whisker plots, pie-charts and bar charts. No inferential statistical analysis was undertaken. Hence, no statistical significance test was used in the study. Information will be collected on computer software programme of SPSS 11 frequencies and percentages calculated to express the results.

Results

The majority (87%) of the antenatal women felt that the labor pain is the worst possible pain and nothing can be done about it. Only 70% of pregnant women said pain should be relieved. Majority of the women 81% were not aware about pain relief methods. Among very few (18%) who came to know about labor analgesia were during previous child birth (59%). The source of information was from doctors, (54%).

The awareness and utilization during previous child birth were 18% and 50% respectively. Reasons for nonutilization were many but majority (45%) was because they did not aware about it. After awareness, presently 69% were wishing to have painless labour. Reasons for nonacceptance were many but majority (47%) were thought its harmful to baby. We could see difference of 13% increase of acceptance rate after counseling. Post counseling, main reason for refusal was due to thought that it may be harmful to baby, (Table 01–17).

Table 1: Demography

Clinical Variables	No. of Patients (n = 240)
Age in years	
20–24	89 (37.1%)
25–29	91 (37.9%)
30–34	60 (25.0%)
Education	
No education	0
< 7^{th}	71 (29.6%)
<10^{th}	63 (26.3%)
12^{th}	58 (24.2%)
Graduation & more	48 (20%)

Table 2: Occupation

Occupations	Percentages
Home Maker	187 (77.9%)
Medical Profession Related	0
Nonmedical Profession Related	53 (22.1%)

Table 3: Income

Per capita income	No. of cases
6574 & above	0%
3287–6573	0%
1972–3286	12 (5%)
986–1971	80 (33.33%)

Table 4: Geography

Geographical distribution	No. of cases
Urban	165 (68.8%)
Rural	75 (31.1%)

Table 5: Parity

Parity	No. of cases
1	167 (69.6%)
2	66 (27.5%)
3	7 (2.9%)
4 or more	0

Table 6: Previous delivery

Previous delivery was in	No. of cases
Primary care-center	103 (42.9%)
Secondary carecenter	47 (19.6%)
Teritiary care-centre	77 (32.1%)
Private hospital	11 (4.6%)
Home delivery	2 (0.8%)

Table 7: Severity of pain

Severity of pain in previous labor	No. of cases
No pain	0
Mild	28 (11.7%)
Moderate	140 (58.3)
Severe	56 (23.3%)
Unbearable	16 (6.7)

Table 8: Should pain relieved

Should labor pain be relieved	No. of cases
Yes	168 (70.0%)
No	58 (24.2%)
No opinion	14 (5.8%)

Table 9: Know pain-relief methods

Do you know of labor pain-relief methods	No. of cases
Yes	44 (18.3%)
No	196 (81.7%)

Table 10: Awareness about labor analgesia

When did you come to know about labor analgesia?	No. of cases
Current pregnancy	4 (9.1%)
Previous Pregnancy	8 (18.2%)
Previous child birth	26 (59.1%)
After previous child birth in hospital wards	6 (13.6%)

Table 11: Source of information

What is the source of information?	No. of cases
Media	0
Neighbors/relatives	6 (13.6%)
Anganiwadi workers	0
Doctors	24 (54.5%)
Nurses	14 (31.8%)
Mothers in the wards	0

Table 12: Awareness and utilization

Awareness & utilization of Labor analgesia during previous pregnancies	
Awareness	44/240 (18.3%)
Utilization	22/44 (50%)
Satisfaction with LA	21/22 (95%)

Table 13: Reasons for nonutilization

If no, what is the reason	*n* = 22
Cost related	1 (4.5%)
Did not know about it before delivery	10 (45.5%)
Service not provided	3 (13.6%)
Harmful to the baby	5 (22.7%)
Refusal by family	3 (13.6%)
Methods do not work	0
Others	0

Table 14: Wish to have presently

Do you wish to have painless labor this time	No. of cases
Yes	167 (69.6%)
No	73 (30.4%)

Table 15: Reasons for nonacceptance

Reasons	*n* - 73
May harm normal labor	7 (9.6%)
Harmful to the baby	35 (47.9%)
Against the will of God	11 (15.1)
Refusal by family	13 (17.8)
Side-effects later in life	6 (8.2)
No response	1 (1.4%)

Table 16: Pre and postcounseling acceptance

Response	Precounseling	Postcounseling	% Difference
Yes	167 (69.6%)	199 (82.9%)	13.3%
No	73 (30.4%)	41 (17.1%)	

$p < 0.001$ Chi-square.

Table 17: Reasons for refusal after counseling

If no why	*n* = 41
May harm normal labor	1 (2.4%)
Harmful to the baby	27 (65.9%)
Against the will of God	2 (4.9%)
Refusal by family	6 (14.6%)
Side-effects later in life	4 (9.8%)
No response	1 (2.4%)

Discussion

The mechanism of labor pain has both visceral and somatic component. Uterine contractions, cervical dilatation and stretching of the lower uterine segment are responsible for pain during the first stage of labor. Visceral afferent *C*-type fibers accompanying the sympathetic nerves carry the pain impulses and enter the spinal cord at the T10-L1 levels. In the second stage of labor, somatic afferent fibers from the vagina and perineum convey pain impulses in the pudendal nerves to the S2-S4 spinal nerve roots.[6]

In our study, we had around 240 parturients, most of them were home makers. Regarding education, majority were under seventh grade and only 20 % were graduates. Around 68% were from urban background and 31% were from rural. Majority were primiparous (69%) among them 23% experienced severe pain and 58% had moderate pain. Most of the parturients (81%) were not aware of labor pain relief techniques and only 18% were aware. Most women became aware during their previous child birth. The source of information was available through doctors. 95% were satisfied with local anesthesia during previous child birth. Around 45% did not utlize labor analgesia because of lack of knowledg. Now, after awareness 69% were ready to accept labor analgesia and 39% were not ready to accept. In James JN et al.[6] study shows half of the participants were in favor of using labor analgesia techniques. Postcounseling we saw around 13% increase in acceptance. Postcounseling most common reason for denial was fear of thought of harmful to baby.

However, studies pertaining to this topic are sparse. By creating awareness, we found there was increase in acceptance for labor analgesia. Utilization of labor analgesia techniques can be increased more by creating awareness during ante natal visits by doctors.

Conclusion

Obstetricians and Anesthesiologist should work as a team with consolidated and coordinated approach to help all pregnant women who come for ante natal visits either by counseling or display aids regarding labor analgesia techniques and services available in hospital and should create awareness and address all their concerns and fears. Team must ensure all parturients to utilize the labor analgesia services adequately and efficiently.

Support: Nil

References

1. Flood P, Rollins MD. Anesthesia for obstretics. In: Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Young WL, Wiener-Kronish JP, Editors. Miller's Anesthesia. 8th edition. Philadelphia: Elsevier Saunders; 2015.p.2339.
2. ACOG Committee Opinion #295 Pain-relief during labor. Obstet Gynecol 2004;104:213
3. Brownridge P. The nature and consequences of childbirth pain. Eur J Obstet Gynecol Reprod Biol 1995;59:9–15.
4. Shidhaye RV, Galande M, Bangal VB, et al. Awareness and attitude towards labor analgesia of Indian pregnant women. Anesth Pain and Intensive Care 2012;16(2):131–36.
5. Pandey VK, Aggarwal P, Kakkar R. Modified BG Prasad's Socio-economic Classification-2018. The need of an update in the present scenario. Indian J Comm Health 2018;30(1):82–84.
6. James JN, Prakash KS, Ponnia M. Awareness and attitudes towards labor pain and labor pain-relief of urban women attending a private antenatal clinic in Chennai, India. Indian J Anesth 2012;56(2):195–98.

Original Research Article

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Predictors of Difficult Airway Intubation A Prospective Observational Study of 202 Patients Undergoing General Anesthesia

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Abstract

Unanticipated difficult tracheal intubation is a significant source of morbidity and mortality in anesthesia practice. Identifying situations and patients at risk for airway management problems is a key to optimal care. This study compares the parameters described to identify a difficult intubation to look for the best predictors or combinations thereof. *Materials and Methods:* The preoperative airway assessment used multiple parameters like Mallampati test, Thyromental Distance, Head and neck Movement, Interincisor Gap, Lahey & McCormick Scale. The results were evaluated on the basis of sensitivity, specificity, positive and negative predictive value of these tests. During intubation a cumulative Intubation Difficulty Scale rating greater than 5 was used to classify a patient as a difficult intubation to validate the scores. *Results:* Amongst all the parameters studied individually, the Upper lip bite test was found to have the highest sensitivity of 48.48% and specificity of 97.3%. When multiple parameters were taken into consideration, the combination of Mallampati score, Upper lip bite test and Neck circumference to thyromental distance ratio was found to have the highest sensitivity of 75.76% and specificity 91.12%. *Conclusion:* Application of multiple predictors can reduce the frequency of unanticipated difficulty and also unnecessary interventions related to over prediction of airway difficulty.

Keywords: Intubation; Difficult airway predictors; Mallampati test; Thyromental distance; Upper lip bite test; Height to thyromental distance ratio; Neck circumference to thyromental distance ratio; Multiple test predictors.

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Introduction

The management of the airway with induction of anesthesia is the primary responsibility of the anesthesiologist.[1]

Unanticipated difficult tracheal intubation is a significant source of morbidity and mortality in anesthesia practice. The incidence of difficult intubation has been reported to range from 1% to 18%.[2,3] The incidence of abandoned/failed intubation is approximately 0.05%–0.35%.[4,5] Approximately 30% of deaths in patients with difficult airway/intubation were caused by hypoxic brain damage secondary to inability to maintain a patent airway.[2] Increases in the incidence of morbid events have also been noted in patients who have undergone difficult tracheal intubation. These events included desaturation, hypertension, oesophageal intubation, pharyngeal trauma,

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dental injury, cancelation of surgery, prolonged hospital stay and increased rate of unexpected ICU admission.[6–8]

Unexpected difficult intubations may be the result of a lack of accurate predictive tests for difficult intubation and inadequate preoperative examinations of the airway.[3] Identifying situations and patients at risk for airway management problems is the key.[8]

Preoperative evaluation of the airway can be accomplished by various measurements of the anatomical landmarks or noninvasive clinical tests performed during physical examinations. Initially the airway assessment was carried out by a single parameter like Mallampati's oropharyngeal classification,[5,9] Thyromental distance,[10] Inter incisor gap, protrusion of the mandible,[11] Head and neck movement[12] etc. But the consideration of multiple parameters is being increasingly recommended.[14–16]

The need for development of a scoring system, which factors in the multiple parameters, to best predict a difficult airway, necessitates an understanding of the relative importance of all the individual parameters.

Aims

Our study aims to identify the relative importance of parameters that predict difficult intubation and combinations thereof.

Objectives

(1) To evaluate the predictors of difficult airway in patients undergoing general anesthesia.

(2) To compare these scores with the Intubation difficulty score obtained in real time in the operation theatre during intubation under General Anesthesia.

(3) To compare the sensitivity, specificity, negative predictive value and positive predictive value of these factors and scoring systems .

(4) To find the most sensitive combination of these factors for use as an optimal predictor for difficult intubation in our tertiary hospital setting.

Materials and Methods

Study Design: Prospective Observational Study;

Place of Study: Department of Anesthesiology, St. John's Medical College and Hospital, Bangalore, India;

Duration of Study: April 2018 to February 2019.

Patient Selection

(A) Inclusion Criteria:

- ASA physical status I and II;
- Patients aged between 18 and 60 years, inclusive of both sexes;
- Patients scheduled to receive general anesthesia requiring endotracheal intubation for elective orthopedic, urologic, ENT, neurological and abdominal surgeries.

(B) Exclusion Criteria:

- Patients younger than 18 years and older than 60 years of age;
- Patients with abnormal head and neck anatomy; those with a laryngeal or Pharyngeal mass; or with a mass in the oral cavity; pregnant women (due to upper airway edema); or those unable to open the mouth, or with limitation of cervical movement;
- Patients requiring a rapid sequence induction or awake intubation;
- Patients posted for emergency surgical procedures.

The study was approved by Institutional Ethical Review Board (IERB No.114/2018. date 24th March 2018) and written informed consent was obtained from every patient prior to the study. This study included 202 patients, a detailed history and general physical examination was performed in each of them.

The Sample size was estimated based on the study by Cattano et al.[1] using Buderers Formula[17] was 204. Preoperative airway examination was performed using multiple screening tests to predict difficult airway. These tests were performed for all patients by the same anesthesiologist to avoid interobserver variability (Table 1).

These preoperative tests results were recorded and the difficulty of intubation assessed by experienced anesthesiologists in the operation theatre, shows in Table 2, and the results were compared after compilation of the data.

Table 1: Factors studied in each patient

S. No	Factors studied
1.	Weight (kg), height (cm) and age (years).
2.	American Society of Anesthesiologists (ASA) physical status.
3.	Inter-incisor gap (between the central incisors).
4.	Thyromental distance.
5.	Sternomental distance.
6.	Mallampati score. *Class 1:* soft palate, fauces, uvula and pillars visible. *Class 2:* soft palate, fauces and uvula visible. *Class 3:* soft palate and base of uvula visible. *Class 4:* none of the soft palate visible.
7.	Neck movements:[6] This criterion was graded into ≤ 80° or > 80°).
8.	Mandibular length (from the angle of mandible to middle of the chin).
9.	Height to thyromental distance ratio.
10.	Upper lip bite test (biting the upper lip with the lower incisors). *Gra*de 1: lower incisors can bite the upper lip above the vermilion line. Grade 2: lower incisors can bite the upper lip below the vermilion line. Grade 3: lower incisors cannot bite the upper lip.
11.	Neck circumference to thyromental distance ratio (neck circumference measured at the level of cricoid cartilage perpendicular to the long axis of neck).
12.	Difficult of laryngoscopy as per Cormack and Lehane grading. *Grade 1:* Most of the glottis is seen. *Grade 2:* Only the posterior part of the glottis is visible. *Grade 3:* The epiglottis is visible, but none of the glottis can be seen. *Grade 4:* Epiglottis not visible.

Table 2: The criteria for assessing a difficult intubation

Number	Criteria for Assessing a Difficult Intubation
N1	Number of additional intubation attempts;
N2	Number of additional operators;
N3	Number of alternative intubation techniques used;
N4	Laryngoscopy view as defined by Cormack and Lehane. (Grade 1, N4 = 0; Grade 2, N4 = 1; Grade 3, N4 = 2; and Grade 4, N4 = 3)
N5	Lifting force applied during laryngoscopy (N5 = 0 if inconsiderable and N5 = 1 if considerable).
N6	Need to apply external laryngeal pressure to improve glottic pressure. (N6 = 0 if no external pressure or only the Sellick's manoeuvre was applied and N6 = 1 if external laryngeal pressure was used).
N7	Position of the vocal cords at intubation (N7 = 0 if abducted or not visible and N7 = 1 if adducted).

Intubation Difficulty Scale (IDS) The IDS score is the sum of N1 through N7.

IDS score < 5 (i.e. easy intubation) IDS score ≥ 5 (i.e. difficult intubation).

Results

Demographics of groups

A total of 202 patients were included in this study and preoperative assessment of the airway was done to predict the difficulty in intubation. Based on the Intubation Difficulty Scale (IDS),[18] the study population was divided into two groups for the purpose of comparison into an 'Easy Intubation Group' - Group A (IDS < 5) and a 'Difficult Intubation Group' - Group B (IDS ≥ 5). There were no cases of desaturation or failed intubation in our study. The prevalence of difficult intubation in our study was 16.3% (33 patients). These two groups were also compared on various parameters such as age, American Society of Anesthesiologists (ASA) physical status grading, presence/absence of snoring and dentition issues.

The mean age in Group A was 39.24 years and in Group B was 42.58 years. This difference was not significant. (p = 0.139). Of the 202 patients studied, 112 (55.4%) were males and 90 (44.6%) were females. In Group B, 24 (72.7%) were males and 9 (27.3%) were females and this difference was significant (p = 0.029). The mean BMI of the study population was 26.10kg/m.^{2} In Group A, the BMI was 25.57 ± 5.25, which was lower than Group B (28.85 ± 6.10). In Group B, 10 (30.30%) patients had a BMI < 25.0; 7 (21.21%) patients had BMI between 25.0–30.0 and 16 (48.48%) patients had a BMI > 30.0.–This difference was statistically significant (p = 0.002).

Table 3 shows the comparison of study variables (ASA Grade, snoring and dentition) between the two study groups. In Group A, ASA Grade I patients had 97 (57.4%) ASA Grade II patients had 12 (36.4%), while in Group B ASA Grade 1 patients had 72 (42.6%) and Grade II patients 21 (63.6%). This difference was significant with p = 0.027. History of snoring was obtained in 7/169 (4.1%) and 3/33 (9.1%) patients in Group A and B respectively (p = insignificant). Patients with Dentition problems were 6/69 in the Easy Intubation Group (3.6%) and 3/33(9.1%) in the Difficult Intubation Group, (p = insignificant). All 108 patients with CL Grade 1 had easy intubation and 60 out of 61 patients with CL Grade 2 had easy intubation. Whereas 29 out of 30 patients with CL Grade 3 had difficult intubation and all 3 patients with CL Grade of 4 had difficult intubation.

Table 3: Comparison of study variables (ASA Grade, Snoring and Dentition) between the two groups (n = 202)

Variables	Group A (n = 169)	Group B (n = 33)	p - value
ASA Grade I	97 (57.4%)	12 (36.4%)	0.027*
ASA Grade II	72 (42.6%)	21 (63.6%)	
Snoring	7 (4.1%)	3 (9.1%)	
Dentition problems	6 (3.6%)	3 (9.1%)	

Table 4 reflects the comparison of predictors of difficult intubation parameters between the two study groups. In Group A there were 87 (51.5%), 73 (43.2%), 9 (5.3%) and 0 patients having Mallampati Class I, II, III and IV respectively. In Group B there were 3 (9.1%), 17 (51.5%), 13 (39.4%) and 0 having Mallampati class I, II, III and IV respectively, (p - value < 0.001 significant). There was only 1 (0.6%) patient with restricted Neck movement < 80° and the intubation was found to be easy. There were 168 (99.4%) patients with Neck movement > 80° whose intubation was easy and 33 (100%) with Neck movement > 80° whose intubation was difficult, (p - value 1, insignificant).

The mean Interincisor Gap was 5.07 ± 3.14 cms in Group A and 4.22 ± 0.56 cm in Group B. (p = 0.126 insignificant). The mean ML in Easy Intubation Group was 11.66 ± 1.00 cm and 12.15 ± 1.19 cm in Difficult Intubation Group, (p = 0.014. significant). The mean values of Thyro Mental Difference (TMD), SMD, HT/TMD and NC/TMD in Group A were found to be 9.86 ± 0.99 cm, 17.98 ± 1.26 cm, 16.43 ± 2.09 and 3.82 ± 0.63 respectively. The mean value in Group B was found to be 8.01 ± 0.90 cm, 14.88 ± 1.45 cm, 20.34 ± 2.38 and 5.10 ± 0.76 respectively, (p < 0.001 significant difference).

Table 4: Comparison of predictors of difficult intubation studied between the two groups (n = 202).

Variables	Group A (n = 169)	Group B (n = 33)	p - value
Mallampati (MP) class			
I	87 (51.5%)	3 (9.1%)	
II	73 (43.2%)	17 (51.5%)	< 0.001
III	9 (5.3%)	13 (39.4%)	
IV	0	0	
Neck Movements (degrees)			
< 80	1 (0.6%)	0 (0%)	1.000
> 80	168 (99.4%)	33 (100%)	
Upper Lip Bite Test (ULBT) Grade			
I	83 (49.1%)	4 (12.1%)	
II	82 (48.5%)	13 (39.4%)	< 0.001
III	4 (2.4%)	16 (48.5%)	

Variables	Group A (n = 169)	Group B (n = 33)	p - value
Interincisor Gap (IIG) in cm	5.07 ± 3.14	4.22 ± 0.56	0.126
TMD (cm)	9.86 ± 0.99	8.01 ± 0.90	< 0.001
ML (cm)	11.66 ± 1.00	12.15 ± 1.19	0.014
SMD (cm)	17.98 ± 1.26	14.88 ± 1.45	< 0.001
HT/TMD	16.43 ± 2.09	20.34 ± 2.38	< 0.001
NC/TMD	3.82 ± 0.63	5.10 ± 0.76	< 0.001

TMD - Thyromental distance; ML- Mandibular length; SMD - Sternomental distance; HT/TMD - Height to Thyromental distance ratio; NC/TMD - Neck Circumference to Thyromental distance ratio in cm.

Table 5 summarizes the Difficult intubation predictor statistics based on standard cut-off values. Mallampati class 3 or above had a sensitivity of 39.39% and a specificity of 95.81%, with p - value of < 0.001. ULBT Grade 3 showed 48.48% sensitivity and 97.63% specificity. p - value was significant (< 0.001). Neck movements < 80° had 0% sensitivity and 99.41% specificity with a p - value of 1.0. IIG of < 3.5 cms showed sensitivity and specificity of 21.21% and 99.41% respectively with p - value of < 0.001.

Table 5: Difficult intubation predictor statistics based on standard cut-off values (n = 202)

Variables	Standard cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	p - value
MP	3 or above	39.39	95.81	65.00	88.89	86.50	< 0.001
ULBT	Class 3	48.48	97.63	80.00	90.66	89.60	< 0.001
Neck Extension	< 80°	0.00	99.41	0.00	83.58	83.17	1.000
IIG (cm)	< 3.5 cm	21.21	99.41	87.50	86.50	86.63	< 0.001
TMD (cm)	< 6.5 cm	6.06	100.00	100.00	84.50	84.65	0.026
ML(cm)	< 9 cm	0.00	97.63	0.00	83.33	81.68	1.000
SMD (cm)	< 13.5 cm	21.21	99.41	87.50	86.60	86.63	< 0.001
8. HT/TMD	> 23.5	9.1	98.02	60.00	84.77	84.16	0.032
9. NC/TMD	> 5.0	45.45	97.63	78.95	90.16	89.13	< 0.001

MP - Mallampati Grade; ULBT - Upper Lip Bite Test; IIG - Interincisor Gap; TMD - Thyromental Distance; ML - Mandibular Length; SMD - Sternomental Distance; HT/TMD - Height to Thyromental Distance Ratio; NC/TMD - Neck Circumference to Thyromental Distance Ratio.

Standard cut off values of TMD (6.5 cms), ML (<9 cms) and SMD (<13.5 cms) had sensitivity of 6.06%, 0% and 21.21% respectively, specificity of 100%, 97.63% and 99.41% respectively. Their p values were 0.026, 1.0 and <0.001 respectively.

Standard cut-offs values of the ratios of HT/TMD (≥ 23.5) and NC/TMD (> 5.0) showed 9.1% and 45.45% sensitivity respectively with specificity of 98.02% and 97.63% respectively. Amongst all the above parameters, the ratio of NC/TMD >5 had the highest sensitivity of 45.45% and TMD < 6.5 cms had the highest specificity of 100. Table 6 shows, the predictor statistics using the new cut-off values which were derived using the ROC curve to find the optimum sensitivity and specificity of each parameter. IIG with new cut-off value (≤ 4.8 cm) showed a higher sensitivity (87.88%) and a lower specificity (56.55%) as compared to the earlier cut-off (< 3.5 cm) having 39.39% and 95.81% respectively.

Table 6: Diagnostic statistics based on cut-off values using ROC curve analysis, (n = 202)

Variables	New cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Area under curve	p - value
1. IIG (cm)	≤ 4.8	87.88	56.55	28.43	95.96	61.69	0.771	< 0.001
2. TMD (cm)	≤ 8.5	75.76	92.31	65.79	95.12	89.60	0.915	< 0.001
3. ML (cm)	> 11.5	69.70	49.11	21.10	89.25	52.48	0.614	0.042
4. SMD (cm)	≤ 16.5	87.89	91.72	67.44	97.48	91.09	0.947	< 0.001
5. HT/TMD	> 18.6	75.76	90.53	58.14	95.03	87.25	0.887	< 0.001
6. NC/TMD	> 4.1	96.97	79.29	45.07	99.24	80.20	0.935	< 0.001

Similarly, TMD (≤ 8.5 cm) showed a higher sensitivity and lower specificity as compared to the standard cut-off (< 6.5 cm), 75.76% and 92.31% *v/s* 6.06% and 100% respectively. ML (> 11.5 cm) provided a sensitivity (69.70%) higher than standard cut-off value (0%) and specificity (49.11%) lower than the standard value (97.63%). The sensitivity of the SMD using the new cut-off value (≤ 16.5 cm) was higher (87.89%) as against cut-off value < 13.5 cm (21.21%) but the specificity (91.72%) was found to be lower as compared to 99.41% by using standard cut-off.

The sensitivity of new HT/TMD ratio here (75.76%) and new NC/TMD ratio here (96.97%) was higher than that given by standard cut-off values (9.1 and 45.5 % respectively) and their specificity (HT/TMD–90.53% *versus* 98.02%, NC/TMD-79.29% *versus* 97.63%) was found to be lower. The *p* - value of all parameters with new cut-off value was < 0.001 except that of ML (*p* - value = 0.042). Table 7 summarizes the prediction of difficult intubation of combinations of the above mentioned parameters. The combination of (MP + ULBT + NC/TMD) and (MP + ULBT + TMD + NC/TMD) showed the highest sensitivity (75.76%), specificity (91.12%), PPV (62.50%) and NPV (95.06%). The *p* - value of all combinations was found to be significant (*p* < 0.001).

Table 7: Predictor statistics based on combinations of standard cut-off values (*n* = 202)

Variables	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	*p* - value
1. MP +ULBT	66.67	92.31	62.86	93.41	86.12	<0.001
2. MP+TMD	45.45	94.67	62.50	89.89	86.63	<0.001
3. MP+NC/TMD	60.61	93.49	64.52	92.48	88.12	<0.001
4. ULBT+TMD	54.55	97.63	81.82	91.67	90.58	<0.001
5. ULBT+ NC/TMD	69.70	95.27	74.19	94.15	91.09	<0.001
6. TMD+NC/TMD	45.45	97.63	78.95	90.16	89.11	<0.001
7. MP+ULBT+TMD	72.73	92.31	64.86	94.55	89.11	<0.001
8. MP+ULBT+NC/TMD	75.76	91.12	62.50	95.06	88.61	<0.001
9. MP+TMD+NC/TMD	60.61	93.49	64.52	92.40	88.12	<0.001
10. ULBT+TMD+NC/TMD	69.70	95.27	74.19	94.15	91.09	<0.001
11. MP + ULBT + TMD + NC/TMD	75.76	91.12	62.50	95.06	88.61	<0.001

NC/TMD – 45.45%) and specificity (TMD- 100%) using standard cut off values were used.

Parameters which had the highest individual sensitivities (MP- 39.39%, ULBT -48.48% and NC/TMD – 45.45%) and specificity (TMD- 100%) using standard cut off values were used.

Discussion

The significance of difficult or failed intubation is very well-recognized as a cause of morbidity and mortality. A test to predict difficult intubation should have high sensitivity, so that, it will identify most patients in whom intubation will truly be difficult. It should also have a high positive predictive value, so that, only a few patients with an airway actually easy to intubate are unnecessarily subjected to the protocol for management of a difficult airway. The ideal model for prediction of difficult intubation would have high sensitivity and specificity. Sensitivity and specificity are dependent on each other, an increase in one of them usually results in a decrease in the other. High specificity may also increase the positive predictive value despite low-sensitivity.

A parameter with high-sensitivity, low-specificity, and low-positive predictive value would incorrectly classify patients as having a difficult airway. However, these may only be a fraction of those that accompany the potentially serious outcome of unanticipated difficult tracheal intubation. Therefore, the sensitivity of a parameter is more important than the specificity.[19]

Defining a good predictive parameter for difficult intubation is challenging because many factors affect visualization of the larynx at intubation, such as the maximum mouth-opening distance, the circumference and length of the neck, and several other characteristics that may be difficult to accurately quantify. These include the compressibility of the tongue and soft tissues of the floor of the mouth and the extent of subluxation of the temporomandibular joint during laryngoscopy.

In addition, the ability of the person performing the intubation, cannot be easily incorporated into a standardized assessment.[1]

The present study, included 202 patients for preoperative assessment of the airway; we found that 16.3% (33 out of 202) of them had difficult intubation. There were no cases of failed intubation. The prevalence of difficult intubation in earlier studies was reported to be 1%–18%[2–5] depending on the criteria used to define it. A total of 33 patients had difficult intubation, out of which 24 were males. The preponderance of males with difficult intubation in our study could be due to the difference in anthropometry, muscularity and laxity of soft tissue in the neck between males and females. Equivocal results are available in literature.[15,17] The mean BMI of patients in Group A was significantly lower (p = 0.002) than that of patients with difficult intubation, which is at variance with other studies in literature[16,22]

In our study, 97 (57.4%) ASA Grade I patients had easy intubation and 12 (36.4%) had difficult intubation. Seventy two (42.6%) patients with ASA Grade II had easy intubation and 21 (63.6%) had difficult intubation. This difference was significant with p - value of 0.027. This too is at variance with other studies in literature. [23] We propose that this can be attributed to the effects of systemic diseases on the airway.

We compared Cormack-Lehane (CL) Grades with difficulty in intubation. None of the 108 patients with C-L Grade 1 had difficult intubation, while 1 out of 61 patients with C-L Grade 2 had difficult intubation. 96.67% (29 out of 30) patients with C-L Grade 3 and all 3 patients with C-L Grade 4 had difficult intubation.

In our study, there was a general increase in difficulty with intubation with increasing MP score 87 out of 90 patients with Malampatti Grade I , 73 out of 90 patients with MP Grade II had easy intubation and 13 out of 22 patients with MP III had difficult intubation. This was statistically significant (p - value < 0.001). There were no patients with MP Grade V in our study.

Sensitivity and Specificity of Individual tests

Mallampati et al.[9] found a significant correlation between preoperative grading and ease of laryngoscopy in their study done on 210 patients, reporting a sensitivity of 50% and specificity of 99% for the MP score. Cattano et al.[1] found the sensitivity, specificity, PPV and NPV of Mallampati score as 35%, 91%, 8% and 98% respectively in their study done on 1956 patients. Sensitivity and specificity in our study was similar, 39.39% and 95.81% respectively. The Positive Predictive Value was found to be higher (65%) and Negative Predictive Value (88.89%) lower. The Mallampati score was accurate in predicting easy intubation but could predict difficult intubation in only 39.39% of cases. Hence, it cannot be considered to be an accurate predictive test of difficult intubation. The is in concordance with the findings of Naquib et al.[20]

The Upper Lip Bite Test (ULBT), when tested initially had the potential to evaluate both jaw movement and buck teeth simultaneously, providing additional support for airway assessment. Khan et al.[11] compared ULBT with modified Mallampati classification in 300 patients and found that ULBT had higher accuracy. It had sensitivity, specificity, PPV and NPV of 76.5%, 88.7%, 28.9% and 98.4% respectively. In our study, it could predict 48.48% of difficult intubations and 97.63% of easy intubations, whereas PPV and NPV was 80% and 90.66% respectively.

Nichol and Zuck[12] suggested atlanto-occipital distance as a major anatomical factor that determines head extension. They stressed the importance of the position of the head and neck in direct laryngoscopy in order to achieve proper alignment of the axes of the oral cavity, pharynx and larynx. Tse et al.[21] found the sensitivity, specificity, PPV and NPV of neck extension ≤ 80° to be 21%, 93%, 18% and 87% respectively. We did not find any patients with difficult neck extension ≤ 80°, thus the sensitivity and PPV was 0.

The sensitivity, specificity, PPV and NPV of thyromental distance (< 6.5 cm) test in our study was found to be 6.06%, 100%, 100% and 84.5% respectively. It successfully predicted all patients with easy intubation. Among all the morphometric measurements, TMD has been studied as a predictor of difficult intubation with equivocal results.[3,22]

Reciever Operating Characteristic curves (ROC) are a graphical method to represent Sensitivity and Specificity of a test and the Area Under the Curve (AUC) is considered a good indicator of the overall efficiency of a test.[23]

When an ROC curve was used to determine a better cut-off for TMD; the sensitivity increased to 75.76% although the specificity decreased to 92.31% with the new cut-off (≤ 8.5 cm). Krobbuaben et al.[22] did not find any significant association between difficult laryngoscopy and Interincisor Gap (IIG ≤ 3.5 cm), unlike in our study (p < 0.001). IIG as

a parameter to predict difficult intubation had sensitivity of 21.21%, specificity of 99.41%, PPV of 87.50% and NPV of 86.50% . Using the ROC curve to determine the best cut-off value it was seen that with IIG ≤ 4.8 cm, the sensitivity increased to 87.88% and specificity decreased to 56.55%.

Interestingly, we did not find any correlation between mandibular length (ML< 9 cm) and difficult intubation. Merah et al.[24] also did not find any correlation between ML and difficult intubation but suggested that ML of atleast 9 cm should guarantee easy intubation. Kurtipek et al.[25] concluded that ML if used on its own, does not have much predictive value.

Sternomental Distance (SMD) can be a predictor of head and neck mobility; Ramdhani et al.[26] studied this parameter and found it to be superior to other tests in predicting difficult intubation. However, the patient group in their study was limited to women of childbearing age only. We found SMD (< 13.5 cm) to have sensitivity of 21.21%, specificity of 99.41%, PPV of 87.50% and NPV of 86.63%. The ROC curve showed a sensitivity of 87.89% and specificity of 91.72%, when new cut-off was taken as ≤ 16.5 cm.

Krobbuaben et al.[21] in their study found HT/TMD ≥ 23.5 was a determining factor for predicting a poor laryngeal view among Thai patients, with sensitivity, specificity, PPV and NPV of 77%, 66%, 24% and 95% respectively. HT/TMD (≥ 23.5) in our study showed low-sensitivity of 9.1%, specificity of 98.02%, PPV of 60% and NPV of 84.77%. ROC curve analysis was used to determine a new cut-off value (> 18.6), and it was found that the sensitivity increased to 75.76% and specificity decreased to 90.53%. This discrepancy may be due to the difference in morphologic charachteristics of Indian population.

Neck circumference to thyromental distance ratio (NC/TMD) was studied by Kim et al.[15] and evaluated as a new index on the assumption that obese patients with both a large neck circumference and a short-neck, might be more difficult to intubate than patients with a large-neck circumference or a short-neck alone. They found NC/TMD > 5 to have sensitivity, specificity, PPV and NPV of 88.2%, 83%, 45.5% and 97.8% respectively. This parameter showed a high-sensitivity (45.45%) in our study. Specificity, PPV and NPV was found to be 97.63%, 78.95% and 90.16%. The new cut-off, NC/TMD > 4.1 (as determined by the ROC curve) had higher-sensitivity (96.97%) but lower-specificity (79.29%).

It is evident from the discussion on individual clinical parameters that each of these tests are based on different anatomical factors of the airway and hence, combinations of individual tests may have higher predictive value in comparison with the value of each test alone. Several authors have combined predictive parameters and devised multivariate risk-index systems such as the El-Ganzouri or Wilson scores.[6–8] These scores contain multiple risk-factors, they are more time consuming to perform. All combination analysis showed a dramatic improvement in predictive values. Combining Mallampati test and Upper lip bite test improved the sensitivity to 66.67% and specificity to 92.3% and it has a better predictive value (PPV and NPV of 62.86% and 93.41% respectively) which is of definite significance.

Combination of ULBT and NC/TMD ratio gives indices of: sensitivity 69.70%, specificity 95.27%, PPV 74.19% and NPV-94.15%. This combination could predict more number of difficult intubations than any other two parameters combined together. Mallampati test and thyromental distance help in determining the relationship of the tongue with oral cavity and to determine the anterior mandibular space respectively. This combination had a sensitivity of 45.45%, specificity of 94.67%, PPV of 62.5% and NPV of 89.89%. Mallampati test and NC/TMD ratio when combined together could predict 60.61% of the difficult intubation and 93.49% of the easy intubation. It had 64.52% PPV and NPV of 92.48%.

We selected a total of four parameters, as suggested by Rudin Domi,[27] which had the highest-sensitivity or specificity individually (MP - sensitivity of 39.39%, ULBT - sensitivity of 48.48%, NC/TMD - sensitivity of 45.45%, TMD - specificity 100%) from our study. When MP class, ULBT and NC/TMD ratio were combined together, it could predict difficult intubation in 75.76% and easy intubation in 91.12%. It had a PPV of 62.50% and NPV of 95.06%. This combination provided the best sensitivity of predicting difficult intubation. We are in the process of developing a scoring system based on these findings and which is undergoing validation.

Conclusion

We studied various parameters like Mallampati class, Neck movements, Upper lip bite test, Interincisor gap, thyromental distance, mandibular length, sternomental distance, Height to thyromental distance ratio and Neck circumference to thyromental distance ratio to predict difficult

intubation. Amongst them, Upper lip bite test was found to predict highest number of difficult intubation (48.48%). A combination of Mallampati class, upper lip bite test, neck circumference to thyromental distance ratio, had the highest predictive value (sensitivity - 75.76%, specificity - 91.12%, Postive Predictive Value - 62.5% and Negative Predictive Value - 95.06%). We suggest that if the ROC of a parameter were used, it would give a more precise estimate of sensitivity and specificity.

References

1. Cattano D, Panicucci E, Paolicchi A, et al. Risk-factors assessment of the difficult airway: An Italian survey of 1956 patients. Anesth Analg 2004;99:1774–779.
2. Shiga T, Wajima Z, Inoue T, et al. Predicting difficult intubation in apparently normal patients: A meta-analysis of bedside screening test performance. Anesthesiology 2005;103:429–37.
3. Rose DK, Cohen MM. The airway: Problems and predictions in 18,500 patients. Can J Anesth 1994;41:372–83.
4. Lienhart A, Auroy Y, Pequignot F, et al. E. Survey of anesthesia-related mortality in France. Anesthesiology 2006;105:1087–97.
5. Mallampatti SR, Gatt SP, Gugino LD, et al. A clinical sign to predict difficult tracheal intubation: A prospective study. Can Anesthe Soc J 1985;32:429–34.
6. Wilson ME, Spiegelhalter D, Robertson JA, et al. Predicting difficult intubation. Br J Anesth 1988;61:211–16.
7. El Ganzouri AR, Mc Carthy RJ, Tuman KJ, et al. Preoperative airway assessment: Predictive value of a multivariate risk-index. Anesth Analg 1996;82:1197–1204.
8. Arne J, Descoins P, Fusciardi J, et al. Preoperative assessment for difficult intubation in general and ENT surgery: Predictive value of a clinical multivariate risk-index. Br J Anesth 1998;80:140–46.
9. Mallampatti SR. Clinical assessment of the airway. Anesthesiology Clinics of North America 1995;13(2):301–08.
10. Chou H, Wu T. Thyromental distance: Shouldn't we redefine its role in the prediction of difficult laryngoscopy? Acta Anesthesiol Scand 1998;42:1.
11. Khan ZH, Kashfi A, Ebrahimkhani E. A Comparison of the Upper Lip Bite Test (a simple new technique) with modified mallampati classification in predicting difficulty in endotracheal intubation: A prospective blinded study. Anesth Analg 2003;96:595–59.
12. Nichol HC, Zuck D. Difficult laryngoscopy: The "anterior" larynx and the atlanto-occipital gap. Br J Anesth 1983;55:141–43.
13. Krobbuaban B, Diregpoke S, Kumkeaw S, et al. The predictive value of the height ratio and thyromental distance: Four predictive tests for difficult laryngoscopy. Anesth Analg 2005; 101:1542–45.
14. Khan ZH, Mohammadi M, Rasouli MR, et al. The diagnostic value of the Upper Lip Bite Test combined with sternomental distance, thyromental distance, and interincisor distance for prediction of easy laryngoscopy and intubation: A prospective study. Anesth Analg 2009;109:822–24.
15. Kim WH, Ahn HJ, Lee CJ, et al. Neck circumference to thyromental distance ratio: A new predictor of difficult intubation in obese patients. Br J Anesth 2011;106(5): 743–38.
16. Rocke DA, Murray WB, Rout CC, Gouws E. Relative risk-analysis of factors associated with difficult intubation in obstetric anesthesia. Anesthesiology 1992;77:67–73.
17. Buderer NM. Statistical methodology: I incorporating the prevalence of disease into the sample size calculation for sensitivity and specificity. Acad Emerg Med 1996;3: 895–900.
18. Seo HS, Lee JG, Kim DS, et al. Predictors of difficult intubation defined by the Intubation Difficulty Scale (IDS): Predictive value of 7 airway assessment factors. Korean J Anesthesiol 2012 Dec;63(6):491–97.
19. Parikh R, Mathai A, Parikh S, et al. Understanding and using sensitivity, specificity and predictive values. Indian J Ophthalmol 2008;56(1):45–50. doi:10.4103/0301-4738.37595
20. Naquib M, Scamman FL, O'Sullivan C, et al. Predictive performance of three multivariate difficult tracheal intubation models: A double-blind, case-controlled study. Anesth Analg 2006;102:818–24.
21. Tse JC, Rimm EB, Hussain A. Predicting difficult endotracheal intubation in surgical patients scheduled for general anesthesia: A prospective blind study. Anesth Analg 1995;81:254–58.
22. Krobbuaban B, Diregpoke S, Kumkeaw S, et al. The predictive value of the height ratio and thyromental distance: Four predictive tests for difficult laryngoscopy. Anesth Analg 2005;101:1542–45.
23. Park SH, Goo JM, Jo CH. Receiver Operating Characteristic (ROC) curve: Practical review for radiologists. Korean J Radiol 2004;5(1):11–18. doi:10.3348/kjr. 2004.5.1.11)
24. Merah NA, Foulkes-Crabbe DJ, Kushimo OT, et al. Prediction of difficult laryngoscopy in a population of Nigerian obstetric patients. West Afr J Med 2004;23: 38–41.

25. Kurtipek O, Isik B, Arslan M, et al. A study to investigate the relationship between difficult intubation and prediction criterion of difficult intubation in patients with obstructive sleep apnea syndrome. J Res Med Sci 2012;17:615–20.
26. Ramadhani SAL, Mohammed LA, Rocke DA, et al. Sternomental distance as the sole predictor of difficult laryngoscopy in obstetric anesthesia. Br J Anesth 1996;77: 312–26.
27. Rudin Domi. A comparison of Wilson sum score and combination Mallampati, Thyromental and Sternomental Distances for predicting difficult intubation. Macedonian Journal of Medical Sciences 2009 Jun 15;2(2):141–44.

Original Research Article

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A Comparative Study of Injection 0.5% Bupivacaine and Injection 0.75% Ropivacaine for Their Duration of Anesthesia/Analgesia in Transversus Abdominis Plane Block for Unilateral Inguinal Hernia Repair under Ultrasound Guidance

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Abstract

Background: The transversus abdominus plane block is a regional anesthesia technique first described in 2001. It is useful in procedures requiring nerve block in the anterior abdominal wall region from T6-L1. It was first used as a blind landmark technique. But more recently it has been performed under ultrasound guidance. TAP blocks are important because they can be used as an alternative analgesic solution in surgery. The purpose of our study was to evaluate effectiveness of TAP block to provide effective postoperative analgesia in patients undergoing inguinal hernia repair surgery. *Materials and Methods:* Our study was conducted in our institution under ultrasound guidance. Total 40 patients undergoing unilateral inguinal hernioplasty surgery under spinal anesthesia were included in the study. Patients were divided into 2 groups of 20 each. *Group B* - Patients receiving USG-TAP block at the end of surgery with 20 ml Inj. Bupivacaine 0.50% - 20 patients. *Group R* - Patients receiving USG-TAP block at the end of surgery with 20 ml Inj. Ropivacaine 0.75% - 20 patients. Patient monitored every two hours upto 24 hours postoperatively for pulse rate, BP, pain by VAS score and complications if any. Pain was assessed by visual analog score from 0 to 10. Recession of motor block noted by movement of ankle and knee joint. *Results:* The mean pain score on VAS in Group B and Group R was 4.75 and 4.89 respectively, 24 hours after surgery. The difference in the two groups was statistically insignificant (p - value > 0.05). VAS score was the same in both the groups at all the time in first 24 hours. *Conclusion:* About 15 ml of 0.5 % bupivacaine or 15 ml of 0.75 % ropivacaine for transverse abdominis plane block produces satisfactory and comparable sensory block, related to duration, analgesia and VAS score. The hemodynamics were stable in both the groups. The lower CNS and cardio toxicity of ropivacaine may help in reducing the risk to the patients. There was no much clinical difference in duration, dose of analgesia and VAS score among both the groups, when injected in equal volume for TAP block under ultrasound guidance. Ropivacaine has a potentially improved safety profile when compared with Bupivacaine.

Keywords: Transversus abdominus plane block; TAP block; Ropivacaine; Bupivacaine.

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Introduction

The abdominal wall forms a major source of pain following abdominal surgery. Even a small surgery like inguinal herniorrhaphy may be followed by risk of chronic pain in about 5–10% patients with significant effect on daily activities if postoperative analgesia is not taken care of. The usual trend is to prescribe an opioid or a NSAID for postoperative analgesia. The opioids have number of side effects like respiratory depression, emesis, reduction in gut motility, sedation etc. NSAIDS have certain side-effects like hemostasis alteration, renal dysfunction, gastrointestinal hemorrhage, etc. However, in regional analgesic technique, drugs have peripheral site of action and hence minimal systemic side-effects. Hence, regional anesthetic technique has gained wide spread importance in postoperative analgesia regimen. Transversus Abdominis Plane (TAP) block is one of such regional blocks. It provides analgesia after lower abdominal surgery particularly where parietal wall pain forms major component of pain. It is physician's duty to rescue the patients from surgical pain by the most possible mean. Now, postoperative pain control is generally best managed by anesthesiologists, because they offer regional anesthetic techniques as well as pharmacological expertise in analgesics.

Inguinal hernia repair surgery is one of the most common surgery performed in general population. Postoperative analgesia is essential to provide comfort and restoration of functions like breathing, cough, movement and communication effectively. Use of opioids and NSAIDS can result in significant adverse effects. Other techniques like rectus abdominis sheath block, paravertebral block, ilioinguinal/iliohypogastric block, local anesthetic infiltration etc. are also tested. Yet, these have disadvantages as they are not easy to perform, do not give adequate analgesia, do not produce long enough analgesic duration etc. The latest trend is the practice of two or more analgesic approach simultaneously called multimodal analgesia. It can produce better pain control, reduce the individual dose of the agent and thereby lowers cost, low side effect and more therapeutic safety. Over recent years, Transversus Abdominis Plane (TAP) block became a part of multimodal analgesia.

TAP is a neuro fascial plane between the Internal Oblique (IO) and Transversus Abdominis (TA) muscle of the abdominal wall through which all sensory nerves supply the parietal peritoneum, skin and muscles of anterior abdominal wall. So, it is a novel approach to block these sensory nerves by injecting local anesthetic within the Transversus Abdominis Plane (TAP), termed as TAP block.[1] Because the sensory afferent nerves run between the abdominal muscles, these nerves can be blocked and postoperative pain can be managed. This has been found to be an effective method in colon surgery, cesarean section with midline incision and prostatectomy and it is also effective in managing pain following inguinal hernia surgeries. TAP block was first described by Rafi et al.[2] in 2001 and was further developed and tested by McDonnell et al. in 2004.[3] Ultrasonography guided nerve blocks offer the advantage of real-time imaging of the needle and injection spread. Use of ultrasonography for placement of the needle and drug distribution can lower the risks associated with TAP block and increases the safety and effectiveness of the block particularly in obese patients.[4]

TAP block is easy to perform, technically simple, pharmacologically safe, effective and economically cheap. TAP block is a part of multimodal analgesic regimen and provides improved analgesia, decrease opioid consumption and its side-effects during postoperative period. McDonnell et al.[5,6] demonstrated that the Transversus Abdominis Plane (TAP) block reduces morphine use after abdominal surgery, including cesarean delivery. He also stated that landmark based TAP block can be used successfully to provide postoperative pain relief after cesarean delivery.

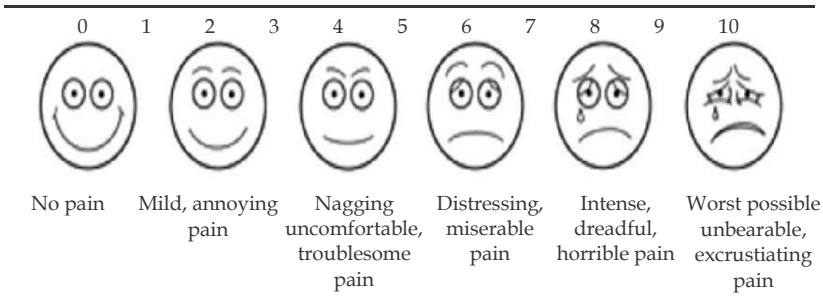

Fig. 1: VAS Score

Grade 0 (0–1): Good analgesia;

Grade 1 (1–4): moderate analgesia;

Grade 2 (4–7): mild analgesia;

Grade 3 (7–10): No analgesia.

Materials and Methods

Our study was conducted in our institution under ultrasound guidance. Total 40 patients undergoing unilateral inguinal hernioplasty surgery under spinal anesthesia were included in the study. Patients were divided into 2 groups of 20 each. *Group B* - Patients receiving USG - TAP block at the end of surgery with 20 ml Inj. Bupivacaine 0.50% - 20 patients. *Group R* - Patients receiving USG - TAP block at the end of surgery with 20 ml Inj. Ropivacaine 0.75% - 20 patients.

Inclusion Criteria

i. Male & Female patients giving written and informed consent for the study;
ii. ASA Grade I & II;
iii. All patients of age group 20 to 65 years of age;
iv. Patients undergoing unilateral inguinal hernia surgery under spinal anesthesia.

Exclusion Criteria

1. Patient refusal;
2. Bleeding disorders;
3. Allergy to local anesthetics;
4. Infection at local site of block;
5. Hemodynamic instability;
6. Contraindications for spinal anesthesia;
7. ASA III & above.

Materials Required

1. Ultrasound machine with a linear transducer (7–13 MHz);
2. Sterile gloves;
3. Ultrasound probe cover;
4. Antiseptic solution for skin disinfection;
5. Ultrasound gel;
6. 23-gauge spinal needle;
7. 20 ml syringe with injection tubing.

A written informed consent was obtained in each case in their vernacular language.

Methodology

After Ethical Committee approval, we investigated forty patients undergoing unilateral inguinal hernioplasty. The patients were randomized and allotted to two groups by computer generated tables to undergo TAP block with bupivacaine (n = 20) [Group B] *vs* ropivacaine (n = 20) [Group R].

Blinding was maintained as the person injecting the solution while giving TAP block was unaware of whether it is bupivacaine or ropivacaine as it was prepared by another person in operation theatre. As well as the person evaluating the VAS score was not knowing whether the subject had received bupivacaine or ropivacaine.

Consent and fasting status were confirmed. In the operation theatre, standard monitoring including ECG, noninvasive BP, pulse oximeter were attached. Peripheral line was taken with 18G IV cannula. As per the institutional protocol, patients were premedicated with intravenous ranitidine and intravenous ondansetron. All patients received standardized spinal anesthesia with 0.5% bupivacaine 3.5 ml in sitting position. Level of analgesia achieved noted. Block assessed by pin prick method. Patients monitored intraoperatively. Hypotension was taken as fall in systolic blood pressure > 20% of base line and treated with incremental doses of mepheneteramine 6 mg and bolus of 200 ml ringer lactate. No analgesic or sedation was given to patient intraoperatively. Vitals were monitored at 5, 10, 15, 30, 45, 60, 75, 90, 120... mints till the end of surgery. Any complications like bradycardia, hypotension were observed. At the end of surgery, Petits triangle was identified on the side of surgery and USG guided TAP block performed.

Results

Majority of the patients were in age group of 30–50 years in both the group. Both groups were comparable in terms of age, weight and height. The mean age in Group B and Group R was 39.73 years and 40.14 years respectively. There was no statistically significant difference in mean age (p = 0.137), The mean weight in Group B and Group R was 70.41 kg & 73.24 kg respectively. There was no statistically significant difference in mean weight (p = 0.325). The mean height in Group B and Group R was 163.54 cm and 164.25 cm respectively. There was no statistically significant difference in mean weight (p = 0.128).

Mean duration of surgery in Group B was 61.49

Table 1: Comparision of both groups in terms of age, weight and height

Characteristics	Group B	Group B	*p* - value
Age	39.73 ± 6.78 years	40.14 ± 7.25 years	0.137
Weight	70.41 ± 5.24 kg	73.24 ± 4.21 kg	0.325
Height	163.54 ± 3.1 cm	164.25 ± 3.2 cm	0.128

min and 61.58 min in Group R respectively. There was no statistically significant difference in total duration required for surgery ($p = 0.541$).

Table 2: Mean duration of surgery

Mean Duration of Surgery	Group B	Group R	*p* - value
Duration of Surgery	61.49 ± 9.54 min	61.58 ± 8.21 min	0.541

The mean pain VAS Score in Group B and Group R was 0.03 and 0.05 respectively 30 minutes after surgery. The difference in the two groups was statistically insignificant (p - value > 0.05). The mean pain VAS Score in Group B and Group R was 0.23 and 0.35 respectively, 60 mins after surgery. The difference in the two groups was statistically insignificant (p - value > 0.05). The mean pain VAS Score in Group B and Group R was 0.32 and 0.34 respectively 2 hour after surgery. The difference in the two groups was statistically insignificant (p - value > 0.05). The mean pain VAS Score in Group B and Group R was 1.63 and 1.59 respectively 4 hrs after surgery. The difference in the two groups was statistically insignificant (p - value > 0.05). The mean pain VAS Score in Group B and Group R was 2.43 and 2.32 respectively 6 hours after surgery. The difference in the two groups was statistically insignificant (p - value > 0.05). The mean pain VAS Score in Group B and Group S was 3.62 and 3.72 respectively 8 hours after surgery. The difference in the two groups was statistically insignificant (p - value > 0.05). The mean pain VAS Score in Group B and Group R was 4.12 and 4.16 respectively 12 hours after surgery. The difference in the two groups was statistically insignificant (p - value > 0.05). The mean pain VAS Score in Group B and Group R was 4.62 and 4.69 respectively, 18 hours after surgery. The difference in the two groups was statistically insignificant (p - value > 0.05). The mean pain score on VAS in Group B and Group R was 4.75 and 4.89 respectively, 24 hours after surgery. The difference in the two groups was statistically insignificant (p - value > 0.05). VAS score was the same in both the groups at all the time in first 24 hours.

Table 3: Mean VAS Score

Time Interval	Group B	Group R	*p* - value
0 Min	0.00	0.00	> 0.05
30 Min	0.03 ± 0.18	0.05 ± 0.6	> 0.05
60 Min	0.23 ± 0.43	0.35 ± 0.3	> 0.05
2 Hr	0.32 ± 0.64	0.34 ± 0.6	> 0.05
4 Hr	1.63 ± 0.45	1.59 ± 0.9	> 0.05
6 Hr	2.43 ± 0.5	2.32 ± 1.4	> 0.05
8 Hr	3.62 ± 0.45	3.72 ± 1.8	> 0.05
12 Hr	4.12 ± 0.91	4.16 ± 1.4	> 0.05
18 Hr	4.62 ± 0.62	4.69 ± 1.3	> 0.05
24 Hr	4.75 ± 0.56	4.89 ± 0.8	> 0.05

Discussion

Elective inguinal hernia repair is one of the most common surgical procedures performed. Adequate postoperative analgesia facilitates earlier patient mobilization and earlier fulfilment of discharge criteria from postoperative wards. Pain after inguinal hernia repair is more pronounced in the first two postoperative days. Patients undergoing inguinal hernia repair commonly receive intravenous opioids for postoperative analgesia. However, systemic

opioids provide only static analgesia; but do not alleviate the dynamic component of pain. Dynamic analgesia is provided mainly by regional anesthetic techniques in the postoperative period. With the advent of truncal nerve blocks there seem to be an alternative to epidural analgesia to provide postoperative pain relief. However, failure rate is high in truncal nerve blocks in anatomic landmark based approaches. The most common approach to postoperative pain relief is multimodal using NSAIDs, opioids and local infiltration of local anesthetic. Opioids are effective for treatment of postoperative pain but can cause adverse effects such as nausea, vomiting, decreased gastrointestinal motility, respiratory depression and sedation which further increase the morbidity of the patient. Local infiltration does not relieve deep muscular pain and NSAID are nephrotoxic. Peripheral nerve blocks with local anesthetics are a method that may be used in inguinal hernia surgeries for pain management. Now-a-days, transverse abdominal plane blocks are being performed more commonly for such procedures. However, no uniform opinion exists between the choice of drugs to be used and it is still not extensively implemented due to the complications encountered during the procedure. In our study, we have compared the efficacy of two different drugs i.e., 0.5% bupivacaine and 0.75% ropivacaine in ultrasound-guided TAP blocks performed for patients undergoing unilateral inguinal hernioplasty.

Based on the observation and results obtained in our study involving 20 patients in each group, results of our study were discussed in detail by comparing with the obtained data and available evidence in the literature. Immediate pain relief by TAP block in the postoperative period has several implications in recovery of these patients, such as VAS score, reduced side effects of opioids and analgesics and better quality of analgesia.

Mean duration of surgery in Group B was 61.49 ± 9.54 min and Group R 61.58 ± 8.21 min. There was no statistically significant difference in total duration required for surgery in two groups (p = 0.541). There was no significant difference between the two groups with respect to the duration of surgery.

In patients under the bupivacaine group, 60% belonged ASA I & 40% to ASA II. In the ropivacaine group, 55% belonged to ASA I & 45% to ASA II. Thus, majority of the patients were of ASA I category and there was no statistically significant difference between both the groups.

The mean pain score on VAS in Group B at 0, 30 min, 60 min, 2 hr, 4 hrs, 6 hrs, 8 hrs, 12, 18 and 24 hrs were 0, 0.03 ± 0.18, 0.23 ± 0.43, 0.32 ± 0.64,1.63 ± 0.45, 2.43 ± 0.5, 3.62 ± 0.45, 4.12 ± 0.91, 4.62 ± 0.62 and 4.75 ± 0.56 respectively.

The mean pain score on VAS in Group R at 0, 30 min, 60 min, 2 hrs, 4 hrs, 6 hrs, 8 hrs,12 hrs, 18 hrs and 24 hrs were 0, 0.05 ± 0.6, 0.35 ± 0.3, 0.34 ± 0.6, 1.59 ± 0.9, 2.32 ± 1.4, 3.72 ± 1.8, 4.16 ± 1.4, 4.69 ± 1.3 and 4.89 ± 0.8 respectively. The difference in the two groups was statistically insignificant (p - value > 0.05). Thus, the mean pain VAS score was the same in both the groups at all the time in first 24 hours. This demonstrates that the US-TAP block in both groups provide same effect & prolonged analgesia in the initial postoperative period. This study very well correlates with the study of Siddiqui et al. who in his analysis of seven randomized, double-blinded studies of both blind and ultrasound guided TAP technique for postoperative analgesia in infraumbilical surgeries demonstrated average and significant reduction in IV PCA requirement as a part of multimodal analgesic regimen. He also demonstrated reduced VAS score both at rest and movement in the early postoperative period. He also found out there was reduced incidence of postoperative nausea, vomiting and sedation.

Conclusion

About 15 ml of 0.5 % bupivacaine or 15 ml of 0.75 % ropivacaine for transverse abdominis plane block produces satisfactory and comparable sensory block, related to duration, analgesia and VAS score. The lower CNS and cardio toxicity of ropivacaine may help in reducing the risk to the patients. There was no much clinical difference in duration, dose of analgesia and VAS score among both the groups, when injected in equal volume for TAP block under ultrasound guidance. Ropivacaine has a potentially improved safety profile when compared with Bupivacaine.

References

1. Paul Bidhan, Banik Debasis, AKM Shamsul Alam. TAP block in postoperative analgesia, a first time clinical trial in Bangladesh. JBSA 2014;27(1):3–11.
2. Rafi A. Abdominal field block: A new approach *via* the lumbar triangle. Anesthesia 2001;56: 1024–1026.
3. McDonnell J, O' Donnell B, Tuite D, et al. The regional abdominal field infiltration (RAFI)

technique: Computerized tomographic and anatomical identification of a novel approach to the transverses abdominis neuro-vascular fascial plane. Anesthesiology 2004;101:A 899.

4. Shibata Y, Sato Y, Fujiwara Y, et el. Transversus abdominis plane block Anesth Analg 2007;105:883.
5. O' Donnell BD, McDonnell JG, Mc Shane AJ. The Transversus Abdominis Plane (TAP) block in open retropubic prostatectomy. Regional Anesthesia and Pain Medicine 2006;31:91.
6. Carney J, McDonnell JG, Ochana A. The transversus abdominis plane block provides effective postoperative analgesia in patients undergoing total abdominal hysterectomy. Anesthesia Analgesia 2008;107:2056–60.

Original Research Article

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Use of Surgical Plethysmographic Index to Assess the Effect of Dexmedetomidine on Hemodynamic Response to Intubation and Surgical Stress

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Abstract

Aims: To study the use of surgical plethysmographic index in assessing the effects of dexmedetomidine in attenuating the hemodynamic stress response. *Materials and Methods:* A two group comparative study was done on 60 patients of ASA I and II patients undergoing elective laproscopic cholecystectomy under general anesthesia in a tertiary referral hospital setting. Group F received 100 ml of normal saline while Group D received 0.5 μg/kg of dexmedetomidine in 100 ml normal saline. *Results:* We found that rise in Heart Rate, Systolic and Diastolic BP and Mean Arterial Pressure was significantly attenuated in the dexmedetomidine group. The Surgical plethysmographic index (SPI) was also reduced. The SPI changed earlier than heart rate and blood pressure in response to stimulation. Opioid and propofol need was also significantly reduced. Endocrine stress response was also attenuated as noted by the lower readings of blood sugar during the surgery in the dexmedtomidine group. *Conclusion:* Surgical Plethysmographic Index is an effective indicator of analgesic depth. Dexmedetomidine attenuates the hemodynamic and neuroendocrine stress response to intubation and surgery and has opioid and anesthetic sparing effects.

Keywords: Surgical plethysmography index; Dexmedetomidine; Heart rate; Mean arterial pressure; Endocrine stress response.

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Introduction

Painful stimulation causes sympathetic responses of the autonomic nervous system. During a surgery, such responses are normally suppressed by analgesic medication. If administration of analgesia is inadequate relative to the level of the stimulation, the patient may show responses such as increased heart rate and peripheral vasoconstriction.[1]

Dexmedetomidine was introduced in clinical practice in the USA in 1999 and was initially approved by the FDA only as a short-term (< 24 hours) sedative for ventilated adult patients in the ICU but is now used widely in anesthesia practice as an analgesic.[2]

In our study, we seek to assess the analgesic effectiveness in adding dexmedetomidine to the standard anesthetic medication by measuring the attenuation of changes in the heart rate and blood pressure and the Surgical Plethysmograhic Index

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(SPI) during endotracheal intubation and first surgical incision. The SPI is a novel index which derives the changes in heart rate and blood pressure from the plethysmographic signal that is measured by a pulse oximeter.[3]

The opioid and anesthetic sparing effects of dexmedetomidine were also assessed and effectiveness in attenuating endocrine stress response was measured indirectly by change in blood glucose levels.

Objective

1. To compare the hemodynamic response in relation to heart rate and mean arterial pressure in patients following intubation and first surgical incision;
2. To estimate the difference in surgical plethysmographic index between the two groups following tracheal intubation and first surgical incision;
3. Correlation of surgical plethysmographic index with heart rate and mean arterial pressure;
4. To compare propofol consumption in the two groups;
5. To compare opioid consumption in the two groups;
6. To compare neuroendocrine stress response by estimating blood glucose levels in the two groups one hour after incision.

Materials and Methods

After the approval from the hospital ethics committee, on 23rd November 2017, this two group comparative study was conducted in a tertiary referral hospital setting on 60 patients posted for elective laproscopic cholecystectomy, over a period of 15 months from January 2018 to June 2019. Written informed consent was obtained from all patients who participated in the study. The operative surgeon also was duly informed.

Inclusion Criteria

- ASA I and II class of patients. Age between 18 and 60 years.

Exclusion Criteria

- Conversion to open procedure. Patients with chronic obstructive pulmonary disease;
- Patients with anticipated difficult airway. Day care patients. Obese patients BMI > 30 kg/m^2. Patients with hypothyroidism. Pregnant and lactating mothers.

Sample size

Based on the study by Bajwa et al.[4] and using the formula. Ref. Kumar & Bhalerao[5]

$$n = \frac{2(Z_\alpha + Z_{1-\beta})^{2\sigma^2}}{\Delta^2}$$

In order to get a 5% level of significance and 80% power, the number of patients required in each group was 30, with a total of 60 patients.

Method of allocation used: Sequential. The first 30 consecutive patients were allotted to Group F and the next 30 were allotted to Group D.

Protocol

Preanesthetic evaluation, Written and informed consent was done on the evening before surgery as per our hospital protocol. Patients were allocated into either of Two Groups, Group D and group F of 30 patients each. Group D received 0.5 μg/kg of dexmedetomidine. Group F received normal saline. Premedication was done as per the hospital protocol for both groups similarly. On receiving the patient, Electrocardiogram (ECG), Noninvasive Blood Pressure (NIBP), pulse oximeter and temperature probe were connected from AISYS-CS^2 (R) machine. Surgical Plesthysmographic Index (SPI) recording was turned on. Baseline readings were noted.

Heart rate, systolic, diastolic and mean arterial blood pressure, and surgical plethysmographic index were recorded during the administration of the drug, after premedication, after induction, every minute for the first 5 minutes after intubation, thereafter, every 5 minutes, on surgical incision and every minute for the first 5 minutes after incision and thereafter, for every 5 minutes. Random blood sugar was recorded at surgical incision and 1 hour postincision.

On receiving the patients in PACU, HR, SBP, DBP, MAP and Modified Ramsay Sedation Score were noted on arrival, 30 min and 60 min after arrival.

Results

The mean age of patients in Group F was 41.83 years and that of patients in Group D was 37.2 years. Not

significant (p = 0.100). The number of males and females in Group F were 14 and 16 respectively and in Group D were 14 and 16 respectively. Not significant. (p = 1.000)

The mean BMI of patients in Group F was 25.37 kg/m^2 and that of Group D was 25.39 kg/m^2. Not significant, (p = 0.975).

The mean heart rate of patients in the both groups was comparable at baseline (p = 0.703). We observed that the percentage drop in heart rate from baseline to after premedication in Group F was 6.85% and that of Group D was 10.75%, which was not significant (p = 0.146). At intubation, the mean heart rate in Group D was 73.83 bpm which was significantly lower than that of Group F's mean 83.43 bpm (p = 0.002). From "1 minute postintubation" to "5 minutes postintubation", and from "0 minutes at incision to 5 minutes postincision" and at 30 minutes, 60 minutes and 90 minutes postcompletion of drug administration the heart rate of patients in Group D was significantly lower than that of Group F (p < 0.001). These differences normalized at 120 minutes, shown in (Table 1).

Table 1: Comparison of Heart rate (bpm) between the two groups

Heart rate (bpm)	Group F	Group D	p - value
Baseline	82.93 ± 16.63	81.60 ± 9.28	0.703
After premedication	76.90 ± 13.61	72.67 ± 7.88	0.146
Intubation			
0 min	83.43 ± 14.07	73.83 ± 8.79	0.002**
1 min	101.57 ± 13.61	73.40 ± 8.72	< 0.001**
2 min	98.43 ± 13.33	72.73 ± 9.62	< 0.001**
3 min	94.60 ± 13.96	72.10 ± 8.81	< 0.001**
4 min	92.87 ± 13.80	71.37 ± 9.79	< 0.001**
5 min	88.97 ± 13.83	70.37 ± 8.78	< 0.001**
Incision			
0 min	87.60 ± 11.90	68.70 ± 9.40	< 0.001**
1 min	99.13 ± 12.43	68.70 ± 8.73	< 0.001**
2 min	97.63 ± 12.83	68.17 ± 9.14	< 0.001**
3 min	93.97 ± 12.19	67.10 ± 8.34	< 0.001**
4 min	91.07 ± 9.87	67.90 ± 9.03	< 0.001**
5 min	88.80 ± 9.75	67.20 ± 9.09	< 0.001**
Postdrug#			
30 min	86.80 ± 9.69	66.20 ± 6.83	< 0.001**
60 min	91.77 ± 9.02	66.53 ± 5.41	< 0.001**
90 min	80.73 ± 13.44	63.97 ± 12.98	< 0.001**
120 min	73.17 ± 10.37	67.83 ± 4.62	0.013*

#: Post drug - time after completion of administration of premedication.

The Mean Arterial Blood Pressure (MAP) in both the groups at baseline was comparable. After premedication, MAP in Group D was significantly lower than Group F (p = 0.001). The MAP in Group F at intubation i.e. 0 minutes was significantly lower than Group D. MAP from 1 minute postintubation to 3 minutes and 4 minutes postintubation was significantly higher in Group F when compared to Group D (p < 0.001). At 5 minutes postintubation, there was no significant difference in the MAP between the two groups (p = 0.953).

From 1 minute postincision to 4 minutes postincision, MAP in Group F was significantly higher as compared to Group D (p < 0.001). MAP at 30 minutes and 60 minutes postdrug administration in Group D was significantly lower than Group F. MAP in Group F was lower than Group D at 90 minutes, however, the difference was only moderately significant (p = 0.022). At 120 minutes, there was no statistically significant difference in the MAP between the two groups (p = 0.504), (Table 2).

Table 2: Comparison of SBP (mm Hg) between the two groups

SBP (mm Hg)	Group F	Group D	*p* - value
Baseline	129.20 ± 13.29	126.27 ± 9.66	0.240
After premedication	123.10 ± 12.58	112.93 ± 8.82	0.001**
Intubation			
0 min	104.53 ± 9.46	109.00 ± 8.59	0.061 +
1 min	143.83 ± 11.14	111.63 ± 7.48	< 0.001**
2 min	136.60 ± 9.82	109.77 ± 8.79	< 0.001**
3 min	125.63 ± 9.56	108.23 ± 8.33	< 0.001**
4 min	114.43 ± 9.11	107.30 ± 9.09	0.004**
5 min	103.97 ± 9.12	105.63 ± 8.45	0.466
Incision			
0 min	100.23 ± 8.38	102.27 ± 7.79	0.334
1 min	133.43 ± 11.22	101.83 ± 9.01	< 0.001**
2 min	130.57 ± 12.31	101.10 ± 8.86	< 0.001**
3 min	121.37 ± 11.39	101.60 ± 8.61	< 0.001**
4 min	105.23 ± 8.70	100.77 ± 8.31	0.047*
5 min	99.83 ± 6.52	100.13 ± 8.82	0.881

The baseline systolic blood pressure in both groups were comparable (p = 0.240). After completion of premedication, SBP in Group D was significantly lower than Group F (p < 0.001). At intubation (0 minutes), the SBP in Group F fell by 18.88% from the baseline. At 1 and 4 minutes postintubation, systolic blood pressure in Group D was significantly lower than Group F (p = 0.004). Difference in systolic blood pressure at 5 minutes postintubation and at 0 minutes at incision was statistically insignificant.

The SBP was significantly higher in Group F from 1 minute postincision to 3 minutes postincision (p < 0.001). At 4 minutes postincision, the difference in systolic blood pressure in both groups was only moderately significant (p = 0.047). By the 5^{th} minute postincision, systolic blood pressure was comparable in both the groups (p = 0.881), (Table 3).

Table 3: Comparison of MAP (mm Hg) between the two groups

MAP (mm Hg)	Group F	Group D	*p* - value
Baseline	94.10 ± 7.44	91.83 ± 7.36	0.109
After premedication	89.70 ± 6.71	83.60 ± 6.48	0.001**
Intubation			
0 min	74.30 ± 5.97	81.53 ± 5.83	< 0.001**
1 min	103.00 ± 8.28	83.13 ± 6.52	< 0.001**
2 min	95.73 ± 8.29	81.93 ± 7.04	< 0.001**
3 min	90.03 ± 7.35	80.30 ± 6.08	< 0.001**
4 min	84.60 ± 7.30	79.10 ± 6.59	0.003**
5 min	77.93 ± 6.52	78.03 ± 6.69	0.953
Incision			
0 min	75.23 ± 6.21	76.07 ± 5.50	0.584
1 min	97.17 ± 7.85	74.77 ± 6.70	< 0.001**
2 min	91.83 ± 8.09	74.37 ± 7.80	< 0.001**
3 min	86.60 ± 8.50	72.83 ± 7.18	< 0.001**
4 min	79.40 ± 7.30	72.67 ± 6.09	< 0.001**
5 min	75.50 ± 6.32	72.30 ± 6.84	0.065 +
Postdrug			
30 min	75.70 ± 6.49	70.90 ± 7.19	0.009**
60 min	84.20 ± 7.27	72.63 ± 6.64	< 0.001**
90 min	70.27 ± 5.34	73.80 ± 6.21	0.022*
120 min	80.83 ± 5.97	81.93 ± 6.68	0.504

The Diastolic Blood Pressure (DBP) in both groups were comparable at baseline (p = 0.532). After premedication, DBP in Group D was lower than Group F but it was only moderately significant (p - 0.031). DBP at intubation (0 minutes) was significantly lower in Group F when compared to Group D (p < 0.001). At 1, 2, and 3 minutes postintubation, DBP in Group F was significantly higher than Group D (p = 0.001). At 4 minutes postintubation, DBP was lower in Group D but the difference was only moderately significant (p = 0.019). At 5 minutes postintubation, there was no significant difference in DBP in both the groups (p = 0.746).

At incision (0 minutes), there was no significant difference between the two groups (p = 0.827). From 1 minute to 4 minutes postincision, DBP in Group F was significantly higher as compared to Group D (p < 0.001). At 5 minutes postincision, the difference between the groups was only moderately significant (p = 0.015), (Table 4).

Table 4: Comparison of DBP (mm Hg) between the two groups

DBP (mm Hg)	Group F	Group D	p - value
Baseline	76.53 ± 8.61	75.20 ± 7.79	0.532
After premedication	73.13 ± 7.44	69.10 ± 6.68	0.031*
Intubation			
0 min	59.13 ± 5.68	67.80 ± 5.71	< 0.001**
1 min	82.70 ± 8.15	68.90 ± 7.19	< 0.001**
2 min	75.27 ± 8.89	68.07 ± 7.46	0.001**
3 min	72.20 ± 8.16	66.23 ± 6.36	0.003**
4 min	69.70 ± 8.63	64.9 ± 6.61	0.019*
5 min	64.90 ± 7.54	64.30 ± 6.72	0.746
Incision			
0 min	62.67 ± 7.24	63.03 ± 5.59	0.827
1 min	79.03 ± 8.07	61.27 ± 6.54	< 0.001**
2 min	72.50 ± 8.11	61.07 ± 8.25	< 0.001**
3 min	69.07 ± 9.06	58.53 ± 7.64	< 0.001**
4 min	66.50 ± 8.21	58.70 ± 6.40	< 0.001**
5 min	63.30 ± 7.80	58.47 ± 7.06	0.015*

The surgical plethysmographic index at baseline were comparable (p = 0.750). At 1 minute and 2 minutes postintubation, SPI was significantly higher in Group F when compared to Group D (p < 0.001). At 3 minutes the difference was only moderately significant (p = 0.012). At 4^{th} and 5^{th} minute postintubation, there was no significant difference between the two groups. At incision (0 minutes), SPI in Group F was significantly higher than Group D. Also, there was a significant rise in SPI at 0 minutes from the previous value. This reactivity of SPI was attenuated by using dexmedetomidine in Group D. From 1 minute to 3 minutes postincision, there was a significant difference in SPI between the two groups. At 4^{th} minute postincision, SPI started returning towards baseline and the difference between the two groups at this timeline was only moderately significant (p = 0.030). At 5^{th} minute postincision, there was no significant difference between the two groups (p = 0.183), (Table 5).

Table 5: Comparison of SPI between the two groups

SPI	Group F	Group D	p - value
Baseline	40.67 ± 11.67	42.17 ± 11.86	0.750
After premedication	38.33 ± 9.31	39.90 ± 10.10	0.240
Intubation			
0 min	36.20 ± 9.63	38.67 ± 9.61	0.325
1 min	55.83 ± 8.97	36.07 ± 10.22	< 0.001**
2 min	45.10 ± 11.41	34.03 ± 10.16	< 0.001**

SPI	Group F	Group D	*p* - value
3 min	39.93 ± 9.89	33.53 ± 9.31	0.012*
4 min	33.30 ± 7.80	32.50 ± 9.65	0.725
5 min	30.53 ± 8.21	32.17 ± 9.33	0.475
Incision			
0 min	39.83 ± 6.46	31.50 ± 9.16	< 0.001**
1 min	53.40 ± 8.22	32.73 ± 8.84	< 0.001**
2 min	47.27 ± 8.17	31.53 ± 9.64	< 0.001**
3 min	40.77 ± 8.31	29.80 ± 8.28	< 0.001**
4 min	34.53 ± 7.03	29.93 ± 8.91	0.030*
5 min	32.47 ± 7.95	29.77 ± 7.56	0.183

The total fentanyl and morphine used in Group D was significantly lower than Group F ($p < 0.001$). The total propofol consumption in Group D was also significantly lower when compared to Group F ($p < 0.001$), (Table 6). The baseline RBS in both groups were comparable ($p = 0.137$). At one hour postincision, the rise in RBS was higher in Group F as compared to Group D ($p = 0.001$), (Table 7).

Table 6: Comparison of total fentanyl (μg), total morphine (mg) and total propofol (mg) requirement between the two groups

	Group F	Group D	*p* - value
Total fentanyl (μg)	176.67 ± 23.21	139.67 ± 19.91	< 0.001**
Total morphine (mg)	4.47 ± 0.73	0.10 ± 0.55	< 0.001**
Propofol (mg)	84.67 ± 17.32	63.17 ± 12.63	< 0.001**

Table 7: Comparison of RBS (mg/dl) levels between the two groups

RBS (mg/dl)	Group F	Group D	*p* - value
0 hr	110.77 ± 20.05	102.67 ± 21.54	0.137
1 hr	128.73 ± 18.61	110.77 ± 20.67	0.001**

In our study, out of the 30 patients allotted to Group F, 24 of them received a score of 2 on the Modified Ramsay Sedation Scale on arrival to PACU. Six out of the 30 received a score of 3 on arrival to PACU. Whereas in Group D, 18 out of 30 received a score of 2 and 12 received a score of 3. The difference in sedation score in both the groups was only suggestive of significance at this timeline ($p = 0.094$). Thirty minutes after arrival in PACU, all patients in Group F received a score of 2 on MRSS. In Group D, 25 out of 30 patients received a score of 2. Five out of 30 received a score of 3. The difference in sedation score between both groups at this timeline was moderately significant ($p = 0.019$). At the end of one hour in PACU, all patients in both groups received a score of 2 on MRSS, (Table 8).

Table 8: Comparison of MRSS between the two groups

MRSS	Group F	Group D	*p* - value
on Receiving	2.20 ± 0.41	2.40 ± 0.50	0.094 +
30 min	2.00 ± 0.00	2.17 ± 0.38	0.019*
1 hour	2.00 ± 0.00	2.00 ± 0.00	–

Since, there was maximum response at 1 minute postintubation and 1 minute postincision, we looked at correlation of heart rate vs surgical plethysmographic index and heart rate *vs* mean arterial pressure at those timelines. In both groups, there was only trivial to small correlation between HR and SPI, and MAP and SPI, (Table 9).

Table 9: Correlation between SPI and heart rate, SPI and MAP at baseline, 1 minute postintubation and 1 minute postincision

Pair	Group F		Group D	
	r - value	*p* - value	*r* - value	*p* - value
Heart rate vs SPI				
HR *vs* SPI @ baseline	0.270	0.148	-0.043	0.822
HR *vs* SPI @ 1 min Intubation	0.025	0.894	0.081	0.671
HR *vs* SPI @ 1 min Incision	0.267	0.154	0.049	0.795
MAP vs SPI				
MAP *vs* SPI @ baseline	–0.254	0.176	0.398	0.029*
MAP *vs* SPI @ 1 min Intubation	0.042	0.825	0.220	0.242
MAP *vs* SPI @ 1 min Incision	–0.169	0.372	0.106	0.577

Discussion

Laryngoscopy, intubation and surgical incision induce a stress response characterized by cardiovascular response in the form of hypertension and tachycardia. This sympathoadrenal stress response results in increased myocardial O_2 demand leading to ischaemia and acute heart failure in susceptible individuals. Alpha-2 receptor agonists (such as Dexmedetomidine) are known to decrease heart rate and blood pressure, cause arousable sedation and provide analgesia without causing significant respiratory depression and are widely used in clinical practice in anesthesiology and critical care.[6]

We noted a significant attenuation of hemodynamic response (HR, SBP, MAP, DBP) to intubation and surgical incision with dexmedetomidine at a low-dose of 0.5 μg/kg as compared to the control group ($p < 0.001$).

SBP was significantly lower in Group D. However, at intubation (0 minutes), the mean SBP was lower in Group F when compared to Group D. This may probably be due to a higher requirement of propofol in Group F. Hence, the difference in systolic blood pressure between the two groups was only suggestive of significance at this timeline ($p = 0.061$). The systolic blood pressure in Group F from 1 minute postintubation to 3 minutes postintubation and from 1 minute postincision to 3 minutes postincision was significantly higher ($p < 0.001$). This is suggestive of pressor response being blunted better in Group D.

MAP was significantly lower in Group D. Findings from baseline to 5 minutes postincision were similar to that of SBP. MAP at 30 minutes postdrug administration in Group D was significantly lower than Group F ($p = 0.009$). At this timeline, percentage change in MAP was greatest among all timelines. However, the lowest recorded MAP at this timeline was 61 mm Hg. At 120 minutes, there was no statistically significant difference in the MAP between the two groups ($p = 0.504$). Findings of DBP were similar to that of SBP and MAP.

Bajwa SS[3] et al. in their study used dexmedetomidine in the dose of 1 μg/kg and found that dexmedetomidine significantly decreased the hemodynamic response to intubation. They also, demonstrated a decrease in fentanyl and isoflurane dose required in their study group. Although, we used a lower-dose in our study, our findings were consistent.

Keniya VM et al.[6] found that dexmedetomidine in a dose of 1 μg/kg lowered the percentage increase in systolic blood pressure, diastolic blood pressure and heart rate significantly. In our study, we also studied, the effect of dexmedetomidine on a novice index known as Surgical Plethysmographic Index (SPI).[7] SPI is a noninvasive, inexpensive technique which gives beat to beat information of the depth of analgesia of the patient.

Both the heart rate and the plethysmographic amplitude are normalized in order to decrease interpatient variability by applying a histogram transformation on the raw time serial data. Then a linear combination of the normalized values is computed as SPI = 100-(0.7*PPGAnorm + 0.3*HBInorm), in which PPGAnorm is the normalized plethysmographic pulse wave amplitude and HBInorm the normalized heart beat interval. Surgical Plethysmographic Index has been validated as a tool to guide analgesia.[8–11]

In our study, we found that SPI was significantly higher in Group F when compared to Group D ($p < 0.001$). At incision (0 minutes), SPI in Group F was significantly higher than Group D. Also, there was a significant rise in SPI at 0 minutes from the

previous value. Whereas, there was no such change in heart rate or MAP, indicating SPI reacts almost immediately to nociceptive stimuli even before there is a change in heart rate. This occurs as SPI not only takes into account heart beat interval, but also pulse wave amplitude which depends on peripheral vasoconstriction. This reactivity of SPI was attenuated by using dexmedetomidine in Group D.

In the present study, since, there was maximum response at 1 minute postintubation and 1 minute postincision, we looked at correlation of heart rate *vs* surgical plethysmographic index and heart rate *vs* mean arterial pressure at those timelines. In both groups, there was only trivial to small correlation between HR and SPI, and MAP and SPI. SPI is not only based on heart beat interval, but also pulse wave amplitude reflecting peripheral vasoconstriction, which may be the reason why SPI did not correlate with heart rate.

Dexmedetomidine mediates analgesia through stimulation of the α_2C and α_2A receptor in the dorsal horn, reducing the release of pronociceptive transmitters, substance P and glutamate, and hyperpolarization of interneurons. Systemic use has an opioid-sparing effect. This effect is advantageous in patients who are prone to postoperative apnea or hypoventilation, such as patients undergoing bariatric surgery. In our study, we compared the requirement of opioids in the two groups. There was a significant reduction in consumption of both fentanyl and morphine ($p < 0.001$). This finding was similar to that of Bajwa SS[3] et al. who used dexmedetomidine in the dose of 1 μg/kg as premedication and found that the requirement for fentanyl and isoflurane were both reduced in the patients who received dexmedetomidine.

Dexmedetomidine is also known to decrease the anesthetic requirement during general anesthesia. In our hospital, loss of verbal contact with the patient is used as end point of induction of propofol. We found that the total dose of propofol required in study Group D was significantly lower ($p < 0.001$). As a higher-dose of propofol was used in the Group F that did not receive dexmedetomidine, hypotension was seen more in this group. Our findings were similar to that of Morgan Le Guen et al. [12] who also demonstrated a decrease in propofol and remifentanil requirement during their study.

Turgut N et al.[13] used dexmedetomidine in a bolus dose of 0.6 µg/kg before induction and 0.2 μg/kg/hr by infusion. They found that propofol dosages for induction and maintenance of anesthesia were lower with dexmedetomidine. The fentanyl group patients required supplemental analgesia earlier than the dexmedetomidine group.

Suvadeep Sen et al.[14] also, in their study demonstrated a reduction in propofol requirement in patients who received dexmedetomidine. Surgery and anesthesia cause an endocrine stress response leading to release of multiple hormones like renin, glucagon, ACTH, cortisol, ADH, GH, etc. There is also inhibition of insulin release. This eventually leads to hyperglycemia. In our study, we looked at rise in serum glucose levels in both groups to see if dexmedetomidine decreased the endocrine stress response. We found that serum glucose levels was significantly lower in the group receiving dexmedetomidine ($p < 0.001$). This finding was similar to the study conducted by Ahmed G Yacout et al.[15] They evaluated the effect of intravenous dexmedetomidine infusion on stress response markers as plasma interleukin-6, cortisol and blood glucose level. Postoperatively, the levels of interleukin-6, cortisol and blood glucose were significantly lower in the group that received dexmedetomidine.

On the contrary, Kumkum Gupta et al.[16] found no difference in blood glucose levels between the two groups they studied. One group received intravenous dexmedetomidine 1 μg/kg and and other received fentanyl 2 μg/kg. Blood glucose concentration has shown 20% increase after surgery. The differences between the groups were not statistically significant as observed by analyzing the variation of serial perioperative blood glucose estimation.

Conclusion

1. On the basis of the study, we conclude that intravenous dexmedetomidine significantly attenuates hemodynamic response to intubation and surgical incision.
2. Surgical plethysmographic index, an index to measure depth of analgesia was also attenuated with dexmedetomidine.
3. There is no correlation of heart rate and mean arterial pressure with surgical plethysmographic index.
4. Surgical plethysmographic index detects noxious stimulation prior to heart rate and blood pressure.
5. Opioid requirement is significantly lowered by use of dexmedetomidine as a premedicant.
6. Dexmedetomidine decreases anesthetic

requirement significantly.

7. Dexmedetomidine attenuates neuroendocrine stress response to anesthesia and surgery as seen by lower blood glucose levels in the study group.
8. Hypotension and bradycardia requiring intervention was not seen in the dexmedetomidine group as a low-bolus dose was administered.
9. Postextubation, patients of the dexmedetomidine group were more sedated than the fentanyl group on arrival at PACU, however, at the end of two hours, there was no difference between the two groups.

References

1. Kovac AL. Controlling the hemodynamic response to laryngoscopy and endotracheal intubation. J Clin Anesth 1996;8:63–79.
2. Kallio A, Scheinin M, Koulu M, et al. Effects of dexmedetomidine, a selective alpha 2-adrenoceptor agonist, on hemodynamic control mechanisms. Clin Pharmacol Ther 1989 Jul;46(1):33–42.
3. Bonhomme V. Comparison of the Surgical Pleth Index™ with hemodynamic variables to assess nociception-antinociception balance during general anesthesia. Br J Anesth 2011: 105;101–111.
4. Bajwa SS, Kaur J, Singh A, et al. Attenuation of pressor response and dose sparing of opioids and anesthetics with preoperative dexmedetomidine. Indian J Anesth 2012;56: 123–28.
5. Kadam P & Bhalerao S. Sample size calculation. International Journal of Ayurveda Research 2010;1(1):55.
6. Kenya VM 57 Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathodrenal response to tracheal intubation and reduces perioperative anesthetic requirement. Indian J Anesth 2011;55:352–57.
7. Struys MM, Vanpeteghem C, Huiku M, et al. Changes in a surgical stress index in response to standardized pain stimuli during propofol–remifentanil infusion. Br J Anesth 2007;99:359–67.
8. Chen X, Thee C, Gruenewald M, et al. Comparison of surgical stress index-guided analgesia with standard clinical practice during routine general anesthesia: A pilot study. *Anesthesiology* 2010;112(5):1175–83. DOI:10.1097/ALN.0b013e3181d3d641.
9. Xinzhong Chen, Carsten Thee, Matthias Gruenewald, et al. Correlation of surgical pleth index with stress hormones during propofol-remifentanil anesthesia. The Scientific World Journal 2012; Article ID 879158. doi:10.1100/2012/879158.
10. Mustola S. Performance of Surgical Stress Index during Sevoflurane-Fentanyl Anesthesia. Anesthesiology Research and Practice 2010; Article ID 810721, 5 pages.
11. Höcker J et al. Surgical stress index in response to pacemaker stimulation or atropine. Br J Anesth 2010;105:150–54.
12. Morgan Le guen, Ngai Liu, Felix Tounou, et al. Dexmedetomidine reduces propofol and remifentanil requirements during bispectral index-guided closed-loop anesthesia: A double-blind, Placebo-controlled trial. Anesth Analg 2014 May;118(5):946–55.
13. Turgut N, Turkmen A, Gökkaya S, et al. Dexmedetomidine-based *versus* fentanyl-based total intravenous anesthesia for lumbar laminectomy. Minerva Anestesiol 2008 Sep; 74(9):469–74.
14. Sen Suvadeep, Chakraborty Jayanta, Santra Sankari, et al. The effect of dexmedetomidine infusion on propofol requirement for maintenance of optimum depth of anesthesia during elective spine surgery. Indian J Anesth 2013;57(4):358–63.
15. Ahmed G Yacout, Hasan A Osman, Mamdouh H Abdel-Daem, et al. Effect of intravenous dexmedetomidine infusion on some proinflammatory cytokines, stress hormones and recovery profile in major abdominal surgery. Alexandria Journal of Medicine 2012 Mar;48(1):3–8. http://dx.doi.org/10.1016/j.ajme.2011.11.001.
16. Gupta Kumkum, Maggo Aman, Jain Manish, et al. Blood glucose estimation as an indirect assessment of modulation of neuroendocrine stress response by dexmedetomidine *versus* fentanyl premedication during laparoscopic cholecystectomy: A clinical study. Anesth Essays Res 2013 Jan–Apr;7(1):34–38. DOI: 10.4103/0259-1162.113985.

Original Research Article

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Comparative Study of Intravenous Dexmedetomidine (0.5 Microgram/ Kg) *Vs* Intravenous Midazolam (0.05 Mg/Kg) as Premedicant in Spinal Anesthesia with 0.5% Bupivacaine for Gynecological Surgeries

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Abstract

Introduction: Surgeries like direct and indirect inguinal hernia repair, lower limb surgeries, urological surgeries and gynecological surgeries are commonly done under spinal anesthesia. It is a selective α_2-adrenoceptor agonist and is currently used for its sedative, analgesic and sympatholytic properties. Intravenous Dexmedetomidine decreases the inhalational anesthesia and opioid requirements during general anesthesia**.** *Aims:* To compare the postoperative effect of intravenous dexmedetomidine in comparison with intravenous midazolam on intrathecal bupivacaine in patients undergoing gynecological surgeries under spinal anesthesia. *Materials and Methods:* Prospective randomized study between March 2017 and August 2018. This study was conducted in 100 patients belonging American Society of Anesthesiologists (ASA) physical status classification class 1 & 2 and undergoing gynecological surgeries under spinal anesthesia were included. *Results:* Postoperative analgesia was significantly prolonged with the use of intravenous dexmedetomidine premedication than with intravenous midazolam. Heart rates were lesser in dexmedetomidine Group A when compared to midazolam Group B, but overall requirement of anticholinergics was similar in both groups. Mean arterial pressures were lower with dexmedetomidine Group A when compared with midazolam Group B. *Conclusion:* Intravenous dexmedetomidine premedication prolongs the duration of sensory and motor blockade during the spinal anesthesia with Bupivacaine with good sedation and postoperative analgesia than with intravenous midazolam premedication in patients undergoing gynecological surgeries under spinal anesthesia.

Keywords: Dexmedetomidine; Midazolam; Bupivacaine; Premedication, Spinal anesthesia.

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Introduction

Surgeries like direct and indirect inguinal hernia repair, lower limb surgeries, urological surgeries and gynecological surgeries are commonly done under spinal anesthesia. Different adjuvants are used in spinal anesthesia along with intrathecal bupivacaine, with the possible advantages of prolonged action, reduced postoperative pain and lesser analgesic requirement postoperatively. Dexmedetomidine, an α_2-agonist, has been used for premedication and as an adjunct to general anesthesia. It is a selective

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α_2-adrenoceptor agonist and is currently used for its sedative, analgesic and sympatholytic properties 4. Intravenous Dexmedetomidine decreases the inhalational anesthesia and opioid requirements during general anesthesia.[1] Also, it has been used safely as premedication agent in patients undergoing surgical procedures under different regional anesthesia techniques. Dexmedetomidine has an inhibitory effect on the locus ceruleus (A6 group) located at the brain stem 6. This supraspinal action could explain the prolongation of spinal anesthesia after intravenous administration of Dexmedetomidine. Part of the mechanism by which Dexmedetomidine produces an antinociceptive effect is by acting directly on the locus ceruleus.[2] There is a growing interest in the use of α_2-adrenoceptor agonists as sedatives because of their favorable properties which include their relatively short half-life, analgesic effects, cardiorespiratory stability and rapid reversal of sedation on discontinuation of drug.[3]

Although a synergistic interaction between intrathecal Dexmedetomidine and local anesthetics has been observed in previous studies, there are few clinical studies with sample size of 25 per group regarding the effect of intravenous Dexmedetomidine premedication on the duration of sensory and motor block during spinal anesthesia.

This clinical study is to assess the effects of intravenous Dexmedetomidine premedication on spinal block duration and postoperative analgesia in patients undergoing surgeries under spinal anesthesia. To isolate dexmedetomidine's analgesic effects from its sedative effects, a comparison will be made with a benzodiazepine i.e., midazolam given by intravenous route to provide sedation. In this study, dexmedetomidine will be administered by intravenous route over 10 min., as rapid administration of dexmedetomidine may cause tachycardia, bradycardia, hypertension or hypotension. Hence, in this study 0.5 micrograms/kg. Dexmedetomidine is administered intravenously. Midazolam 0.05 milligram/kg. administered intravenously gives enough sedation and amnesia without any adverse effects on hemodynamics and respiration in patients undergoing surgeries under spinal anesthesia. Therefore, midazolam 0.05 milligram/kg. is administered intravenously to the patients in this study.

Materials and Methods

Prospective randomized study done as Hospital based, between March 2017 and August 2018. This study was conducted in Modern Maternity Hospital, Hyderabad, Telangana. 100 patients belonging American Society of Anesthesiologists (ASA) physical status classification class 1 & 2 and undergoing gynecological surgeries under spinal anesthesia were included. Using a computer-generated randomization schedule, the patients were randomly divided into two groups:

Group A: The first group are of 50 patients who were administered intravenous Dexmedetomidine 0.5 micrograms/kg. 15 minutes prior to spinal anesthesia with intrathecal bupivacaine 0.5% 3 ml. (n = 50).

Group B: The second group are of 50 patients who were administered intravenous midazolam 0.05 milligrams/kg. 15 minutes prior to spinal anesthesia with intrathecal bupivacaine 0.5% 3 ml (n = 50).

Inclusion Criteria

Healthy adult patients aged between 18 and 50 yrs. of either sex, Patients belonging to ASA class I/II.

Exclusion Criteria

Patients aged <18 years or > 50 years, ASA class III/IV, Use of any opioid or sedative medications in the week prior to surgery, History of alcohol or drug abuse, Known allergy to dexmedetomidine, midazolam or Bupivacaine, Contraindication to spinal anesthesia (e.g., coagulation defects, infection at puncture site, Preexisting neurological deficits in the lower extremities), Cardiovascular, Respiratory, Neurological, Endocrine, Hepatic, Renal disease or other comorbid conditions, Patients having inadequate subarachnoid blockade and who are later supplemented by General anesthesia, Patients with excessive blood loss and needing blood transfusion and Pregnant women.

This study was conducted under the guidance of senior anesthesiologist. All the emergency drugs and equipment were kept ready in the operating room. Patients were shifted to operation theatre and monitors connected. Monitors included Electrocardiography, Noninvasive blood pressure measurement and Pulseoximetry. The same monitor was used for all the patients in the study. After intravenous insertion of an 18-G catheter in the operating room, all patients received 20 ml/kg of lactated Ringer's solution intravascular volume loading before spinal anesthesia. Each group was premedicated with Dexmedetomidine and Midazolam 15 minutes before spinal anesthesia. The Group A or Group B drugs were premixed to

a total volume of 50 ml. with 0.9% NS and were administered intravenously as infusion over a 10 min period as a single-dose. Five minutes after the end of the infusion, the patients were placed in the left lateral position and lumbar puncture performed at the L3-L4 interspace using a standard midline approach with a 25-G Quincke spinal needle. Hyperbaric Bupivacaine 0.5% 3 ml (15 mg.) was injected intrathecally and the patients received oxygen 5 L/min throughout the procedure by Hudson facemask. Recordings were done by the same anesthesiologist from the beginning of the procedure till 24 hours after completing the surgery. Parameters observed will be:

Hemodynamic status

Heart Rate (HR), Mean Blood Pressure (MAP), Oxygen Saturation (SpO_2), and Respiratory Rate (RR) were recorded before premedication, 5 min after premedication, immediately before and after dural puncture, and every 5 min for first 60 min, every 10 min next 60 min and every 15 min for next 60 min after spinal anesthesia. Vasopressor and anticholinergic drug requirements were noted.

Hypotension (defined by a decrease in MAP below 20% of baseline or systolic pressure < 90 mm Hg) were treated with intravenous Ephedrine 6 mg and Ringer Lactate solution of 200 ml over a 5 minute period. Bradycardia of HR < 50 beats/ min was treated with intravenous atropine 0.6 mg intravenously.

Sensory blockade

Onset of action of Sensory blockade after spinal anesthesia was assessed at every 2 min for the first 15 min or until two consecutive levels of sensory blockade were identical (i.e. fixation of the level) and thereafter every 10 min during surgery and postoperatively using pinprick sensation bilaterally in the mid-axillary line. Time for maximum sensory level was noted. Recovery time for sensory blockade defined as regression of anesthesia from the maximum level was recorded. Time for sensory regression of two dermatomes was noted. The time for the first request for analgesia and the number of patients who required supplemental analgesia was recorded.

Quality of sensory block

Postoperative pain was assessed by the patient using the Visual Analog Scale or VAS scale postoperatively. Patients with a VAS score of 3 or more received Inj. Diclofenac 1 mg/kg. intramuscularly. The time for first request for postoperative analgesia and number of patients who required supplemental analgesia were recorded.

Motor blockade

Onset of Motor blockade was assessed every 2 min for the first 15 min or till blockade of Modified Bromage Scale 3 is noted, whichever was earlier. Motor blockade duration is the time for return to Modified Bromage Scale 1.

Modified Bromage Scale

Bromage 0: Patients is able to move hip, knee & ankle;

Bromage 1: Patients is unable to move hip, but able to move knee & ankle;

Bromage 2: Patient is unable to move hip & knee but able to move ankle;

Bromage 3: Patient is unable to move hip, knee & ankle.

Ramsay Sedation Score

The scores were reevaluated every 10 min for up to 120 min. Excessive sedation recorded as a score greater than 4:

1. Patient is anxious and agitated or restless or both;
2. Patient is cooperative, oriented and tranquil;
3. Patient responds to commands only;
4. Patient exhibits brisk response to light glabellar tap or loud auditory stimulus;
5. Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus;
6. Patient exhibits no response.

The presence of any complication in the preoperative and postoperative periods was noted, particularly in relation to respiratory or cardiovascular problems, nausea or vomiting and headache.

Statistical analysis

The raw data was entered and mean and standard deviation values were analyzed using Microsoft Office Excel Worksheet (.xlsx) 2016 on Microsoft Windows 10 and p - value was analyzed using unpaired t - test in GraphPad InStat 3 (Trial). For statistical significance a p - value of 0.05 or lesser is taken as being statistically significant.

Results

All patients were comparable for age, weight and height and the difference was statistically not significant in both groups, shows in (Table 1).

Heart rate decreased in both the groups after spinal anesthesia, but the fall in heart rate in (Dexmedetomidine) Group A was statistically significant than with (Midazolam) Group B with the *p* - values as mentioned, shown in (Fig. 1).

Table 1: Demographic details in present study

Parameters	Group A	Group B	*p* - value	Statistical significance
No. of patients	50	50	–	–
Age (in years)	40.78 ± 6.27	38.44 ± 6.17	0.0629	Not significant
Weight (in kgs)	67.88 ± 7.95	69.66 ± 7.93	0.2532	Not significant
Height (in cms)	160.40 ± 5.31	159.96 ± 4.93	0.6686	Not significant

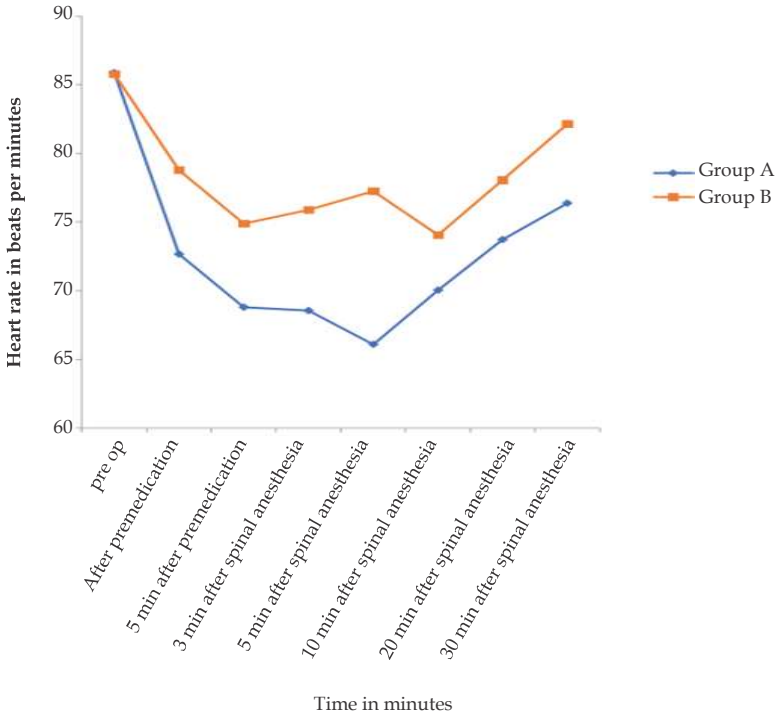

Fig. 1: Heart rate variation between two groups in present study

Mean arterial pressure decreased in both the groups after spinal anesthesia, but the fall in (Dexmedetomidine) Group A was statistically significant than with (Midazolam) Group B, shown in (Fig. 2 and Table 2).

Table 2: Time period during observation post operatively

Duration	Group A	Group B	*p* - value	Statistical significance
Time for onset of sensory blockade	228 ± 25.56	224 ± 35.31	0.517	Not significant
Two segment regression time (in min)	134.02 ± 25.26	110.72 ± 22.64	< 0.0001	significant
Motor blockade duration (in min)	175 ± 14.56	162 ± 15.48	< 0.0001	significant
First request of analgesia (in min)	230.52 ± 21.52	203.14 ± 24.99	< 0.0001	significant

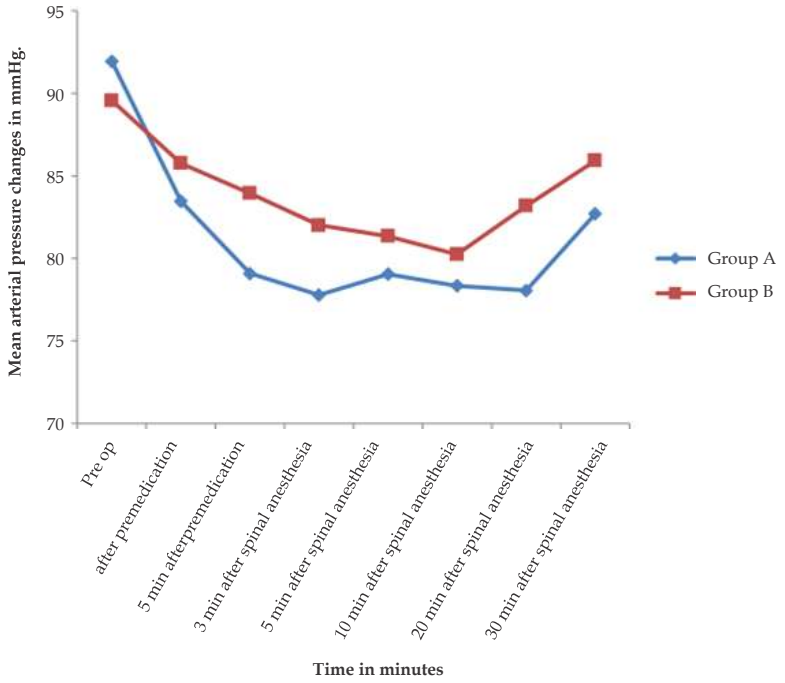

Fig. 2: Mean Arterial pressure variation between two groups in present study

Time for onset of sensory blockade is insignificant when compared in both groups.

On Comparision of side-effects in two groups it is observed insignificant, as shown in Table 3.

Table 3: Comparision of side-effects in two groups

Side-effects	Group A	Group B	Statistical significance
Bradycardia	8%	8%	Not significant
Hypotension	8%	8%	Not significant
Nausea/Vomiting	6%	6%	Not significant
Respiratory depression	0%	0%	Not significant

Discussion

Different drugs have been used as adjuvants with local anesthetic agents in order to prolong the duration of spinal anesthesia. Clonidine an α_2 agonist, has been widely used in the intrathecal, oral and intravenous routes to prolong the duration of spinal anesthesia. It is known to have prolonging effect on sensory and motor blockade when used as an oral premedication within 2 hours before bupivacaine spinal anesthesia. The intravenous administration of clonidine within 1 hr after the spinal blockade prolonged bupivacaine spinal analgesia for approximately 1 hour without adverse effect.[4]

Dexmedetomidine, also an α_2-agonist, is pharmacologically related to clonidine, has 8 times more affinity for α_2-receptors than clonidine. It produces sedation and anxiolysis by binding to α_2-receptors in the locus ceruleus, which diminishes the release of norepinephrine and inhibits sympathetic activity, thus decreasing heart rate and blood pressure. It produces analgesia by binding to adrenoreceptors in the spinal cord. It has been used as adjuvant to local anesthesia in the intrathecal route and has significant effect on onset and duration of spinal anesthesia.

Dexmedetomidine has an onset of action of 30 min when the maintenance dose is used intravenously. Use of standard loading dose (1 μg/kg/hr infused over 10 minutes), decreases the time for onset of action. Side-effects of dexmedetomidine, such as hypotension and bradycardia, are dose dependent. Infusion of loading dose over 10 min and then infusing the maintenance dose decreases the incidence of those side-effects. Jorm CM, Stamford

JA found that dexmedetomidine has an inhibitory effect on the locus ceruleus (A6 group) located at the brain stem.[5] This supraspinal action could explain the prolongation of spinal anesthesia after intravenous administration of dexmedetomidine. The noradrenergic innervation of the spinal cord arises from the noradrenergic nuclei in the brain stem including the locus ceruleus, the A5 and the A7 noradrenergic nuclei. Neurons in the locus ceruleus are connected to the noradrenergic nuclei in the brain stem. Axon terminals of the noradrenergic nuclei reach lamina VII and VIII of the ventral horns of the spinal cord.

The activity of the noradrenergic neurons is decreased by agonists acting at α_2-adrenergic receptors on the locus ceruleus cell bodies. Therefore, inhibition of the locus ceruleus results in disinhibition of the noradrenergic nuclei and exerted descending inhibitory effect on nociception in the spinal cord.

The mechanism of motor blockade is unclear, the analgesic effects of α_2-adrenergic agonists could be mediated through supraspinal, spinal and peripheral actions.[6] Dexmedetomidine results in direct inhibition of impulse conduction in the large, myelinated Aα fibers and the 50% effective concentration (EC50%) measured approximately 4-folds of that in small, unmyelinated C fibers. This could explain the lesser duration of motor blockade compared with sensory blockade, as conduction of motor nerve fibers was less inhibited than sensory nerve fibers at the same concentration of dexmedetomidine. This would explain the prolongation of sensory blockade than motor blockade. Dexmedetomidine is known to have sedative effect providing better conditions for the surgeon and the patient. This study indicated that premedication with intravenous dexmedetomidine prolonged the duration of bupivacaine induced sensory blockade during spinal anesthesia. In addition, dexmedetomidine increased the time until first request of analgesic for postoperative pain relief. It also provided sedation comparable to midazolam premedication. It is recommended to administer dexmedetomidine over 10 min, as rapid administration might produce tachycardia or bradycardia, hypotension.[7]

Furthermore, previous studies describe an evaluation of the analgesic effect of different doses of intravenous dexmedetomidine (0.25, 0.5 and 1 mcg/kg.) on ischemic pain in healthy volunteers demonstrated moderate analgesia with a ceiling effect at 0.5 mcg/kg. With this in mind, dexmedetomidine, 0.5 mcg/kg was given intravenously over 10 min in this study. Administration of midazolam 0.05 mg/kg. was reported to give enough sedation and amnesia without any adverse effects on hemodynamics and respiration in patients aged 30–70 yrs, under spinal anesthesia.[8] Therefore, midazolam 0.05 mg/kg was given intravenously over 10 min in this study.

Midazolam has been reported to have an antinociceptive effect through the neuroaxial pathway. However, the effects of midazolam on nociception may depend on the route of administration, with analgesia observed after spinal or epidural application, but not after systemic administration of this agent.[9] In this study also, intravenous administration of midazolam did not enhance the analgesic effect of intrathecal injection. Finally, the use of dexmedetomidine premedication before spinal anesthesia seems to offer clinical advantages compared with midazolam premedication, since dexmedetomidine provides additional analgesia. During lumbar puncture, it is preferable that patients be able to alert the anesthesiologist of any paresthesia and pain on injection, both of which have been associated with postoperative neurologic deficit.

Midazolam may cause restlessness and disinhibition instead of sedation in some patients and this is referred to as a paradoxical reaction.[10] Thus, surgery will then become extremely difficult. In this study, no patients experienced a paradoxical reaction with midazolam. The sedation produced by dexmedetomidine differs from other sedatives, as patients may be easily aroused and remain cooperative.[11] Midazolam has a potent anterograde amnesic effect, and dexmedetomidine infusion also may result in impairment of memory and psychomotor performance. However, the amnesic effect of midazolam rapidly diminished with time.

Rapid or bolus intravenous administration of dexmedetomidine produces sudden hypotension and bradycardia until the central sympatholytic effect dominates, resulting in moderate decreases in both MAP and HR from baseline. This study observed no significant cardiovascular variability in this study consisting mainly of healthy patients. This might be attributed to sympathetic blockade associated with spinal anesthesia, slow administration of a low-dose and sufficient preoperative hydration. However, further studies are needed to investigate the efficacy of dexmedetomidine in geriatric patients or medically compromized patient populations. In previous studies, it has been shown that dexmedetomidine

caused no or minimal respiratory depression. However, midazolam is known to cause apnea and arterial desaturation in sedative doses. In this study, there was no respiratory depression in any patients and respiratory parameters remained within normal limits throughout the procedure.

Nevertheless, it was concluded within the constraints of the present design that the addition of intravenous dexmedetomidine before spinal blockade provided similar pain relief with delayed-onset of postoperative pain and significantly less analgesic requirements.

In this study, we have shown that a single-dose of intravenous dexmedetomidine given as premedication prolonged the duration of sensory blockade of bupivacaine induced spinal anesthesia. It also provided sedation and additional analgesia The heart rate decreased significantly after the start of intravenous infusion loading dose and extended in the PACU. This decrease in the heart rate was clearer and more significant in Group A in comparison with Group B. The lower heart rate observed in Group A could be explained by the decreased sympathetic outflow and circulating levels of catecholamines that are caused by dexmedetomidine.[12] Other studies support the finding that the bradycardia effect of dexmedetomidine is long lasting when used as a premedication drug. In conclusion, supplementation of spinal anesthesia with intravenous dexmedetomidine produces significantly longer sensory and motor blockade than intrathecal bupivacaine along with intravenous midazolam. Adverse side-effects were avoided by the slow infusion of loading dose of dexmedetomidine. All patients reached good sedation levels that enabled their cooperation and better operating conditions for the surgeon without significant respiratory depression.

Conclusion

Intravenous dexmedetomidine premedication prolongs the duration of sensory and motor blockade during the spinal anesthesia with Bupivacaine with good sedation and postoperative analgesia than with intravenous midazolam premedication in patients undergoing gynecological surgeries under spinal anesthesia.

References

1. Fragen RJ, Fitzgerald PC. Effect of dexmedetomidine on the Minimum Alveolar Concentration (MAC) of sevoflurane in adults age 55 to 70 years. J Clin Anesth 1999 Sep;11(6):466–70.
2. Guo TZ, Jiang JY, Buttermann AE, et al. Dexmedetomidine injection into the locus ceruleus produces antinociception. Anesthesiology 1996 Apr;84(4):873–81.
3. Scheinin H, Aantaa R, Anttila M, et al. Reversal of the sedative and sympatholytic effects of dexmedetomidine with a specific alpha 2-adrenoceptor antagonist atipamezole: A pharmacodynamic and kinetic study in healthy volunteers. Anesthesiology 1998 Sep;89(3):574–84.
4. Korkmaz M, Gurbet A, Sahin S. Comparision of sedative effects of midazolam and dexmedetomidine during regional anesthesia. Dicle Med J 2011;38(2):148–54.
5. Jorm CM, Stamford JA. Actions of the hypnotic anesthetic, dexmedetomidine, on noradrenaline release and cell firing in rat locus ceruleus slices. Br J Anesth 1993 Sep;71(3):447–79.
6. Roberts TL. Dexmedetomidine. J Pharm Soc Wis 2003 Nov/Dec;47–52.
7. Memiş D, Turan A, Karamanlioğlu B, et al. Adding dexmedetomidine to lidocaine for intravenous regional anesthesia. Anesth Analg 2004 Mar;98(3):835–40.
8. Grant SA, Breslin DS, MacLeod DB, et al. Dexmedetomidine infusion for sedation during fiberoptic intubation: A report of three cases. J Clin Anesth 2004 Mar;16(2):124–26.
9. Rhee K, Kang K, Kim J, et al. Intravenous clonidine prolongs bupivacaine spinal anesthesia. Acta Anesthesiol Scand 2003 Sep;47(8):1001–1005.
10. Ghai B, Makkar JK, Chari P, et al. Addition of midazolam to continuous postoperative epidural bupivacaine infusion reduces requirement for rescue analgesia in children undergoing upper abdominal and flank surgery. J Clin Anesth 2009 Mar;21(2):113–19.
11. Ho KM, Ismail H. Use of intrathecal midazolam to improve perioperative analgesia: A meta-analysis. Anesth Intensive Care 2008 May;36(3):365–73.
12. Povey HM, Jacobsen J, Westergaard-Nielsen J. Subarachnoid analgesia with hyperbaric 0.5% bupivacaine: Effect of a 60-min period of sitting. Acta Anesthesiol Scand 1989 May;33(4):295–97.

Original Research Article

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Comparison between Dexmedetomidine and Midazolam for Postoperative Analgesia and Sedation in Mechanically Ventilated Patients

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Abstract

Context: Postoperative patients requiring mechanical ventilation in surgical ICU's require adequate sedation and analgesia in order to modulate physiological response to stress and pain, hence reducing morbidity and mortality in the ICU. The consequences of inadequate sedation and analgesia can be sustained, including self-removal of intraluminal tubes and vascular catheters, aggressive behavior by patients against care providers, and poor patient-ventilator synchrony. Oversedation can lead to prolonged duration of mechanical ventilation, more prolonged ICU, and hospital stays. *Aims:* To evaluate the effects of dexmedetomidine and midazolam for sedation in postoperative mechanically ventilated patients. *Study Design:* Arandomized prospective study. *Methods:* 100 patients aged above 18 years after major abdominal or pelvic surgeries requiring a minimum of 6 hours of artificial ventilation admitted to intensive care units were included as subjects, and they were randomly divided into two groups of fifty each. Group D received Dexmedetomidine, a loading dose of 2.5 μg/kg, and a maintenance dose of 0.5 μg/kg/hr, and Group M received Midazolam a loading dose of 0.05 mg/kg and a maintenance dose of 0.025 mg/kg/hr. Both groups were compared for the level of sedation using Ramsay sedation score, hemodynamic variables, safety profile. *Statistical analysis used:* Chi-square test and Student's unpaired *t*-test. *Results:* Ramsay sedation score was within the desired level (2–4) in both dexmedetomidine and midazolam group ($p > 0.05$). Patients who received dexmedetomidine infusion had significantly lower heart rates compared to patients who received midazolam infusion ($p < 0.00$), there were no significant differences in SBP, DBP, MAP and oxygen saturation between two groups. *Conclusion:* Dexmedetomidine and midazolam are safe sedative drugs for postoperative mechanically ventilated patients. Patients were easily aroused to cooperate without signs of irritation within the dexmedetomidine group.

Keywords: Dexmedetomidine; Midazolam; Mechanical ventilation.

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Introduction

The intensive care unit is an environment of high-level stress and discomfort for patients. The use of adequate sedation and analgesia is essential in order to modulate physiological response to stress and pain, hence reducing morbidity and mortality in ICU.[1] Intubated, mechanically ventilated patients in surgical ICU require sedation and analgesia to tolerate tracheal tube, artificial

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ventilation, to suppress cough and to prevent respiratory fighting during procedures such as bronchial suctioning, physiotherapy, and catheter placement.[2] The sedation of patients reduces stress response, provides anxiolysis, improves tolerance of ventilator support, and facilitates nursing care. However, the sedatives have adverse effects and have the potential to prolong mechanical ventilation and also increases health care cost.[3–4]

Dexmedetomidine is an α_2 adrenoreceptor agonist with a unique mechanism of action providing sedation and anxiolysis via receptors within the locus coeruleus, analgesia *via* receptors in the spinal cord and attenuation of stress response with no significant respiratory depression.[5] The recommended dose is an IV infusion bolus of 1 μg/kg body weight over a 10 minute period, followed by a continuous IV infusion of 0.2–0.7 μg/kg/hr. The maintenance dose is titrated until the sedation goal is reached. It has shown to inhibit CYP2 D6 *in vitro*, but the clinical significance of this inhibition is not well-established. Dexmedetomidine appears to have little potential for interactions with drugs metabolized by the cytochrome P450 system. Coadministration of Dexmedetomidine with sevoflurane, isoflurane, propofol, alfentanil, and midazolam may result in the enhancement of sedative, hypnotic or anesthetic effects.

Midazolam is selected as comparator medication owing to its frequent use for short-term sedation and is often identified as the most commonly used sedative in ICU. Gaba receptor agonist medication is the most commonly used sedatives for ICU patients; its preliminary evidence indicates dexmedetomidine advantages.[6] The sedative agents are commonly administered as boluses or by continuous infusion when required in an intensive care unit. However, the latter method of infusion is more common. It also ensures constant levels of sedation, thus reducing the chance of intermittent agitation. However, the studies have shown that continuous infusion is known to prolong the duration of mechanical ventilation and thus prolonging the duration of stay in ICU. The physician has to set the desired sedation score, and patients should be reevaluated regularly. This approach allows titration of the therapy and prevents the chances of over or under sedation.

The treating physician should understand that how much and for how long the sedation is given. The over and under sedation can have deleterious consequences in determining the patient outcome. Over sedation increases the prolonged ventilatory support and also duration of stay in ICU. Under sedation can result in hypercatabolism, immunosuppression, hypercoagulability, and increased sympathetic activity. Hemodynamic responses to measure sedation are unreliable in the critically ill patient, hence the need for formal sedation scoring. There are many clinical scoring systems to assess the depth of sedation in ICU; examples include the Ramsay sedation score, Addenbrookes, Bloomsbury scales, and Richmond Agitation Sedation Scale (RASS). In our study, we have used the Ramsay sedation score, shows in Table 1. The present study is being undertaken in a randomized single-blinded manner to evaluate sedative and analgesic properties, safety profile, cardiovascular responses, ventilation and extubation characteristics with dexmedetomidine compared to midazolam in postoperative mechanically ventilated patients.

Materials and Methods

A randomized prospective study was undertaken Intensive Care Unit Medical College Hospital. A total of 100 ASA 3, ASA 4, ASA 5 patients, aged 18 years and above, after major abdominal pelvic surgeries requiring a minimum of 6 hours of artificial ventilation were included in the study. Morbidly obese patients and patients with neurological deficits, local sepsis were excluded from the study.

About 100 patients who satisfied the inclusion and exclusion criteria were allocated randomly into two groups by using a random numbers table. Group D -Dexmedetomidine group received a loading dose 2.5 mcg/kg and a maintenance dose 0.5 mcg/kg/hr. Group M - Midazolam group received a loading dose 0.05 mg/kg and a maintenance dose 0.025 mg/kg/hr.

Anesthetic technique in the operating room was carried out with 0.5 mg/kg thiopentone, 3–4 mcg/kg fentanyl and vecuronium 0.05 mg/kg. Direct laryngoscopy and endotracheal intubation were done with appropriate endotracheal tubes, maintenance of anesthesia was provided with 33% O_2 + 66% N_2O + intermittent halothane+ intermittent positive pressure ventilation. Neuromuscular blockade was provided with vecuronium as required. At the end of the surgical procedure, the neuromuscular blockade was not reversed, and artificial ventilation was continued. After admission to ICU patients were randomized into either of one group, patients were connected to multiparameter, which records heart rate, noninvasive measurements of SBP, DBP, MAP, continuous ECG monitoring,

and O_2 saturation. Patients were immediately artificially ventilated with synchronized intermittent ventilation with pressure support mode. Sedatives used before study enrolment was discontinued prior to initiation of study drug. Each patient received a study drug after randomization. Optional loading doses(up to 2.5 mcg/kg dexmedetomidine or 0.05 mg/kg midazolam) was administered at the investigators discretion. The starting maintenance infusion dose of study drug was 0.5 mcg/kg/hr for dexmedetomidine and 0.025 mg/kg/hr for midazolam corresponding to the midpoint of allowable infusion dose range. Dosing of the study was adjusted by managing the clinical team based on sedation assessment performed with Ramsay Sedation Score (RSS), a minimum of every 1 hour for the first 6 hours, thereafter every 2 hours till extubation or up to 18 hours. No other sedatives or analgesics or muscle relaxants were allowed during the study period. Study drug infusion was stopped at the time of extubation in both the groups or after a maximum of 18 hours. The following parameters were assessed:

- Level of sedation was assessed by RSS initially every hour for 6 hours, thereafter every 2 hours till extubation or up to 18 hours;
- Hemodynamic parameters (HR, SBP, DBP, MAP, SpO_2);
- Duration of analgesia by pain assessment using Visual Analog Score (VAS);
- Duration of ICU stay;
- Side-effects.

Statistical analysis was done by Unpaired *t*-test, which was used to compare the mean levels between two groups and Chi-square test for categorical data.

Results

A randomized prospective study was conducted in order to evaluate the efficacy and safety of dexmedetomidine in comparison to midazolam in the management of analgesia and sedation for postoperative patients in surgical ICU. A total of 100 postoperative patients were divided randomly into two groups of 50 each. Group D received dexmedetomidine, and Group M received midazolam infusion. The results were obtained as follows:

The mean age of patients in Group D was 41.9 ± 12.4 years, and that of Group M was 41.1 ± 14 years. There was no statistically significant difference between the two groups with respect to age distribution (p = 0.768). In Group D there were 24 male and 26 female patients; in Group M there were 23 male and 27 female patients. There was no significant statistical difference in gender distribution between the two groups (p = 0.84). The mean weight of patients of Group D was 57.2 ± 13.5 kg, and that of Group M was 57.8 ± 12.2 kg. There was no statistically significant difference in the body weight between two groups (p = 0.8).

Shown in Table 1, mean Ramsay sedation score range from 2.3 to 3.5 in Group D, and 2.6 to 3.7 in Group M. sedation score was not statistically significant in two groups (p > 0.05), (Fig. 1).

Table 1: Ramsay sedation score

Score	Response
1	Anxious or Restless or Both
2	Cooperative, Oriented and Tranquil
3	Responds to Commands
4	Brisk Response to Stimulus
5	Sluggish Response to Stimulus
6	No Response to Stimulus

Mean heart rate ranged from 77–97 bpm in Group D and 89–93 bpm in Group M. Statistical evaluation showed a significant fall in heart rate (17 bpm) in Group D immediately after administration of dexmedetomidine, and the fall in heart rate was maintained throughout the study period which was statistically significant (p = 0.00), (Fig. 2).

Fig. 1: Sedation score comparison

Mean SBP ranged from 113.0–117.7 mm of Hg in Group D while in Group M ranged from 110.0–119.6 mm of Hg. Mean DBP ranged from 69.0–72.0 mm of Hg in Group D while in Group M ranged from 65.5–70.8 mm of Hg. Basal MAP ranged from 83.7–87.4 mm of Hg in Group D, whereas in Group M ranged from 80.7–85.7 mm of Hg. Oxygen saturation level ranged from 98.0–99.0% in Group D, whereas in Group M ranged from 98.1–99.1%, there was no statistically significant difference in SBP, DBP, MAP, and SpO_2 among two groups, (Figs. 3–5).

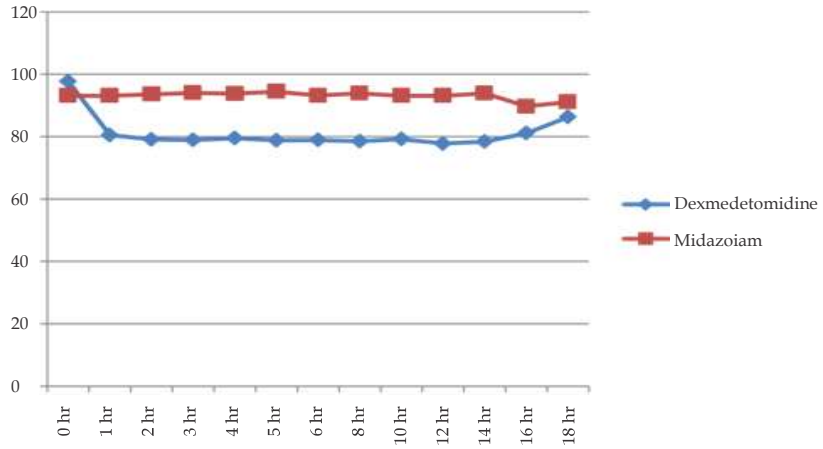

Fig. 2: Heart rate comparison.

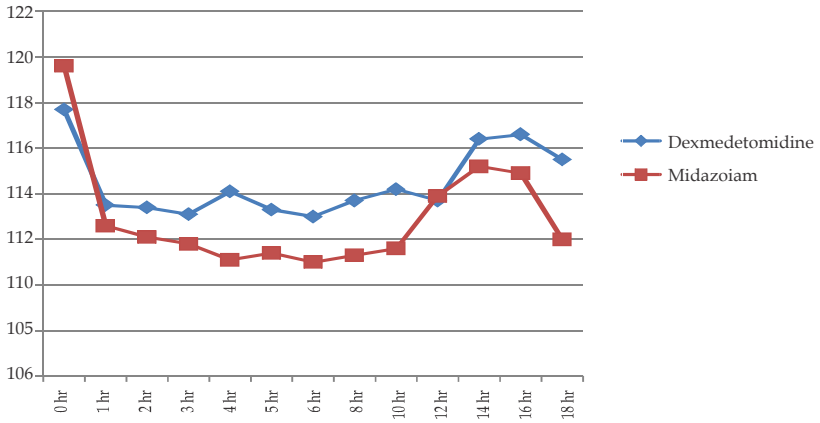

Fig. 3: SBP (Systolic Blood Pressure).

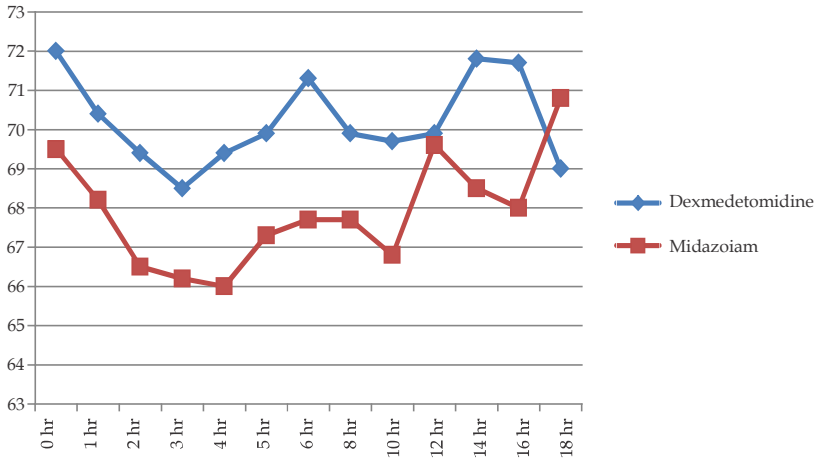

Fig. 4: DBP Comparison.

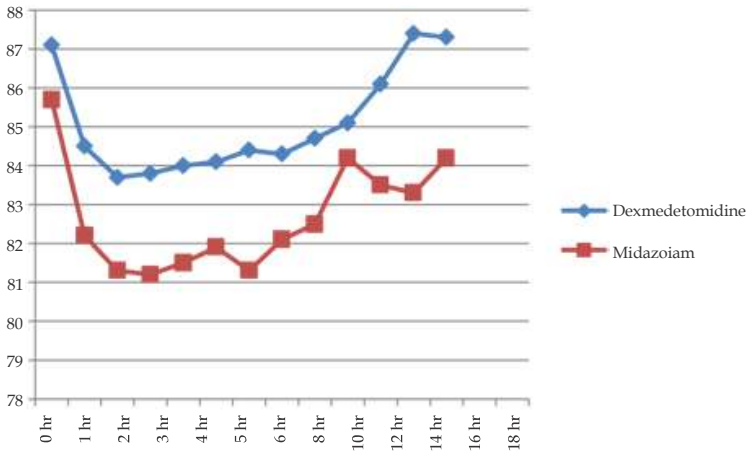

Fig. 5: MAP comparison.

Mean VAS score in Group D ranged from 2.2–3.1 after infusion of dexmedetomidine, whereas in Group M ranged from 2.0–4.0 after infusion of midazolam. There was no statistically significant difference in VAS among the two groups. Fig. 6. The mean ICU stay in Group D was 2.4 days, whereas in Group M was 2.6 days. There was no statistically significant difference in ICU stay among two groups (p = 0.22), (Fig. 7).

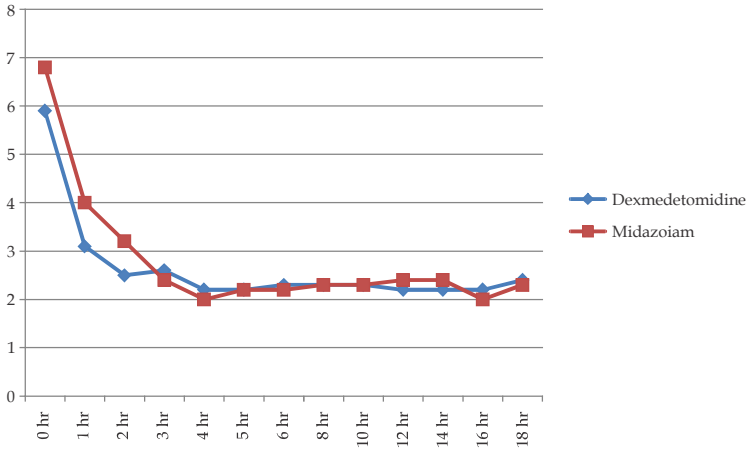

Fig. 6: VAS score comparison.

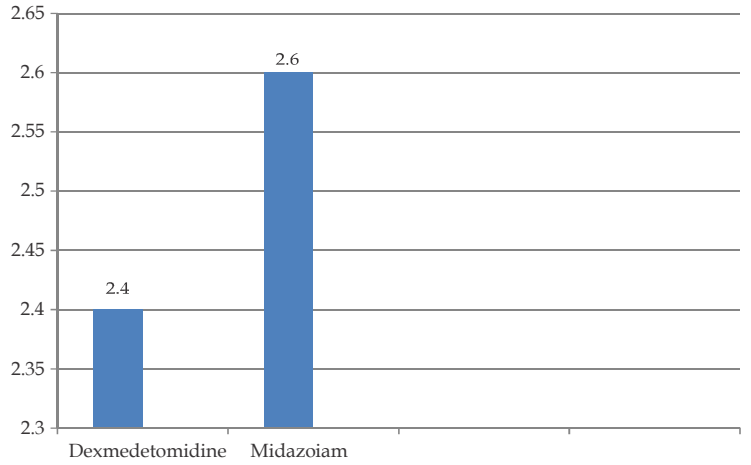

Fig. 7: Number of days of ICU Stay.

Discussion

Postoperative mechanically ventilated patients in surgical ICU require sedation and analgesia in order to modulate physiological response to stress and pain, hence reducing morbidity and mortality in the ICU.[1] Sedation helps in allaying the anxiety, increases tolerance to the endotracheal tubes, suppresses cough, and prevents respiratory fighting during intensive care procedures such as bronchial suctioning, physiotherapy, and catheter placement[2] and improves the outcomes of interventions in the Intensive care Unit.

The available literature has shown that sedative agent should have an action which is rapid in onset, should be effective at providing adequate sedation, allow rapid recovery after discontinuation, easy to administer, lack drug accumulation, have a few adverse effects and interact minimally with other drugs. The consequences of inadequate sedation and analgesia can be substantial, including self-removal of important intraluminal tubes and vascular catheters, aggressive behavior by patients against care providers, and poor patient-ventilator synchrony. Oversedation can lead to prolonged duration of mechanical ventilation, longer ICU and hospital stays, increased incidence of ventilator-associated pneumonia, and the inability of patients to communicate with health care providers or family members. The currently available sedatives include Propofol and benzodiazepines like Midazolam; both will provide adequate sedation, but they also produce many adverse effects. Benzodiazepines are anxiolytic and amnestic agents, but they can also cause paradoxical agitation in the elderly. Benzodiazepines are also associated with respiratory depression and the potential for the drug to accumulate, leading to aprolonged recovery period.

Midazolam is selected as the comparator medication owing to its frequent use for short-term sedation and is often identified as the sedative most commonly used in ICU. *Y*-Aminobutyric acid receptor agonist medications are the most commonly used sedatives for Intensive Care Unit (ICU) patients, yet preliminary evidence indicates that the α_2 agonist dexmedetomidine may have distinct advantages. Even after its beneficial effects, the midazolam has other outward effects, including restlessness, paradoxical reaction, cognitive impairment, amnesia, and respiratory depression.

Many newer sedatives are available in the market. Dexmedetomidine is one such newer sedative which is an α_2a adrenoreceptor agonist with a unique mechanism of action, providing sedation and anxiolysis via receptors within the locus coeruleus, a small nucleus present in the pons, analgesia *via* receptors in the spinal cord and attenuation of the stress response with no significant respiratory depression. Inaddition to sedation, dexmedetomidine provides analgesic effects, a lack of respiratory depression, sympatholytic blunting of the stress response, preservation of neutrophil function, and may establish a more natural sleep-like state. Dexmedetomidine is recently introduced in India (only in 2009) and available as 50 μg/0.5 ml, 100 μg/ml, 200 μg/2ml ampoules (Dexem, Themis Medicare Limited) and not many studies have been done using dexmedetomidine as a sedative in postoperative surgical ICUs.

Hence, the study was undertaken to evaluate the efficacy, hemodynamic variables, and safety profile of Dexmedetomidine as short-term sedative in comparison with most commonly used sedative Midazolam in postoperative mechanically ventilated patients. These studies are scant to prove the role of Dexmedetomidine as a sedative and analgesic in postsurgical patients in ICU. Hence, the study was undertaken to evaluate Dexmedetomidine as a sedative and analgesic in postsurgical patients in ICU. Hence, a randomized prospective study was conducted in order to evaluate the efficacy and safety of Dexmedetomidine in comparison to Midazolam in the management of analgesia and sedation for postoperative patients in surgical ICUs. A total of 100 postoperative patients were divided randomly into two groups of 50 each. Group D received Dexmedetomidine, and Group M received Midazolam infusion.

The mean age of the subjects in this study was 38.2 years in the Dexmedetomidine group and 39.1 years in the Midazolam group. About 52% in Group D and 54% in Group M were males. The mean weight of patients was 60.9 Kgs and 66.4 Kgs in Group D and Group M, respectively. There was no statistically significant difference with regards to mean age, weight, and sex. Hence, the two groups were comparable.

The mean sedation scores were ranged from 2.3 to 3.5 in Group D and 2.6 to 3.7 in Group M. There was no significant difference in Ramsay sedation score between Group D and Group M during the study period. In a similar study conducted by Jacobi J, Fraser GL et al.,[7] and Riker RR, Shehabi Y et al.,[5] dexmedetomidine produced equivalent sedation as Midazolam and the patients who have received Dexmedetomidine, despite artificial ventilation and intubation, were easily aroused to cooperate without showing irritation.

In the present study, there was significant bradycardia in the Dexmedetomidine group compared to the Midazolam group. There was a fall of 17 bpm after dexmedetomidine infusion, and the fall in heart rate was sustained throughout the study period and did not require any treatment. In a similar study, conducted by Vinit K Srivastava et al.[8] and Riker RR; Shehabi Y et al.,[5] heart rate showed a significant reduction in the dexmedetomidine group than in Midazolam group.

In the present study, visual analog scores were within the optimal range. VAS of 2–3 was achieved in both groups without using any other additive analgesia. In a similar study, conducted by McMurray et al.[9], and RM Venn et al.[10], they noted patients who received Midazolam infusions required significantly more analgesics than patients who received Dexmedetomidine infusions.

In the present study, there was no significant difference in length of ICU stay in both groups. In a similar study conducted by Stephen M; noted the recovery time and length of ICU stay were similar in both Dexmedetomidine and Midazolam groups.

Conclusion

The study was undertaken to evaluate the efficacy and safety of Dexmedetomidine compared to Midazolam as a short-term sedative in postoperative mechanically ventilated patients in surgical ICUs. Dexmedetomidine is a new alpha 2 agonist, which was as efficacious and had a safety profile similar to Midazolam.

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Abbreviations

ICU	Intensive Care Unit
GABA	Gama Aminobutyric Acid
HR	Heart Rate
BP	Blood Pressure
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
MAP	Mean Arterial Pressure
SpO_2	Oxygen Saturation
mg	Milligram
μg	microgram
Kg	Kilogram
Hr/hrs	Hour/hours
RSS	Ramsay Sedation Score
bpm	Beats per minute
mm Hg	Millimeter of Mercury
ASA	American Society of Anesthesiologists
VAS	Visual Anolog Scale

References

1. Md Ralib Azrina, Ali Saedah, Nikman Ahmad Mohd, et al. A comparative study of dexmedetomidine and propofol for sedation in the cardiothoracic intensive care unit. Int Med J 2007 Dec;6(2).
2. Elbaradie Samia, H El Mahalawy Faten and H Solyman Amira. Dexmedetomidine *vs* propofol for short-term sedation of postoperative mechanically ventilated patients. Journal of Egyptian Nat Cancer Inst 2000 September;16(3):153–58.
3. Mazzeo AJ. Sedation for the mechanically ventilated patient. Crit Care Clin 1995;11:937–55.
4. Tung A, Rosenthal M. Patients requiring sedation. Crit Care Clin 1995;11:791–802.
5. Riker RR, Shehabi Y, Bokesch PM, et al. Dexmedetomidine *vs* Midazolam for sedation of critically ill patients: A randomized trial. JAMA 2009;301(5):489–99.
6. Parker MM, Schubert W, Shelhamer JH. Perceptions of a critically ill patient experiencing therapeutic paralysis in an ICU. Crit Care Med 1984;12(1):69–71.
7. Jacobi J, Fraser GL, Coursin DB. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. Crit Care Med 2002;30(1):119–41.
8. K Srivastava Vinit, Agrawal Sanjay, Kumar Sanjay, et al. Comparison of dexmedetomidine, propofol and midazolam for short-term sedation in postoperatively mechanically ventilated neurosurgical patients. Journal of clinical and diagnostic research 2014 Sep;8(9):GC04–GC07.
9. McMurray TJ, Collier PS, Carson IW, et al. Propofol sedation after open heart surgery: A clinical and pharma cokinetic study. Anesthesia 1990;45: 322–26.
10. Venn RM, Bradshaw CJ. Preliminary UK experience of dexmedetomidine: A novel agent for postoperative sedation in the intensive care unit. Anesthesia 1999;54:1136–142.

Original Research Article

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Comparing ABG Analysis and Hemodynamics in Patients Undergoing Laparoscopic Cholecystectomy with Either ProSeal Laryngeal Mask Airway or Cuffed Endotracheal Tube as Airway Conduit: A Randomized Trial

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Abstract

Background and Aims: ProSeal Laryngeal Mask Airway (PLMA) has been proven to cause minimal hemodynamic fluctuations and postoperative complications when compared to cuffed Endotracheal Tubes (ETT) in laparoscopic surgeries. Hence, present study was done to compare ABG analysis and hemodynamic parameters in patients undergoing laparoscopic cholecystectomy. *Materials and Methods:* Present study included fifty American Society of Anesthesiologist Class I patients weighing 30–70 kg within age group of 20–60 years posted for elective laparoscopy cholecystectomy after the ethical committee clearance and were randomly allocated to either PLMA (Group I) or ETT (Group II) group with 25 in each group. Hemodynamic responses, ABG analysis and postoperative complications were noted and compared. *Results:* There was no demographic difference. When we analyzed heart rate, systolic and diastolic blood pressure, mean arterial pressure values, they were found to be comparable throughout except for those after insertion ($p < 0.05$). The ABG analysis and $EtCO_2$ before pneumoperitoneum and one hour after pneumoperitoneum showed no significant difference ($p > 0.05$) with either of the device. No case of regurgitation or aspiration found in either group. Postoperative complications were mainly seen with ETT Group. *Conclusion:* Metabolic effects of either PLMA and ETT during laparoscopy cholecystectomy were similar but PLMA affects the hemodynamic parameters to a lesser degree making it a better choice.

Keywords: Ventilatory mechanics; ABG analysis; PLMA; Hemodynamics; ETT.

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Introduction

The airway management of the patients undergoing laparoscopic procedures has progressed from Endotracheal Intubation (ETT) to lesser invasive devices like ProSeal Laryngeal Mask Airway (PLMA). One of the major advantages of these devices is that they are easily available, can be used even by inexperienced personnel and are almost atraumatic to the airway during insertion. The other advantages of supraglottic devices over ETT include tendency of causing less hemodynamic instability at induction and emergence, minimal

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increase in intraocular pressure after insertion, less depth of anesthetic requirements, coughing during emergence is less, improved oxygen saturation at extubation and lower incidence of sore throat.[1]

An understanding of the pathophysiological consequences of increased intraabdominal pressure is important for the anesthesiologist who must ideally prevent or when prevention is not possible, adequately respond to these changes. The raised intraabdominal pressure mandates the requirement of proper glottic seal to prevent pulmonary aspiration and adequate ventilation to eliminate absorbed CO_2. The PLMA provides a significantly higher oropharyngeal leak pressure making it better choice in those patients and situations where a high oropharyngeal leak pressure is required[2], laparoscopic procedure being one of them. This highoropharyngeal leak pressure avoids the leak during positive pressure ventilation and helps maintaining oxygenation well during pneumoperitoneum and hence can be compared with ETT for any changes in $PaCO_2$ in the blood.

One more danger of pneumoperitoneum is tendency to cause regurgitation and gastric distension when combined with positive pressure ventilation. PLMA being a double-lumen, double-cuff LMA provides an additional drain tube permitting access to gastrointestinal tract which further protects against regurgitation.[3]

Combining both adverse effects of ETT insertion and pneumoperitoneum a very well-studied and smooth device like PLMA can be considered, based on this hypothesis and ample of studies with the use of PLMA in laparoscopic surgeries,[4,5] we considered this study.

Materials and Methods

A randomized prospective, double-blind clinical trial was performed. According to a computer-generated plan, patients were then randomly divided into two groups – the ProSeal group as Group I (n = 25) and the ETT Group as Group II (n = 25).

Institutional ethical Committee approval was taken after which informed written consent was taken from fifty patients who were posted for elective laparoscopic cholecystectomy surgery under general anesthesia over a period of 1 year. Patients included were of either sex, ASA-Grade I weighing 30-70 kg and within age group of 20–60 years.

Exclusion Criteria

- *Problems in airway*: Limited mouth opening, anticipated/known difficult airway, reduced mobility of cervical spine, glottic and supraglottic airway obstruction, pharyngeal abscess/hematoma);
- *Increased risk of aspiration*: Full stomach, gastroesophageal reflux disease, delayed gastric emptying due to opioid or pregnancy.

A detailed history and examination of all patients was done one day prior to surgery. All patients were fasted overnight and were given tablet Alprazolam (0.25 mg) at bedtime and 2 hours preoperatively. Patients were given injection diclofenac sodium 75 mg and glycopyrrolate (0.2 mg) intramuscular 45 minutes prior to induction. An intravenous line was secured followed by injection ranitidine (50 mg) and metoclopramide (10 mg), 40 minutes before surgery.

Patient was then shifted to operating room, ringer lactate was started and all routine monitors were attached (ECG, noninvasive blood pressure and pulse oximetry). It was ensured preoperatively that PLMA or ETT to be used was checked and correct size is available. Preoxygenation for 3 minutes was done which was followed by injection propofol 2 mg/kg and suxamethonium 2 mg/kg for induction of anesthesia. Injection tramadol 0.4–0.5 mg/kg was given as analgesic. Then respective device allocated was inserted.

Group I: PLMA (size 3 in females and size 4 in males) using introducer;

Group II: Cuffed ETT (size 7–7.5 ID for females, size 8–8.5 ID for males).

PLMA cuff was thoroughly deflated with a syringe using cuff-deflating tool & lubrication was applied to the posterior cuff surface. After optimal placement in hypopharynx, mask was inflated with 20–30 ml of air to obtain a required seal. Correct placement of both PMLA and ETT was ensured by chest expansion, auscultation, absence of leak on auscultation of epigastrium and neck, leak test by passage of gastric tube into stomach *via* drain tube and $EtCO_2$. The NGT was inserted 10 minutes after the placement of the device and connected to intermittent suction for the duration of surgical procedure in both the groups. Anesthesia was maintained with isoflurane in oxygen and nitrous oxide (1:2) and intermittent boluses of vecuronium (0.1 mg/kg). Ventilation was controlled mechanically using closed circuit with CO_2 absorber and were ventilated with tidal volume of 8 ml/kg. Respiratory rate adjustments in

ventilator were done for $EtCO_2$ levels above 60 mm Hg or SpO_2 below 92% or any adverse hemodynamic changes. Abdominal cavity was then insuffulated with CO_2 and intraabdominal pressure maintained at 10–12 mm of Hg with flow rate between 1.8–2 liters/min. Head up and lateral tilt was provided at the surgeon's request. Hemodynamic parameters - Heart Rate (HR), Systolic, Diastolic & Mean Blood Pressure (SBP, DBP, MAP) and pulse oximetry (SpO_2) were noted at preinduction, after insertion of device, after nasogastric tube (NGT) insertion, before & 10 minutes after pneumoperitoneum and postoperatively.

The presence of any visible secretions or blood on the device was documented, other complications like gastric distension, aspiration etc. were also noted. If secretions present over PLMA their pH was done. Peritoneal insufflation and total anesthetic time were also noted. ABG analysis before pneumoperitoneum and one hour after pneumoperitoneum was also done. Simultaneously, the values of $EtCO_2$ were also noted.

At completion of procedure reversal was given in form of injection neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). Extubation was done after suctioning and removal of NTG when patient responded on command. Postoperative complications such as cough, vomiting, laryngospasm or any intervention required during emergence was also recorded.

Statistical analysis

The data was analyzed with the help of computer software MS-excel and SPSS12.0 for windows. Outcomes were reported as percentages for qualitative variables and mean and standard deviation for quantitative variables. Unpaired "*t*" test/Chi-square/Fisher's exact test were employed to evaluate statistical significance between the two groups. A *p* - value of < 0.05 was considered as statistically significant.

Results

A total of 50 patients were randomized after checking inclusion and exclusion criteria, Fig. 1. Both the groups were comparable in age, sex and

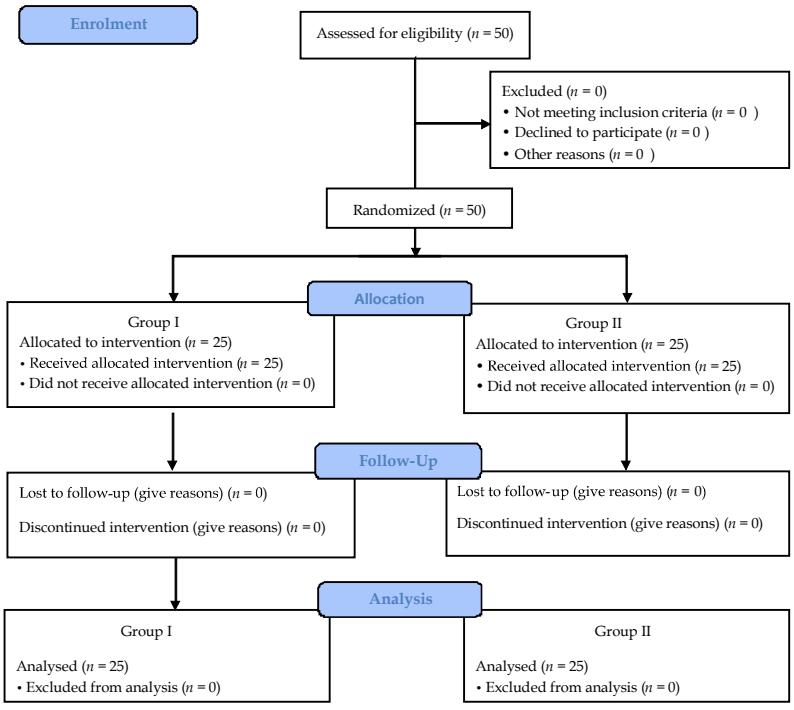

Fig. 1: Consort Flow Diagram.

weight distribution as shown in (Fig. 2).

There was no statistically significant difference in mean values of peritoneal insufflation time being 77.36 ± 16.88 and 80.36 ± 15.6 seconds in Group I and II respectively (*p* - value = 0.51). The total anesthetic time was also comparable in both the groups being 93.44 ± 21 min and 98.12 ± 18.86 min with *p* - value of 0.41, Fig. 2. Insertion success rate for NGT placement in PLMA and ETT Groups was comparable in both the groups i.e. 96% for 1st

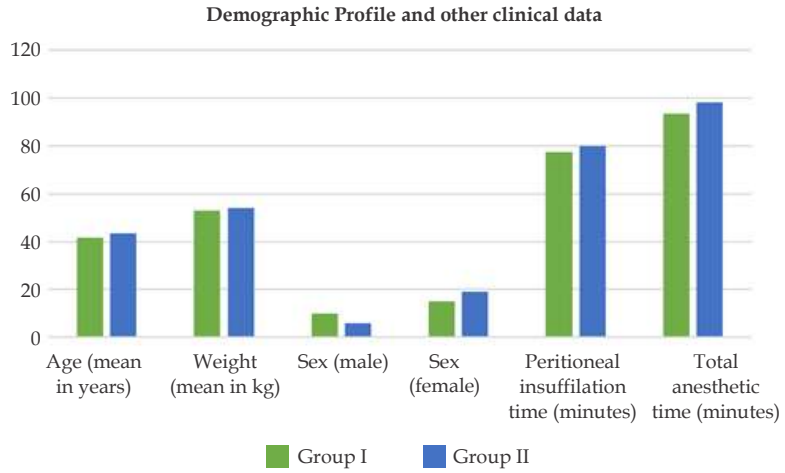

Fig. 2: Showing demographic profile and other clinical data of the two groups.

attempt and 4% for 2nd attempt. No patient required 3rd attempt for any of the devices' placement.

The observations of HR and MAP are shown in Tables 1 and 2, values are in mean ± standard deviation. The SBP and DBP were insignificant between the two groups throughout the surgery except just after insertion of device. The mean SBP was 122.68 ± 12.9 and 138.6 ± 9.98 mm of Hg in Group I and II respectively with a *p* - value of 0.0001

Table 1: Heart Rate (beats per minute) at various intervals

Time intervals	Group I	Group II	*p* - value
Preinduction	88.32 ± 13.7	81.4 ± 11.44	0.06
After insertion	87.8 ± 15.08	88.28 ± 9.97	0.89
After NGT	86.6 ± 13.9	82.08 ± 8.27	0.17
Before pneumoperitoneum	84.32 ± 12.7	81.04 ± 7.85	0.27
After pneumoperitoneum	85.84 ± 13.5	82.88 ± 8.08	0.35
Postoperative	84.12 ± 12.7	80.32 ± 8.23	0.21

Table 2: MAP (mm of Hg) at various intervals

Time intervals	Group I	Group II	*p* - value
Preinduction	92.84 ± 10.18	96.04 ± 8.56	0.23
After insertion	92.92 ± 9.05	104.84 ± 8.13	0.0001
After NGT	92.48 ± 7.62	94.96 ± 4.06	0.15
Before pneumoperitoneum	92.92 ± 8.55	94.04 ± 4.87	0.57
After pneumoperitoneum	95.24 ± 8.29	96.92 ± 5.74	0.40
Postoperative	90.84 ± 7.77	93.72 ± 5.68	0.14

which was significant. The mean DBP was 78.56 ± 9.06 and 88.6 ± 7.82 mm of Hg with $p = 0.0001$ and was significant.

Arterial Oxygen Saturation (SpO_2) was between 94–100% throughout the procedure in both the groups indicating adequate ventilation and any absence of hypoxia. Gastric distension was reported in 1 of our cases in PLMA Group while secretions over PLMA were noticed in 2 of the patients and their pH as determined by litmus paper technique was > 6. There was no case of regurgitation or aspiration noted in any of the patients in each group. Overall incidence of complications was comparable in both the groups with $p = 0.11$.

ABG analysis between the two groups was done before creation of pneumoperitoneum and one hour after pneumoperitoneum and the parameters were comparable between the two groups, Fig. 3. The pH values were comparable in both the groups. The mean pH values before pneumoperitoneum

were 7.39 ± 0.01 and 7.39 ± 0.02 in Group I and II respectively with *p* - value of 1 i.e. not statistically significant. The mean pH values one hour after pneumoperitoneum were 7.41 ± 0.02 and 7.40 ± 0.02 in Group I and II respectively with *p* - value of 0.38 i.e. not statistically significant. $PaCO_2$ values before and one hour after pneumoperitoneum were also not significant with $PaCO_2$ before pneumoperitoneum being 37.92 ± 0.95 mm Hg and 37.84 ± 1.14 mm Hg with *p* - value of 0.78. $PaCO_2$ one hour after pneumoperitoneum being 38.92 ± 1.15 mm Hg and 39 ± 1.55 mm Hg with *p* - value of 0.83. The values of mean $EtCO_2$ were 37.34 and 41.96 in PMLA Group, 36.88 and 40.15 in ETT Group before pneumoperitoneum and one hour after pneumoperitoneum with *p* - value of > 0.05 and was insignificant, and was noted at the same time when ABG sample was withdrawn

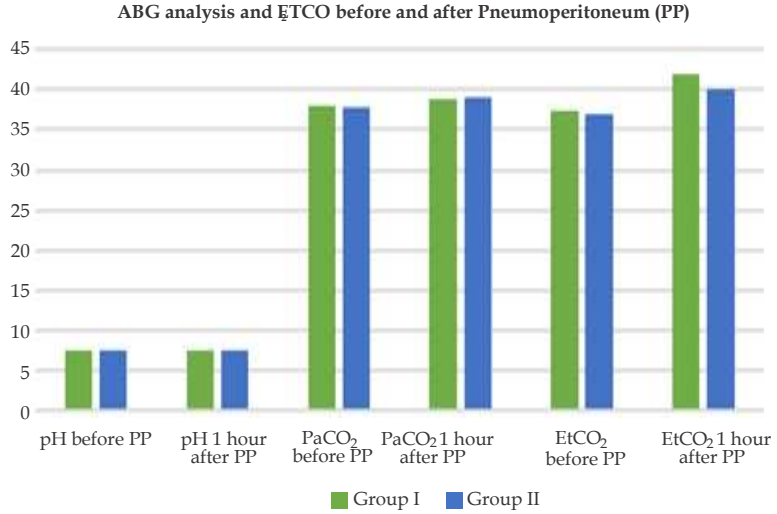

Fig. 3: Showing ABG analysis and $EtCO_2$ before and one hour after pneumoperitoneum.

from the patient. In present study, most of the cholecystectomies were done within 60 minutes and very few extended to 90 minutes hence duration of exposure to CO_2 was comparable in both the groups and also eliminates the bias caused by duration of pneumoperitoneum.

Table 3: Postoperative complications

Complications	Group I	Group II
1. Cough	2/25 (8%)	8/25 (32%)
2. Laryngospasm	none	1/25 (4%)
3. Bronchospasm	none	none
4. Sore throat	3/25 (12%)	6/25 (24%)
5. Vomiting	1/25 (4%)	none

* Values in number (percentage).

Postoperative complications are shown in Table 3. A total of 6 patients in Group I (24%) and 15 patients in Group II (60%) had the complications. Overall incidence of respiratory events at extubation was comparable with *p* - value of 0.47.

Discussion

In literature we found ample of studies comparing PLMA and ETT proving it to be an equally efficacious device as far as insertion characteristics are considered. In present study, we chose laparoscopic procedure because increased intraabdominal pressure from pneumoperitoneum requires the higher airway pressures for which PLMA was originally designed. Moreover, it is proven fact that PLMA can withstand higher oropharyngeal leak pressures,[2] so, we compared it with ETT to see its adequacy in providing good ventilation and oxygenation during laparoscopic surgery.

When hemodynamic parameters were compared in our study there was not much difference in mean heart rate between both the groups, as was shown by Shroff PP et al.[5] also. However, in PLMA Group they found more heart rate which was statistically significant before and after pneumoperitoneum in contrast to ours. The systolic, diastolic and mean blood pressures in our study were comparable at various intervals but were significant after insertion of both devices. The values were much lower in PLMA Group after insertion as compared to ETT Group proving that it causes less stimulation at intubation and was similar to other studies.[5-7] These studies recommended PLMA for patients with cardiac and respiratory diseases because of stable hemodynamics and quicker insertion and considered it to be a safer airway conduit for ventilation during the laparoscopic surgeries. The mechanism for hemodynamic changes associated with ETT/LMA insertion as quoted by most of the authors is due to altered plasma catecholamine levels. ETT insertion leads to stimulation of afferent pathways both pharyngeal and laryngeal, whereas LMA placement causes partial afferent stimulation that is pharyngeal only. As all sympathetic stimuli are mediated by afferent fibers, their stimulation ultimately leads to the release of catecholamines in the blood which are responsible for the pressor responses in the body. Ultimately from above discussion we can comment that PLMA causes less hemodynamic variability and thus giving it an edge over the ETT for laparoscopic surgery.

Arterial oxygen saturation was between 94–100% throughout the procedure in both groups indicating adequate oxygenation and absence of any hypoxia in our study. This was comparable to other studies.[4,5,8] However, Sharma B et al.[8] also reported transient suboptimal oxygenation (SpO_2 - 94%) in one patient undergoing extraperitoneal inguinal hernia repair which was due to extensive subcutaneous emphysema.

CO_2 is 20 times more soluble than air and oxygen and thus more rapidly absorbed from peritoneal cavity and then excreted from lungs. So, if ventilation is not adequate it can lead to CO_2 accumulation (hypercarbia), respiratory acidosis and hemodynamic alterations. $EtCO_2$ is considered as good noninvasive monitoring modality for determining the minute ventilation required to maintain normocarbia and for estimation of $PaCO_2$ especially during pneumoperitoneum but it takes about 15 minutes for $PaCO_2$ to reach a plateau value after creation of pneumoperitoneum.[9,10] Because of high solubility of CO_2, its vascular systemic absorption is also increased from peritoneum during this period. This, combined with decreased lung compliance during laparoscopic procedure (due to upward shift of diaphragm) leads to increased arterial CO_2 levels and decreased pH. In our study, also the pH and $PaCO_2$ altered after pneumoperitoneum but their values were comparable in both the groups showing that patients were equally well-ventilated with PLMA. Also, $PaCO_2$ analysis helps us to assess ventilation because the normal arterial–to-end-tidal CO_2 gradient increases as the dead space is increased. In our study, we maintained our patients on controled ventilation with nitrous oxide 60% in oxygen, isoflurane and vecuronium intermittent boluses as and when required. We did not adjust any ventilatory parameters in any patient of the two groups during the pneumoperitoneum period as all of them maintained $EtCO_2$ below 60 mm of Hg during that period.

Above findings in our study are also supported by Showket et al.[11] but they studied the pediatric population and concluded that at ventilator parameters designed to maintain normocapnia, the PLMA provided adequate seal. Similar results were seen in other studies.[4,8,12] In a study by Shah et al.[1] who compared PLMA and ETT in the patients undergoing beating-heart coronary artery bypass grafting also found that respiratory parameters such as SpO_2, pCO_2, peak airway pressure and lung compliance were comparable in both groups and occurrence of adverse events was also lower in PLMA Group. ABG monitoring to ascertain $PaCO_2$ levels is not a routine part of laparoscopic procedures due to nonavailability of ABG analyzer machine and the associated costs especially in developing countries. There appears correlation between $EtCO_2$ levels and $PaCO_2$ levels in our study thus $EtCO_2$ may be used as a marker of $PaCO_2$ change in case ABG analyser is not available. In intraoperative complications we found 4% (one patient) incidence of gastric distention with PLMA and no case of gastric distention was found in ETT Group as well. Our findings were supported by Shroff et al.[5] who noted 3% gastric distention in PLMA and none in ETT Group.

In our study, we found no case of regurgitation of gastric contents through the drain tube when PLMA was used because we had ensured previously that all our patients received appropriate premedication to minimize and decrease gastric volume and acidity. Also, NGT was inserted and intermittent suctioning was done in all of our patients. There was no case of regurgitation of gastric contents

into the bowl of PLMA which was consistent with various other studies.[5,6,13]

As found in other studies[8,14,15] we also found no case of pulmonary aspiration in PLMA group, danger of an unprotected airway and any risk of aspiration pneumonitis could not be made as volume was too small to determine that. In both the groups of our study, the peritoneal insufflation time and total anaesthetic time were comparable. There are ample of studies where PLMA was used for as long as 300 minutes without any adverse events supporting findings of our study.[4,15] Shah K et al.[1] used PLMA in beating heart coronary artery bypass grafting surgery showing that it can be used for prolonged surgery as an alternative to ETT.

In our study the group with ETT had more postoperative complications as compared to PLMA as such, thus showing smoother extubation with PLMA. Patients in PLMA Group in our study showed lower incidence of cough and sore throat this can be attributed to the fact that no laryngoscopy was required during its insertion and hence atraumatic to the airway. This also leads to low mucosal pressure causing lesser pharyngeal perfusion pressure. Overall respiratory complications when seen with PLMA Group in our study were less. Laryngospasm was reported in one of the patients in ETT Group as was found in other studies too.[2,5,15] However, in studies by N Saraswat et al.[12] and Patodi V et al.[16] frequency of complications during emergence were significantly more in ETT Group.

We found only one patient with vomiting after PLMA removal in our study. No particular reason for vomiting could be ascertained as no treatment was required and it settled of its own. However, Hohlrider et al.[17] showed that PLMA reduced the absolute risk of postoperative nausea and vomiting by 40% also because of the reason that cuff of PLMA is less stimulating to pharyngeal mucosa as compared to ETT cuff causing lesser airway morbidity in PLMA Group.

Limitations of our study were that we did not analyse the influence of duration of surgery and hence the CO_2 exposure which can be done by including different laparoscopic procedures and analysing their effect. Secondly, we did not measure the oropharyngeal leak pressures. Thirdly, we could have measured the bicarbonate levels, lactate, urea and electrolytes to further support our results but because we took a simple procedure without major intercompartmental fluid shifts we did not do it.

Conclusion

In conclusion ProSeal laryngeal mask airway (PLMA) can be used safely and is equally effective airway conduit to Endotracheal Tube (ETT) for patients of laparoscopic cholecystectomy reason being more stable hemodynamics and its ability to maintain adequate ventilation and oxygenation in such procedures.

So, PLMA can be considered as a better choice in high-risk patients with hypertension, ischemic heart disease and obstructive airway diseases for laparoscopic procedures. We recommend further studies with larger sample size to authenticate the above results.

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References

1. Shah K. ProSeal laryngeal mask airway as an alternative to standard endotracheal tube in securing upper airway in the patients undergoing beating-heart coronary artery bypass grafting. Ann Card Anesth 2017;20:61–66.
2. Singh A, Bhalotra AR, Anand R. A comparative evaluation of ProSeal laryngeal mask airway, I-gel and Supreme laryngeal mask airway in adult patients undergoing elective surgery: A randomized trial. Indian J Anesth 2018;62:858–64.
3. Evans NR, Gardener SV, James MFM. ProSeal laryngeal mask protects against aspiration of fluid in the pharynx. British Journal of Anesthesia 2002;88(4):584–87.
4. Maltby JR, Beriault MT, Watson NC. LMA ProSeal is an effective alternative to tracheal intubation for laparoscopic cholecystectomy. Canadian Journal of Anesthesia 2002;49(8):857–62.
5. Shroff PP, Kamath S. Randomized comparative study between the ProSeal laryngeal mask and the endotracheal tube for laparoscopic surgery. Internet Journal of Anesthesiology 2006;11(1).
6. Parekh SS, Parekh Shivam Bipin, Chaula Doshi, et al. ProSeal laryngeal mask airway *versus* cuffed endotracheal tube for laparoscopic surgical procedures under general anesthesia: A random comparative study. Anesth Essays Res 2017;11(4):958–63.
7. Idrees A, Khan FA. A comparative study of positive pressure ventilation *via* laryngeal mask airway and endotracheal tube. J Pak Med Assoc 2000;50:333–38.

8. Sharma B, Sahai C, Bhattacharya A, et al. ProSeal laryngeal mask airway: A study of 100 consecutive cases of laparoscopic surgery. Indian J Anesth 2003;47:467–72.
9. Mutetwa EN, Shumbairerwa S, Crawford, et al. Metabolic effects of carbon dioxide (CO_2) insufflation during laparoscopic surgery: Changes in pH, arterial partial Pressure of Carbon Dioxide ($PaCO_2$) and End Tidal Carbon Dioxide ($EtCO_2$). Cent Afr J Med 2015;61(9–12):61–65.
10. Joris JL. Anesthesia for Laparoscopic Surgery, Miller's Anesthesia, 6th edition. Edited by Miller RD. Elsevier Churchill: Livingstone; 2005.pp.2285–2306.
11. Ahmad Dar Showket, Deka Sangeeta, Das Nilotpal, et al. Proseal LMA *versus* endotracheal tube a clinical comparative study of its different effects in pediatric patients undergoing lower abdominal surgeries. International Journal of Contemporary Medical Research 2016;3(5):1301–305.
12. Saraswat N, Kumar A, Mishra A, et al. The comparison of Proseal laryngeal mask airway and endotracheal tube in patients undergoing laparoscopic surgeries under general anesthesia. Indian J Anesth 2011;55:129–34.
13. Roth H, Genzwuerker HV, Rothhas A, et al. Proseal laryngeal mask airway and the laryngeal tube suction for ventilation in gynecological patients undergoing laparoscopic surgery. Eur J Anesthesial 2005;22(2):117–22.
14. Brimacombe J, Keller C, Berry A. Gastric insufflation with the ProSeal laryngeal mask. Anesthesia Analgesia 2001;92(6):1614–15.
15. Maltby JR, Beriault MT, Watson NC, et al. LMA classic and LMA ProSeal are effective alternatives to endotracheal intubation for gynecologic laparoscopy. Canadian Journal of Anesthesia 2003;50(1):71–77.
16. Patodi V, Singh M, Sethi SK, et al. A comparative study between ProSeal laryngeal mask airway and endotracheal tube for ease of insertion and hemodynamic changes in patients undergoing laparoscopic cholecystectomy under general anesthesia. IJRMS 2016;4(12):5334–340.
17. Hohlrieder M, Brimacombe J, Von Goedecke A, et al. Postoperative nausea, vomiting, airway morbidity and analgesic requirements are lower for the ProSeal laryngeal mask airway than the tracheal tube in females undergoing breast and gynecological surgery. British Journal of Anesthesia 2007;99(4):576–80.

Original Research Article

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A Comparative Study of the Efficacy of Dexmedetomidine and Clonidine as an Adjuvant to Bupivacaine in Supraclavicular Brachial Plexus Block

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Abstract

Background: Supraclavicular brachial plexus block is preferable to general anesthesia in upper limb surgeries. Various adjuvants have been added to improve the quality of the block and prolong postoperative analgesia. Alpha-2 agonists are used as adjuants to local anesthetics to extend the duration of neuraxial and peripheral nerve blocks. We compared clonidine and dexmedetomidine as an adjuvant to bupivacaine in supraclavicular brachial plexus block. *Aims:* To compare the effects of Clonidine and Dexmedetomidine when added as adjuvant to Bupivacaine on onset and duration of sensory & motor block, duration of analgesia and quality of block for Supraclavicular brachial plexus block. *Methods:* In this prospective, double-blinded study 60 ASA I–II patients were randomly divided into two groups of 30 each. First group received 30 ml bupivacaine 0.325% with Clonidine 1 mcg/kg (Group C) and second group received 30 ml bupivacaine 0.325% with dexmedetomidine 1 mcg/kg (Group D) in Supraclavicular brachial plexus. The characteristics for anesthesia and analgesia were assessed for the two groups. *Results:* Onset of sensory block was faster in Group D than in Group C, while onset of motor block was faster in Group C than in Group D, but the difference was not statistically significant. Duration of sensory block and motor block was 234.17 ± 24.11 min and 296.30 ± 25.78 min in Group C as compared with 445.07 ± 67.79 min and 503.10 ± 75.67 min in Group D. Statistically significant longer duration of sensory and motor block was observed in Group D ($p < 0.001$). There was significant increase in duration of analgesia in Group D (477.27 ± 70.11 min) as compared with Group C (285.43 ± 26.88 min). In Group D, 83.3% of the patients achieved Grade IV quality of block as opposed to 43.3% in Group C ($p = 0.006$). *Conclusion:* To conclude, dexmedetomidine prolongs the duration of sensory and motor block and enhances the quality of block as compared with clonidine when used as an adjuvant to Bupivacaine. The added advantage of conscious sedation, hemodynamic stability, and minimal side-effects makes it a potential adjuvant for nerve blocks.

Keywords: Bupivacaine; Clonidine; Dexmedetomidine; Supraclavicular brachial plexus block.

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Introduction

Most of the upper limb surgeries are performed under brachial plexus block. Peripheral nerve blocks provides intraoperative anesthesia and postoperative analgesia without any systemic side-effects.[1] Supraclavicular brachial plexus block provides safe, effective, low-cost anesthesia with good postoperative analgesia.

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Clonidine, a partial α_2 adrenoceptor agonist is used as adjuvant to local anesthetics to prolong the peripheral nerve block duration.[2-4] The $\alpha_2 : \alpha_1$ selectivity of dexmedetomidine is eight times that of clonidine and it has high specificity for α_2 subtype which makes it a much more effective sedative and analgesic agent.[5]

Dexmedetomidine is being used for intravenous (IV) sedation and analgesia for intubated and mechanically ventilated patients in Intensive Care Units (ICUs),[6,7] and nonintubated patients for surgical and other procedures.[8] In previous clinical studies, the use of IV dexmedetomidine lead to significant opioid sparing effects and decrease in inhalational anesthetic requirements.[9] It has been described to improve the quality of intrathecal and epidural anesthesia.[10-13] This study was designed to test the hypothesis that dexmedetomidine when added as an adjuvant to bupivacaine in supraclavicular brachial plexus block increases the sensory and motor block duration, duration of analgesia and block quality when compared with clonidine.

Materials and Methods

A prospective randomized double-blind clinical trial was carried out on sixty ASA I and II patients planned for elective upper limb surgeries under supraclavicular brachial plexus block after obtaining written informed consent and ethical committee approval. They were divided into two groups (Group C and Group D) of 30 patients each.

Group C: Received clonidine 1 μg/kg + bupivacaine 0.325% (30 cc), and

Group D: Received dexmedetomidine 1 μg/kg + bupivacaine 0.325% (30 cc).

Patients with significant neurological & neuromuscular deficit, cardiovascular, pulmonary, alcohol or drug abuse, pregnancy or lactating women and patients on adrenoceptor agonist or antagonist therapy or on sedatives, antipsychotic therapy were excluded from this study. Patient refusal for procedure, morbid obesity, peripheral vascular disease, coagulopathy, or known allergies were also excluded.

On arrival in the operation room, basal Heart Rate (HR), noninvasive Systolic Blood Pressure (SBP) & Diastolic Blood Pressure (DBP), and Oxygen Saturation (SpO_2) were recorded. An 18/20 gauge (G) IV cannula was secured in nonoperated arm and Ringer's lactate was started. Patients were allocated randomly into two groups. Anesthesiologist not involved in the study prepared the drug solutions. The anesthesiologist conducting the block and monitoring the patient was blinded to the treatment group. The same anesthesiologist collected the data who was unaware of the group allocation.

Neural localization was done by using a nerve stimulator (B Braun) connected to a 22 G, 5 cm length stimulating needle (Stimuplex, Braun). The location end point was a distal motor response with an output lower than 0.5 mA in the median nerve region. 30 mL of a solution containing local anesthetic combined with clonidine or dexmedetomidine as mentioned above was injected. Negative aspiration was done every 5 ml to avoid intravascular injection while injecting drug solution. A 3-min massage was performed to avoid an uneven drug distribution.

Sensory block was assessed in the distribution of four nerve territories of median nerve, radial nerve, ulnar nerve and musculocutaneous nerve by pin prick test using a 3-point scale. Sensory block assessment was done at each minute after completion of drug injection until total sensory blockade. Onset of sensory block was appraised when there was a dull sensation to pin prick and complete sensory block was appraised when there was complete loss of sensation to pin prick along the distribution of any of the above mentioned nerves.

Sensory block was graded[25] as:

Grade 0: Sharp pin prick felt;

Grade 1: Analgesia, loss of sensation of pin prick;

Grade 2: Anesthesia, loss of sensation of touch.

Motor block was determined by thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion of elbow (musculocutaneous nerve) according to the modified Bromage scale[14] on a 3-point scale. At each minute motor block assessment was carried out by the same observer until total motor blockade after drug injection.

Motor block was graded as:

Grade 0: Normal motor function with full flexion and extension of elbow, wrist, and fingers;

Grade 1: Decreased motor strength with ability to move the fingers only;

Grade 2: Complete motor block with inability to move the fingers.

Sensory block onset time was defined as the time interval between the end of local anesthetic administration and complete sensory block (score 2 for all nerves). Sensory block duration was defined as the time interval between the complete sensory block and complete resolution of anesthesia on all the nerves (score 0). Motor block onset time was defined as the time interval between total local anesthetic administration and complete motor block (Grade 2). Motor block duration was defined as the time interval from complete motor block to complete recovery of motor function of hand and forearm (Grade 0).

The block was contemplated incomplete when any of the segments supplied by ulnar, radial, median and musculocutaneous nerve did not have analgesia even after 20–30 min of drug injection.

These patients were supplemented with IV fentanyl (1–2 μg/kg) and midazolam (0.02 mg/kg). We considered block failed when two or more nereves unaffected. In this case, general anesthesia was given intraoperatively.

HR, SBP, and DBP were recorded at 0, 15, 30, 60, 90, and 180 min intraoperatively and every 60 min postoperatively. The modified Ramsay Sedation Scale (RSS)[15] was used to assess sedation score from 1–6 as follows:

1 = Anxious, agitated, restless;

2 = Cooperative, oriented, tranquil;

3 = Responds to commands only;

4 = Brisk response to light glabellar tap or loud noise;

5 = Sluggish response to light glabellar tap or loud noise;

6 = No response to stimulus.

Blood loss was calculated by the gravimetric method and replaced if more than the allowable blood loss. Duration of surgery was noted.

The quality of operative conditions were assessed according to the following numeric scale[16]:

Grade 4: No complaint from patient (Excellent);

Grade 3: Minor complaint with no need for the supplemental analgesics (Good);

Grade 2: Complaint that required supplemental analgesia (Moderate);

Grade 1: Patient given general anesthesia (Unsuccessful).

The intra- and postoperative assessment was done by an anesthesiologist who was unaware of the drug used. Duration of Analgesia (DOA) is the time between the complete sensory block and the first analgesic request. Patients were assessed for duration of analgesia as per a numeric rating scale of 0 to 10. Postoperatively, numeric rating scale was recorded every 60 min until the score of 5.

The rescue analgesia was given in the form of Inj. diclofenac sodium (1.5 mg/kg) intramuscularly at the Numeric Rating Scale of 5 and the time of administration was noted. Patients were observed for any side-effects like nausea, vomiting, dryness of mouth and also observed for complications like pneumothorax, hematoma, local anesthetic toxicity and postblock neuropathy in the intra and postoperative periods.

Statistical Methods

Descriptive and inferential statistical analysis has been used in our study. Continuous measurement results are presented on Mean ± SD (Minimum-Maximum) and results on categorical measurements are presented in percentage numbers (%). '*p* - value of less than 0.05' was considered to be significant. The following assumptions on data were made - dependent variables were normally distributed, random sampling from the population was ensured and the cases of the samples were independent.

Student *t*-test (two tailed, independent) and Chi-square/Fisher Exact test were used to assess the significance of study parameters on continuous scale for inter group analysis on metric parameters and categorical scale between two or more groups respectively. Levene's test for homogeneity of variance has been performed to assess the homogeneity of variance and $p \leq 0.01$ was considered to be strongly significant.

Results

Sixty patients fulfilling the inclusion criteria were randomly assigned to one of the two groups. The demographic data and surgical characteristics were comparable in both groups, showed in Table 1, ($p > 0.001$).

The baseline hemodynamic parameters were comparable in both groups. Significantly lower pulse rate was observed at 30, 60 and 90 min, but not less than 60 beats/min, in Group D as compared with Group C, showed in Fig. 1, ($p < 0.001$).

Table 1: Demographic data

Parameters	Group C (n = 30) Clonididne Mean ± SD)	Group D (n = 30) Dexmedetomidine (Mean±SD)	p - value
Age (years)	36.87 ± 10.89	39.67 ± 11.41	0.335 (NS)
Weight (kg)	58.87 ± 7.75	60.77 ± 7.99	0.354 (NS)
Gender (M/F)	18/12	12/18	1.000 (NS)
Type of surgeries			
# Lower end of humerus	6	4	
# Elbow (Olecranon)	4	4	
# Radius & ulna	20	22	

n = Number of patients; SD = Standard Deviation; $p < 0.05$ significant; NS= Not significant; M = Male; F = Female; Kg = Kilogram; # = Fracture.

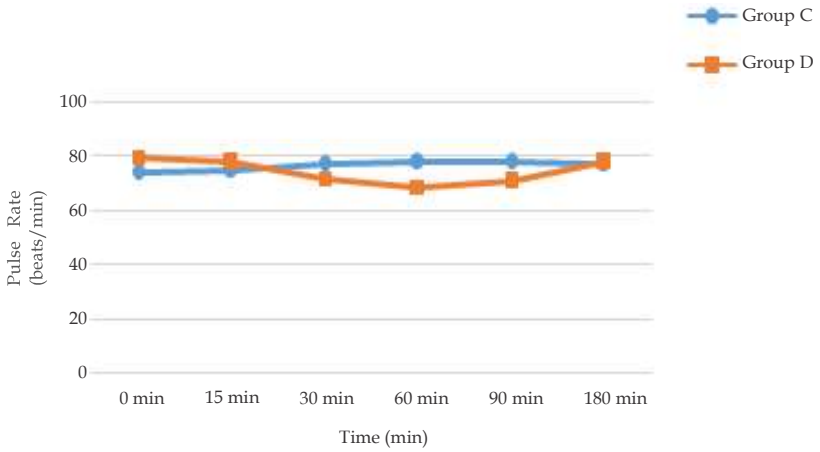

Fig. 1: Comparison of Pulse rate in both the groups.

Systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were found to be significantly lower than baseline from 30 to 90 min in Group D as compared with Group C ($p < 0.001$). Treatment was not required for this fall in blood pressure. The hemodynamic parameters were comparable at the end of 180 min, (Fig. 2).

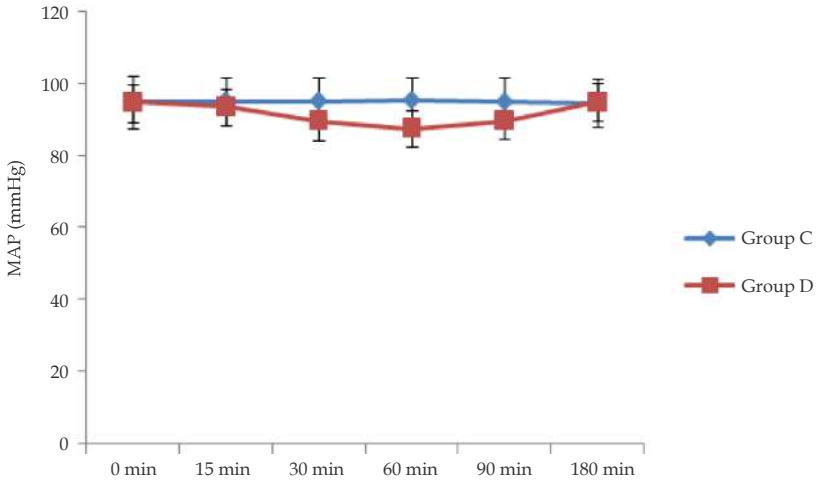

Fig. 2: Comparison of mean arterial pressures in both the groups.

Sensory block onset was faster in Group D than in Group C, while onset of motor block was faster in Group C than in Group D, but statistically the difference was not highly significant, Table 2, ($p >$ 0.001).

Table 2: Onset of Sensory block and Motor block

Onset of block (min)	Group C (Mean ± SD)	Group D (Mean ± SD)	*p* - value
Sensory	2.69 ± 0.55	2.82 ± 0.51	0.348 (NS)
Motor	4.95 ± 1.55	5.75 ± 1.52	0.047+

S = Not significant; SD = Standard deviation; + : Suggestive Significance.

Duration of sensory block was 234.17 ± 24.11 min in Group C as compared with 445.07 ± 67.79 min in Group D. Statistically significant longer duration of sensory block was observed in Group D, showed in Table 3 and Fig. 3, (p < 0.001). The duration of motor block was 296.30 ± 25.78 min in Group C as compared with 503.10 ± 75.67 min in Group D. Again, duration of motor block was significantly longer in Group D, Table 3 and Fig. 3, (p < 0.001).

Table 3: Duration of Sensory and Motor block and duration of analgesia

Duration (min)	Group C (Mean ± SD)	Group D (Mean ± SD)	*p* - value
Sensory	234.17 ± 24.11	445.07 ± 67.79	< 0.001*
Motor	296.30 ± 25.78	503.10 ± 75.67	< 0.001*
Analgesia	285.43 ± 26.88	477.27 ± 70.11	< 0.001*

SD = Standard Deviation; Min= Minutes; * = Highly significant.

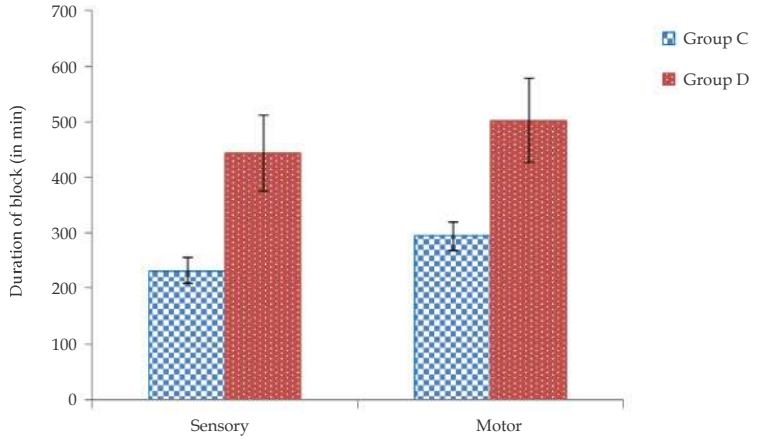

Fig. 3: Comparison of duration of block in both the groups.

There was significant increase in duration of analgesia in Group D (477.27 ± 70.11 min) as compared with Group C (285.43 ± 26.88 min). The difference was statistically significant, Table 3 and Fig. 4, (p < 0.001).

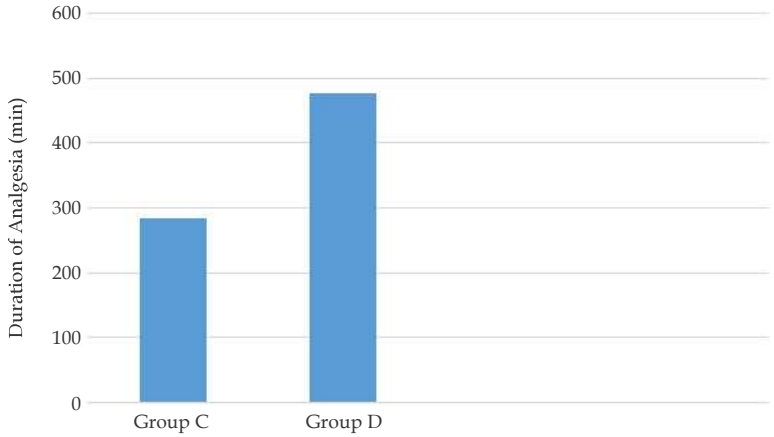

Fig. 4: Comparison of duration of Analgesia in both the groups.

In Group D, 83.3% of the patients achieved Grade IV quality of block as opposed to 43.3% in Group C (p = 0.006). 17 patients in Group C with Grade II and III block and 5 patients in Group D needed sedation or sedation with analgesia. One patient in Group C needed general anesthesia as the block was inadequate, (Table 4).

Side-effects like nausea, vomiting, dry mouth were not reported in the postoperative period in both the groups.

Table 4: Quality of block

Quality of block	Group C		Group D	
	No	%	No	%
I	0	0.0	0	0.0
II	8	26.7	2	6.7
III	9	30.0	3	10.0
IV	13	43.3	25	83.3
Total	30	100.0	30	100.0

No: Number of patients; % = Percentage of patients.

Discussion

In this randomized, double-blinded trial, we compared dexmedetomidine and clonidine as an adjuvant to Bupivacaine in supraclavicular brachial plexus block, and found that there was a significantly increased sensory and motor block duration in the dexmedetomidine group than in the clonidine group.

Mechanism of action of clonidine: Clonidine was used for its antihypertensive properties. The central actions are mediated through α_2 adrenoceptors. Specific peripheral effects of clonidine appear to be less obvious because α_2 adrenoceptors are not present on the axon of the normal peripheral nerve.[4] The mechanism of action of clonidine varies, which are centrally mediated analgesia, α_2 β adrenoceptor-mediated vasoconstrictive effects, attenuation of inflammatory response and direct action on peripheral nerve.[17]

Dalle et al. advocated that clonidine, by enhancing the Na/K pump during repetitive stimulation, increases the threshold for initiating the action potential causing slowing or blockage of conduction.[18] Kosugi et al. studied the effects of various adrenoceptor agonists and antagonist on Compound Action Potential (CAP) recorded from frog sciatic nerve, and found that CAPs were inhibited by α_2 adrenoceptor agents so that, they are able to block nerve conduction.[19] The increased effect of low-dose clonidine on lidocaine-induced inhibition of action potential of C-fibers and Aδ fibers (Gaumann et al., 1992;[20] Butterworth and Strichartz, 1993) together with synergistic mechanism of action with local anesthetics (Eledjam et al., 1991) may be the possible explanation to the direct peripheral action.[21]

Studies shown that clonidine as an adjuvant to bupivacaine prolongs the duration of anesthesia and analgesia in brachial plexus block,[2,3] but with side-effects like bradycardia, hypotension, and respiratory depression. In our study, we observed slight hypotension during 30 to 90 minutes duration.

Mechanism of action of dexmedetomidine

As both dexmedetomidine and clonidine belong to same group i.e. α_2 agonist, there is similarity in the mechanism of analgesic effects. Brumett et al. showed that dexmedetomidine increases duration of bupivacaine anesthesia and analgesia of sciatic nerve block in rats.[17]

Another study showed that perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolonged the duration of analgesia by blocking the hyperpolarization-activated cation, that prevents the nerve from returning from a hyperpolarized state to resting membrane potential for subsequent firing.[22]

Studies have demonstrated side-effects like bradycardia, hypotension with dexmeditomidine. In our study, we observed hypotension during 30 to 90 minutes duration. Baroreceptor reflex and HR response to vasopressors is preserved with the use of dexmedetomidine which helps in the treatment of hypotension and bradycardia easily.

Esmaoglu et al. studied dexmedetomidine with levobupivacaine for axillary brachial plexus block and showed that dexmedetomidine shortens the both sensory and motor block onset, prolongs the duration of block and postoperative analgesia.[23] It may be because peripheral α_2 agonist produces analgesia by reducing release of norepinephrine,

leading to α_2 receptor-independent inhibitory effects on nerve fiber action potentials.[16,24]

Many studies was conducted for α_2 agonist peripheral nerve action and most of them were on animals with few human studies. A study showed increased duration of sensory blockade by adding dexmedetomidine to bupivacaine and levobupivacaine in greater palatine and axillary brachial plexus nerve blocks respectively.[23,24] Archana Tripathi et al.[26] concluded dexmedetomidine (1 μg/kg)as an adjuvant prolongs the duration of sensory and motor block and analgesia duration and improves the anesthesia quality when injected with bupivacaine (39 ml of 0.25%)as compared with clonidine (1 μg/kg) in supraclavicular brachial plexus block. Rajaclimax Kirubahar et al.[27] concluded that dexmedetomidine (2 μg/kg) as an adjuvant to bupivacaine (35 ml of 0.375%) in supraclavicular brachial plexus block shortens the onset time to sensory and motor block and prolongs the analgesia duration when compared to clonidine (2 μg/kg). In our study, we used low-volume of bupivacaine when compared to other studies.

In our study, we compared the addition of clonidine (Group C 1 μg/kg) and dexmedetomidine (Group D 1 μg/kg) to 30 ml of bupivacaine (0.325%) in supraclavicular brachial plexus block. The result of our study shows that all patients in both groups were comparable with respect to demographic profile, duration of surgery and type of surgery. With these doses, we had stable hemodynamics in patients, except for fall in blood pressure during 30 to 90 minutes, fall in blood pressure was more pronounced in dexmedetomidine group than compared to clonidine group.

In our study, sensory block onset was a little faster with Group D as compared with Group C which was statistically insignificant, while motor block onset was a little longer in Group D which was mildly significant statistically. The duration of analgesia was longer in Group D when compared to Group C which was statistically significant. In our study, the quality of block in 83% of the patients in Group D was Grade IV (excellent block) while only 43% in Group C achieved Grade IV quality. This improved quality of block observed in Group D might be the result of various mechanisms of nerve conduction block such as hyperpolarization.[4] decreased CAP[19] and inhibition of voltage gate of sodium pump.

In our study, there was no significant sedation observed, mild arousable sedation was observed during intraoperative and postoperative period. From our study, we would like to suggest that dexmedetomidine can be safely used with bupivacaine in peripheral nerve blocks; Further trials are needed to determine the exact dose and effect of neurotoxicity on the human nerve.

Conclusion

We would like to conclude that dexmedetomidine prolongs the sensory and motor block duration and escalates the quality of block when compared with clonidine as an adjuvant to Bupivacaine in peripheral nerve block. The additional benefit of hemodynamic stability, conscious sedation and minimal side-effects makes it a promisable adjuvant for nerve blocks. Further studies with large sample sizes are warranted to validate these findings.

Support: Nil

Conflicts of interest: Nil

References

1. Damien B, Murhy, Collin JL, et al. Novel analgesic adjuvants for brachial plexus block: A systemic review. Anesth Analg 2000 May;90(5):1122–28.
2. Singelyn FJ, Dangoisse M, Bartholomee S, et al. Adding clonidine to mepivacaine prolongs the duration of anesthesia and anesthesia after brachial plexus block. Reg Anesth 1992;17:148–50.
3. Duma A, Urbanek B, Sitzwohl C, et al. Clonidine as an adjuvant to local anesthetic axillary brachial plexus block: A randomized, controlled study. Br J Anesth 2005;94:112–26.
4. Popping DM, Elia N, Mar E. Plexus blocks: A meta-analysis of randomized trials. Anesthesiology 2009;111:406–15.
5. Virtanen R, Savola JM, Saano V, et al. Characterization of selectivity, specificity and potency of medetomidine as an alpha 2-adrenoceptor agonist. Eur J Pharmacol 1988;150:9–14.
6. Mantz J, Singer M. Importance of patient orientation and rousability as components of intensive care unit sedation. In: Maze M, Morrison P, editors. Redefining Sedation. London, UK: The Royal Society of Medicine Press Ltd; 1998.pp.23–29.
7. Shehabi Y, Ruettimann U, Adamson H, et al. Dexmedetomidine infusion for more than 24 hours in critically ill patients: Sedative and cardiovascular effects. Intensive Care Med 2004;30:2188–96.
8. Shukry M, Miller JA. Update on dexmedetomidine: Use in nonintubated patients requiring sedation for surgical procedures. Ther Clin Risk Manag

2010;6:111–21.

9. Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anesthetic requirement. Indian J Anesth 2011;55:352–57.
10. Kanazi GE, Aouad MT, Jabbour-Khoury SI, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacainespinal block. Acta Anesthesiol Scand 2006;50:222–27.
11. Konakci S, Adanir T, Yilmaz G, et el. The efficacy and neurotoxicity of dexmedetomidine administered *via* the epidural route. Eur J Anesthesiol 2008;25:403–09.
12. Yazbek-Karam VG, Aouad MA. Perioperative uses of dexmedetomidine. Middle East J Anesthesiol 2006;18:1043–58.
13. El-Hennawy AM, Abd-Elwahab AM, Abd-Elmaksoud AM, et al. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Br J Anesth 2009;103:268–74.
14. Swaro Swastika, Karan Daisy, Banerjee Swarna. Comparision of fentanyl and dexmedetomidine as an adjuvant to bupivacaine in supraclavicular brachial plexus block: A randomized double blind prospective study. Asian Journal of Pharmaceutical and Clinical Research. 2016;9:74–77.
15. Sarkar DJ, Khurana G, Chaudhary A, et al. A comparative study on the effects of adding fentanyl and buprenorphine to local anesthetica in brachial plexus block. J Clin Diagn Res 2010;4:3337–43.
16. Ramsay MA, Savage TM, Simpson BR, et al. Controlled sedation with alphaxolone-alphadolone. Br Med J 1974;2:656–59.
17. Memis D, Turan A, Karamanlioglu B, et al. Adding dexmedetomidine to lignocaine for IVRA. Anesth Analg 2004;98:835–40.
18. Brummett CM, Norat MA, Palmisano JM, et al. Perineural administration of dexmedetomidine in combination with Bupivacaine enhances sensory and motor blockade in sciatic nerve block without inducing neurotoxicity in rat. Anesthesiology 2008;109:502–11.
19. Dalle C, Schneider M, Clergue F, et al. Inhibition of the I (h) current in isolated peripheral nerve: A novel mode of peripheral antinociception? Muscle Nerve 2001;24:254–61.
20. Kosugi T, Mizuta K, Fujita T, et al. High concentrations of dexmedetomidine inhibit compound action potential in frog sciatic nerve without α_2 adrenoceptor activation. Br J Pharmacol 2010;160:1662–76.
21. Gaumann DM, Brunet PC and Jirounek P. Clonidine enhances the effect of lidocaine on C fiber action potential. Anesthesia and Analgesia 1992;74:719–25.
22. Eledjam JJ, Deschodt J, Viel EJ, et al. Brachial plexus block with bupivacaine: Effects of added alpha 2-adrenergic agonists: Comparison between clonidine and epinephrine. Canadian Journal of Anesthesia 1991;38:870–75.
23. Brummett CM, Hong EK, Janda AM, et al. Perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolongs the duration of analgesia by blocking the hyper polarization-activated cation current. Anesthesiology 2011;115:836–43.
24. Esmaoglu A, Yegenoglu F, Akin A, et al. Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block. Anesth Analg 2010;111:1548–51.
25. Obayah GM, Refaie A, Aboushanab O, et al. Addition of dexmedetomidine to Bupivacaine for greater palatine nerve block prolongs postoperative analgesia after cleft palate repair. Eur J Anesthesiol 2010;27:280–84.
26. Tripathi Archana, Sharma Khushboo, Somvanshi Mukesh, et al. A comparative study of clonidine and dexmedetomidine as an adjunct to bupivacaine in supraclavicular brachial plexus block**.** Journal of anesthesiology clinical pharmacology 2016;32:344–48.
27. Kirubahar Rajaclimax, Bose Sundari, Kanna Vijay, et al. Comparison of clonidine and dexmedetomidine as an adjuvant to bupivacaine in supraclavicular brachial plexus block for upper limb orthopedic procedures. IJRMS 2016 April;4(4):1172–76.

Original Research Article

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To Study and Compare Induction Characteristics and Hemodynamic Effects of Sevoflurane with Halothane for Inhalational Anesthesia in Pediatric Patients

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Abstract

Induction: and maintenance of general anesthesia in pediatric patients is often managed with an inhaled anesthetic agent, with various inhalational anesthetic agents available having their pros and cons. In this study, we evaluated and compared sevoflurane with halothane in pediatric patients for induction characteristics and hemodyanamic effects. Sixty patients, aged between 2 and 10 years undergoing various surgeries were randomly divided into two groups of 30 each to receive either sevoflurane or halothane anesthesia, induced by using equipotent incremental doses of either of the inhalational agent upto 3 MAC. Anesthesia was then maintained with either of the inhalational agents at 0.5 MAC with nitrous oxide (60%) in oxygen (40%). Induction time, induction scoring and hemodynamic parameters were recorded and analyzed using appropriate statistical method. *Results:* of our study showed that the induction time of sevoflurane was significantly faster than that of halothane (184 ± 56 secs *vs* 302 ± 62 secs) without any major airway problem (salivation, breath-holding and coughing). Excitement and restlessness during induction was found to be more common with sevoflurane than with halothane but this difference was not statistically and did not interfere with the induction. Heart rate and blood pressure were better maintained during sevoflurane anesthesia than the halothane anesthesia. We did not find any significant incidence of cardiac arrhythmias with either of the agents.

Keywords: Inhalational; Induction; Sevoflurane; Halothane; Pediatric; Anesthesia.

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Introduction

Induction and maintenance of general anesthesia in pediatric patients is often managed with an inhaled anesthetic agent, which should ideally produce rapid and smooth induction, rapid emergence and a short postoperative recovery period with minimal adverse effects. Halothane has traditionally been used as anesthetic agent for inhalational induction in children because it produces less airway irritation, but it is not an ideal induction agent because of its potential to cause bradycardia, hypotension and ventricular ectopy.[1,2] The pleasant, nonpungent odour of sevoflurane, its low-blood – gas solubility along with its cardiostable properties and minimal hepatotoxicity suggests that it has most of the

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properties of an ideal inhalational agent and that it may be a suitable alternative to halothane for its use in pediatric anesthesia.[3–6] We designed this study to compare the induction characteristics and hemodynamic effects of sevoflurane with halothane anesthesia in children aged 2–10 years undergoing various commonly performed surgical procedures.

Materials and Methods

Patients in the age group of 2–10 years (ASA Grade 1 & 2), undergoing elective pediatric surgeries under general anesthesia were chosen for the study. Patients with history of any major systemic illness, previous history of hypersensitivity to any anesthetic drug, patients undergoing emergency surgeries were excluded. After a careful preanesthetic checkup, an informed consent was taken from the guardian of the patient. Premedication with oral midazolam 0.5 mg/kg given 1 hour prior to the procedure. The patients were then randomly divided into two groups to receive either sevoflurane or halothane anesthesia.

On reaching the Operation table, the baseline values of PR, BP, SpO_2 were recorded. Intravenous access was established. Anesthesia was then induced with Sevoflurane beginning at 1 MAC (2.5%), increasing by 1% (0.5 MAC) every 3–4 breaths to a maximum of 7.5% (3 MAC) *via* JR circuit using an appropriate sized face mask along with Nitrous oxide (60%) in oxygen (40%). The same protocol was followed during the induction of anesthesia by Halothane.

There again the induction was started at 1 MAC of Halothane (1%) followed by increments of 0.5% (0.5 MAC) every 3–4 breaths to a maximum of 3% (3 MAC). Once the criteria of induction were met with (loss of eyelash reflex, loss of tone, fixed central pupil, automatic respiration), trachea was intubated with an appropriate sized endotracheal tube and oropharyngeal packing done. Anesthesia was maintained with Sevoflurane/Halothane at 0.5 MAC (1.2% and 0.5% respectively) with Nitrous Oxide (60%) in Oxygen (40%). Injection fentanyl 1 μg/kg was given for the intraoperative analgesia. Muscle relaxation was supplemented with Inj. Atracurium besylate 0.2 mg/kg as and when required. In both the groups the volatile anesthetic agent was discontinued at the completion of the last stitch.

The neuromuscular block was then reversed after the dressing with Inj. Neostigmine (0.05 mg/kg) along with Inj. Glycopyrrolate (0.01 mg/kg). A gentle suction was then done under vision followed by removal of oral packing.

The trachea was extubated after the return of the gag reflex, adequate tidal volume, and the return of purposeful movements.

The following parameters were recorded :

1. Heart Rate (HR), Blood Pressure (BP), Oxygen Saturation (SpO_2) were noted at following intervals:
   (a) Preinduction;
   (b) During induction at every 2 min. interval;
   (c) Immediately after intubation;
   (d) 5 mins after intubation;
   (e) Every 10 mins during the maintainance till the recovery.
2. ECG, SpO_2 monitoring was done continuously during the procedure. Any episode of bradycardia (HR < 20% of preinduction level), hypotension (20% of preinduction value), hypoxia (SpO_2 < 90%) were recorded;
3. Induction Time was taken as the time taken from the start of the anesthesia to the loss of eyelash reflex;
4. Induction Scoring was done as follows (Table 1):

The results were compiled and analyzed using the following tests:

Student's t- test: Demographic profile, Systolic blood pressure, Diastolic blood pressure, Induction time, Total Induction scoring.

Chi-square test: Sex ratio, Untoward effects during induction,

Wilcoxan signed rank test: Heart rate.

Results

There was no statistical difference between the two groups with respect to the demographic profile, the number of various surgical procedures done and the mean duration of anesthesia for various procedures, shown in Table 2. There was a statistically significant difference between the two groups with respect to the induction time. The induction time was seconds in sevoflurane group compared to seconds in halothane group. The induction was significantly faster with sevoflurane than with halothane, (Table 3).

Table 1: Symptom

Symptom	Worst (1)	Fair (2)	Best (3)
Salivation	Pouring out	Little wet	None
Coughing	Persistant	Self limiting	None
Breath holding	Persistant	Temporary	None
Laryngospasm	No air entry	Partial air entry	B/L equal air entry
Nausea/Vomiting	Persistant	Temporary	None
Bronchospasm	Unable to ventilate	Wheeze	None
Excitement/Restlessness	Severe	Some problem	None

Table 2: Induction parameters (Induction time)

Parameter	Group H (n = 30)	Group S (n = 30)	p - value*
Induction time (secs)	302 ± 62	184 ± 56	< 0.0001

Table 3: Demographic profile

	Group H (n = 30)	Group S (n = 30)	p - value**
Age (years)*	5.7 ± 21	4.8 ± 3	0.725
Sex (M/F)	20/10	21/9	1
Wt.(kg)*	15.5 ± 3.33	15.2 ± 3.18	0.865
Surgical procedure			
Upper abd Surgery	18	21	
Tonsillectomy	5	2	
Orthopedic surgery	7	7	
Mean duration of anesthesia(min)			
Upper abd surgery	66.71 ± 13.89	75 ± 7.07	0.465
Tonsillectomy	48.27 ± 7.78	48 ± 10.17	0.098
Orthopedic surgery	60.17 ± 22.4	59.28 ± 25.9	0.125

Untoward effects during the induction of halothane anesthesia were seen in the form of salivation (6 pts.), breath holding (3 pts.), cough (3 pts.) and bronchospasm (2 pts.) whereas during sevoflurane anesthesia induction; salivation, breath holding, cough and bronchospasm were observed in 7, 2, 1 and 1 patients respectively, Table 4.

Table 4: Untoward effects during induction

Parameter	Group H (n = 30)	Group S (n = 30)	p - value
N/V	0	0	
Salivation	6	7	1
Breath holding	3	2	1
Cough	3	1	0.612
Laryngospasm	0	0	
Bronchospasm	2	1	1
Excitement/Restlessness	0	2	0.492

Excitement and restlessness which was absent in halothane group was observed in 2 patients in sevoflurane group but this was statistically insignificant, Fig. 1. There was no significant difference between the mean induction scores in the two groups, (Table 5).

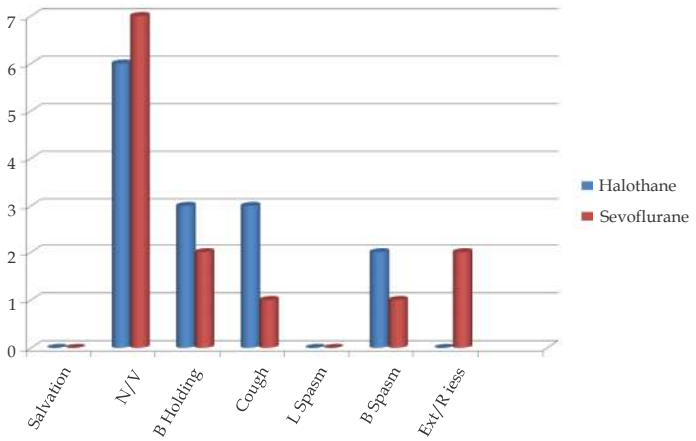

Fig. 1: Untoward effects during Induction

Table 5: Induction score

Score	Group H (*n* = 30)	%	Group S (*n* = 30)	%	*p* - value
21	19	63.33	20	66.66	1
20	8	26.66	8	26.66	1
19	2	6.66	1	3.33	1
18	1	3.33	1	3.33	1
Mean	20.5 ± 0.77		20.5 ± 0.72		0.733

An increase in PR was seen at 2 min during induction in sevoflurane group which is statistically significant. A statistically highly significant increase in the pulse rate was seen immediately after intubation in both the groups which became stable in sevoflurane thereafter. Whereas, in halothane group, fall in pulse rate was seen at 20 mins where it was statistically significant and at 30 min duration it was highly significant in halothane group, (Table 6 and Fig. 2).

Table 6: Heart rate variation

Time	Group H (*n* = 30)	*p* - value* H	Group S (*n* = 30)	*p* - value* S
Preop	110 ± 20.5		114.2 ± 19.08	
At 2 min	115.11 ± 21.2	0.086	120.8 ± 18	0.057
At intubation	125.1 ± 13.3	000	129.57 ± 16.97	000
5 min postintubation	112.7 ± 15.23	0.422	121.6 ± 13.60	0.063
At 10 min	108.4 ± 15.60	0.078	120.2 ± 18.86	0.063
20 min	106.46 ± 13	0.020	119.83 ± 19.44	0.056
30 min	104.2 ± 12.9	0.006	115 ± 15.74	0.750

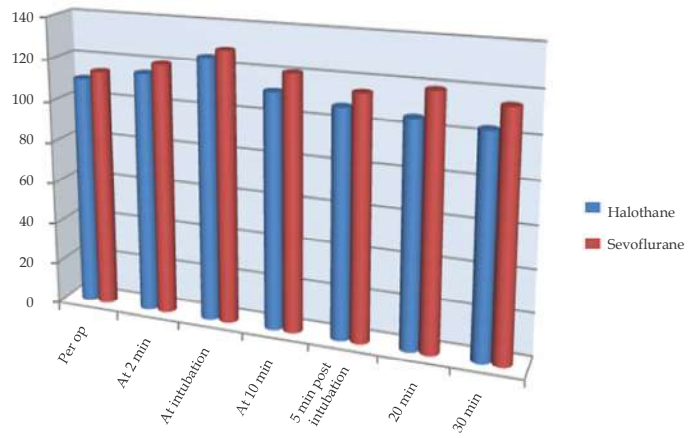

Fig. 2: Heart rate variation.

There was a statistically significant fall in SBP at 2 mins during induction in halothane group. A statistically significant increase in SBP was seen in both the groups immediately postintubation which was more in sevoflurane than in halothane. SBP was stable during rest of the procedure in both the groups, Table 6 and Fig. 3. There was statistically significant increase in Diastolic BP in sevoflurane group which was clinically significant at immediate postintubation time and clinically insignificant at 20 mins, (Table 7 and Fig. 4).

Table 7: Systolic blood pressure variation

Time	Group H (n = 30)	p - value* H	Group S (n = 30)	p - value* S
Preop	108.33 ± 8.20		101.43 ± 8.63	
At 2 min	101.60 ± 12.92	0.05	102.20 ± 8.25	0.514
At intubation	112.8 ± 9.85	0.04	107.40 ± 9.37	0.002
5 min postintubation	107.13 ± 7.24	0.140	103.97 ± 11.05	0.240
At 10 min	108.2 ± 8.08	0.809	103.2 ± 9.76	0.292
20 min	108.13 ± 9.77	0.875	104.66 ± 10.94	0.155
30 min	107.87 ± 9.22	0.822	102.10 ± 8.39	0.698

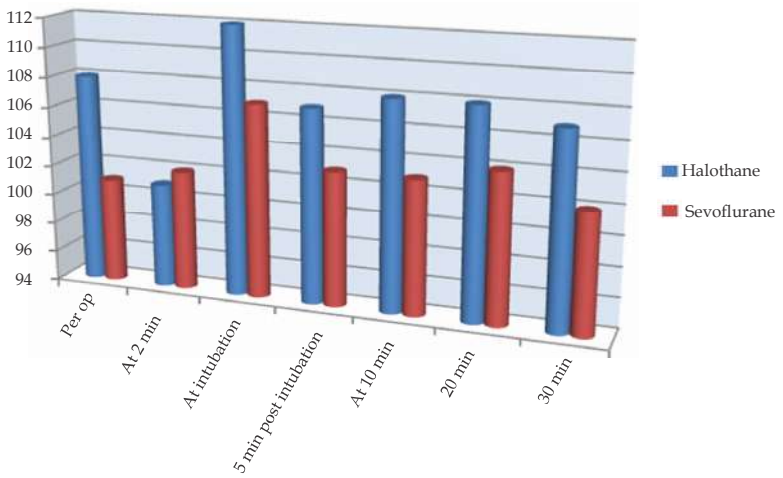

Fig. 3: Systolic blood pressure variation.

Table 8: Diastolic blood pressure variation

Time	Group H (n = 30)	p - Value* H	Group S (n = 30)	p - value* S
Preop	61.13 ± 18.90		54.20 ± 8.24	
At 2 min	54.27 ± 7.59	0.064	55.20 ± 6.40	0.428
At intubation	60.23 ± 7.53	0.800	59.30 ± 9.07	0.012
5 min postintubation	54.77 ± 6.59	0.102	56.23 ± 7.69	0.204
At 10 min	57.47 ± 6.95	0.310	54.70 ± 5.87	0.767
20 min	56.56 ± 6.84	0.219	57.86 ± 8.45	0.049
30 min	54.63 ± 11.91	0.126	56.73 ± 10.86	0.272

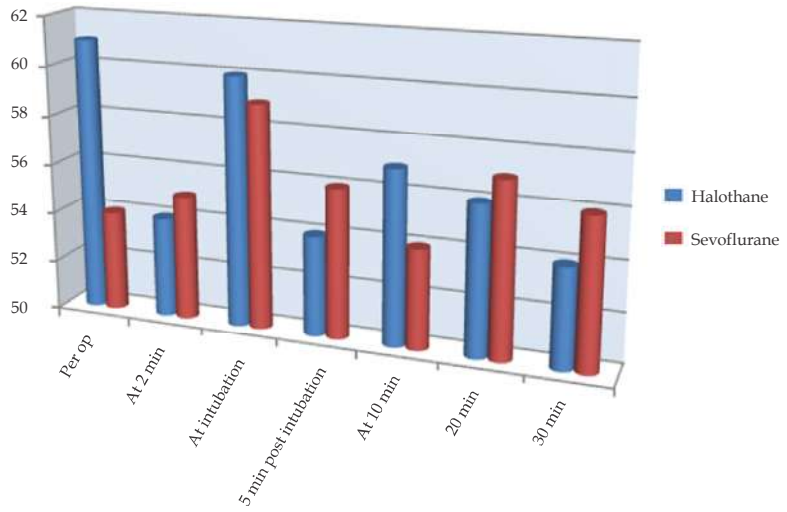

Fig. 4: Diastolic blood pressure variation.

Discussion

We conducted this study to compare the induction and hemodynamic characteristics of sevoflurane and halothane anesthesia in 60 patients of ASA Grade 1 & 2 undergoing various surgeries. Both the groups studied were comparable with respect to the age, sex ratio, weight in kgs, the no. of various surgical procedures done and the mean duration of anesthesia during the various surgical procedures, (Table 2).

In our study the induction was significantly faster in sevoflurane group (184 ± 56 secs) compared to halothane group (302 ± 62 secs), Table 3. This result was found to be statistically significant ($p < 0.05$). This was most probably the consequence of the lower-blood – gas partition coefficient for sevoflurane compared to halothane, particularly since it was a goal to use comparable MAC's for both the agents during the induction as well as the maintenance. Our results were similar to those of PJ Davis et al.[7] GP Johannasson et al.[8] A Black, et al. [9] PE Singston et al.[10] R Muto et al.[11] S Inomoto[12] and Kajal N Dedhia et al.[13] But, Y Naito et al.[14] and Veronique Piat et al.[15] did not find any significant difference between the induction time of sevoflurane and halothane. This difference in result was probably due to the fact that they did not use the equipotent concentrations of the two agents throughout the induction time. The concentration used for halothane was higher compared to the concentration of sevoflurane in all the three studies.

In our study no difference was found between the two groups with respect to the induction score. Untoward effects during induction of halothane anesthesia were seen in the form of salivation (6 patients), breath holding (3 pts.), cough (3 pts.) and mild bronchospasm (2 pts.). Whereas, during sevoflurane induction, salivation, breath holding, cough and bronchospasm were found in 7, 2, 1 and 1 patients respectively, Table 3. These incidences were not statistically significant. Excitement and restlessness which was absent in the halothane group was observed in 2 patients in the sevoflurane group. Though this was clinically significant, it was statistically found to be insignificant. Our results are in accordance with the studies done by Y Naito et al.[14] V Piat,[15] A Black[9] and Kajal N Dedhia. They found no statistically significant difference in the side-effects during the induction of anesthesia in both the groups. PE Singston et al.[10] found a higher incidence of struggling during rapid induction with 5% halothane compared to 8% sevoflurane. This was probably due to the more pleasant odour of sevoflurane which was better tolerated in unpremedicated children. No such observation was made in our study and all our patients were premedicated with oral midazolam. A statistically insignificant incidence of excitement which did not interfere with the course of induction was seen in the sevoflurane group and this was similar to the trend seen in our study. The incidence of breath holding was found in 3 patients in halothane group and 2 in sevoflurane group, whereas cough was observed in 3 patients in halothane group and 1 patient in sevoflurane group. R Muto et al.[11] also found a higher incidence of airway problems in the form of breath holding, coughing and complete refusal in halothane (40%) compared to sevoflurane (7%).

In our study, we found an increase in the heart rate immediately after intubation in both the groups,

Table 5. In sevoflurane group it rose from the baseline value of 114 ± 19.08 per minute to 129.57 ± 16.97 per minute. Similarly, heart rate in halothane group increased from 110 ± 20.5 per minute to 125 ± 13.3 per minute. In both the groups these changes were very highly significant ($p < 0.001$). The increase in heart rate at the time of intubation in both the groups may be due to the stress response to laryngoscopy and intubation. This was also observed by V Piat et al.[15] in sevoflurane group but not in halothane group. The heart rate started returning towards normal in both the groups after intubation and reached the baseline value in halothane group at 5 minutes and in sevoflurane group at 30 minute. A fall in the heart rate below baseline value was observed in halothane group during intraoperative period which was statistically significant at 20 and 30 minutes but was not clinically significant and did not require any treatment. Kajal N Dedhia et al.[13] observed a fall in heart rate in halothane group but no change in sevoflurane group. Our results are similar to other studies. GP Johannasson et al.[8] reported a higher heart rate throughout in the sevoflurane but no change in heart rate was seen in halothane group. This difference in observations may be because of the use of atropine premedication (0.035 mg/kg) in all the patients. In our study, we did not give any atropine to our patients. We gave Inj. Glycopyrrolate only to those patients who had excessive salivation during induction of anesthesia (3 patients in sevoflurane group and 2 patients in halothane group). Studies done by A Black et al. [9] and PE Singston et al.[10] showed no difference in the heart rate between the two groups from the baseline values. Both of them had used atropine premedication in their studies.

In halothane group a fall in systolic and diastolic blood pressure was observed at 2 mins of induction. Thereafter, at intubation, there was an increase in both systolic and diastolic blood pressure. The rise in systolic blood pressure was significant whereas rise in diastolic blood pressure was insignificant. In sevoflurane group, there was a marginal increase in both the systolic and diastolic blood pressures at 2 minutes of induction which increased to significant levels at intubation, Tables 7 and 8. V Piat et al.[15] observed that during the same time interval (induction to intubation) SBP decreased significantly in halothane group whereas it did not change in sevoflurane group. The same results were observed in our study during induction. The increae in blood pressure during intubation found in our study in accordance with the studies done by Kajal N Dedhia et al. [13] and V Piat et al.[15] who also observed an increase in SBP immediately after the insertion of the LMA and after intubation respectively. The systolic and diastolic blood pressures remained stable during intraoperative period, Table 7 and 8, after intubation in our study. Our results are similar to those of A Black et al. [9] who reported stable blood pressure during intraoperative period in both the groups. R Muto et al.[11] and Satoru Tanaka et al.[16] observed a slight decrease in BP in both the groups which was not significant and this was probably due to the use of higher dose of sedative premedication in their study.

No significant arrhythmia, episode of deaturation or any other mishap was observed during the cases in either of the groups.

Conclusion

From our study, we conclude that the induction time of sevoflurane was significantly faster than that of halothane and it was not associated with any major airway problem (salivation, breath-holding and coughing. Heart rate and blood pressure were better maintained during sevoflurane anesthesia than the halothane anesthesia. We did not find any significant incidence of cardiac arrhythmias with either of the agents.

References

1. Eger El, Smith NT, Stoelting RK, et al. Cardiovascular effects of halothane in man. Anesthesiology 1970;396–409.
2. Barash PG, Glanz S, Taunt K, et al. Ventricular function in children during halothane anesthesia. Anesthesiology 1978;79–85.
3. Strum DP, Eger El. Partition coefficients for sevoflurane in human blood, saline, and olive oil. Anesth Analg 1987;66:654–56.
4. Sarner JB, Levine M, Davis PJ. Clinical characteristics of sevoflurane in children: A comparison with halothane. Anesthesiology 1995;82:38–46.
5. Ebert TJ, Messana LD. Absence of renal and hepatic toxicity after 4 hours of 1.25 minimum alveolar concentration sevoflurane anesthesia in volunteers. Anesth Analg 1998;86:662–67.
6. Hirschman CA, Edelstein G. Mechanism of inhalational anesthesia on airways. Anesthesiology 1982;56:107–111.
7. Lerman J, Davis PJ, Welborn LG, et al. Induction, recovery, and safety characteristics of sevoflurane in children undergoing ambulatory surgery: A comparison with halothane. Anesthesiology 1996:84:1332–340.

8. Johannesson GP, Floren M. Sevoflurane for ENT surgery in children: A comparison with halothane. Acta Anesthesiol Scand 1995;39:546–50.
9. Black A, Suri MRJ. A comparison of the induction characteristics of sevoflurane and halothane in children. Anesthesia 1996;51:539–42.
10. Singston PE. Rapid inhalational induction in children: 8% sevoflurane compared with 5% halothane. Br J Anesth 1997;78:362–65.
11. Muto R, Takata M. Comparison of sevoflurane and halothane induction in pediatric anesthesia. Clinical pediatric anesthesia 1997;3:147–52.
12. Inomata S, Yamashita S. Anesthetic induction time for tracheal intubation using sevoflurane or halothane in children. Anesthesia 1998;53:440–45
13. Dedhia KN, Kudalkar A. Comparison of sevoflurane and halothane for induction of anesthesia and laryngeal mask airway insertion in pediatric patients. Indian J Anesth;48(6):465–68.
14. Naito Y, Tamai S, Shingo K. Comparison between sevoflurane and halothane for pediatric ambulatory anesthesia. Br J Anesth 1991;67:387–89.
15. Piat V, Dubois MC, Murat I. Induction and recovery characteristics and hemodynamic responses to sevoflurane and halothane in children. Anesth Analg 1994;79:890–94.
16. Tanaka S, Tsuchida H. The effect of sevoflurane, isoflurane, halothane and enflurane on hemodyanamic responses during an inhaled induction of anesthesia *via* a mask in humans. Anesth Analg 1996;82:821–26.
17. Redhu S, Jalwal GK, Saxena M, et al. A comparative study of induction, maintainance and recovery characteristics of sevoflurane and halothane anesthesia in pediatric patients. J Anesth Clin Pharmacology 2010;26(4):484–87.

Original Research Article

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Clinical Study of Epidural Nalbuphine vs Tramadol for Postoperative Pain Relief in Lower Limb Orthopedic Surgeries

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Abstract

Context: Achieving satisfactory postoperative analgesia with epidural opioids has been the subject of research many times. *Aims:* To evaluate postoperative pain relief in patients administered with epidural nalbuphine or tramadol for lower-limb surgery under combined spinal-epidural anesthesia. *Settings:* Tertiary hospital, Kanchipuram Dist, Tamil Nadu. *Design:*Prospective observational study. *Materials and Methods:* The study was done on patients undergoing lower-limb orthopedic procedures. The patients were assigned to either epidural nalbuphine (N) Group or epidural tramadol (T) Group. The convenience sampling technique was used until each group had 40 subjects. Group N received epidural 0.125 % bupivacaine with nalbuphine 0.2 mg/ml infusion@6ml/hr and Group T with epidural 0.125 % bupivacaine with tramadol2mg/ml infusion@6ml/hr started at sensory regression to T10 for postop analgesia. The pain severity was assessed using Visual Analog Scale (VAS) and sedation was assessed using Pasero Opioid-induced Sedation Scale (POSS). Intravenous paracetamol was used as rescue medication. *Statistical analysis used:* Chi-square test and unpaired *t*-test. *Results:* The mean sedation at 2 hrs was 1.65 ± 0.8 in tramadol and 2.8 ± 0.41 in the nalbuphine group. The difference was statistically significant (p - value < 0.001). The mean VAS at 12 hrs was 1.06 ± 0.4 in tramadol and 1.26 ± 0.44 in nalbuphine. At 24 hrs it was 0.86 ± 0.41 in tramadol and 1.05 ± 0.34 in nalbuphine group, with statistically significant differences (p - value < 0.05). In the tramadol group, 5 (12.5%) had vomiting and 6 (15%) were administered with IV paracetamol. *Conclusions:* Nalbuphine was more effective in providing postoperative pain relief compared to Tramadol. Tramadol was associated with a higher incidence of nausea and vomiting.

Keywords: Nalbuphine; Tramadol; Postoperative Analgesia; Sedation; Nausea; VAS.

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Introduction

Spinal anesthesia is a well-known technique used for lower-limb orthopedic surgeries. It is known for its rapid onset of action, simplicity to perform and good muscle relaxation while requiring lower drug dosage and lower incidence of the failed block.[1,2] However, the duration of spinal anesthesia is shorter which in turn shortens postoperative analgesia. Due to this, various adjuvants are added to improve the quality and duration of spinal blockage.[1] A combined spinal-epidural technique is another option where the local anesthetic opioid combination can be used as an intermittent or continuous epidural infusion to provide postop analgesia.

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Opioids are one of the commonly added adjuvants to the local anesthesia. Tramadol, a centrally acting analgesic, is commonly used for the control of postoperative analgesia.[3] Tramadol has a dual mechanism of action. It acts on opioid receptors as well as inhibits neuronal uptake of norepinephrine and serotonin. Due to this nonopioid action, tramadol has a lesser risk of producing respiratory depression than other opioids.[4] However, a higher incidence of nausea and vomiting is one of the concerns for the use of tramadol in postoperative patients.[5,6]

Nalbuphine is a synthetic opioid analgesic with agonist-antagonist activity and acts as an antagonist at μ-receptors and agonists at *k*-receptors to provide reasonably potent analgesia.[7] Studies have shown that nalbuphine was associated with lesser incidence of nausea and vomiting as compared to tramadol during the postoperative period.[5] However, it was associated with complications like respiratory depression, undesirable sedation, and urinary retention.[1]

Evaluation of postoperative analgesic effect of various adjuvants is of great importance to anesthesia practice and its effectiveness is an essential step toward identifying better pain management strategies and developing guidelines for better practice.[8] Moreover, there are a lack of well-designed Indian studies comparing nalbuphine and tramadol. Hence, the study was done to evaluate and compare the efficacy and safety of epidural infusion of 0.125% bupivacaine with either nabuphine or tramadol.

Subjects and Methods

The study was a prospective observational study conducted among 80 participants admitted in our tertiary care hospital. Adult patients (18–70 years of age) with the American Society of Anesthesiologists physical status class I and II undergoing elective lower limb orthopedic procedures performed under combined spinal-epidural anesthesia were included in the study.

Patients not willing to give consent, patients with bleeding diathesis or on anticoagulant therapy, morbidly obese patients and patients with cardiac, renal, hepatic & neurological disorders were excluded from the study. Convenience sampling was done to recruit the study participants in either epidural nalbuphine or epidural tramadol group. Participants were serially included in the study till both groups had 40 patients each. The study commenced after obtaining institutional ethics committee approval and written informed consent from the patients.

After connecting monitors, the Intravenous line was started. Preanesthetic medications included intravenous glycopyrrolate (4 μg/kg) and ondansetron (0.1 mg/kg). Coloading was done with 500 ml of ringer lactate. Under aseptic precautions first, the epidural catheter was placed in L1-L2 space using the Loss of Resistance technique. Then spinal anesthesia was given with 3.5 ml of 0.5% bupivacaine heavy at L3-L4 space using a 25 g quincke needle.

The patients randomly received either bupivacaine nalbuphine or bupivacaine tramadol epidural infusion for postoperative pain relief. The epideural infusion was started after sensory regression to T11 level.

Group N - 0.125 % bupivacaine with nalbuphine, 0.2 mg/ml infusion@6ml/hr

Group T- 0.125 % bupivacaine with tramadol, 2 mg/ml infusion@6ml/hr

Pain severity was assessed by the Visual Analog Scale (VAS). The score was assessed as 0, no pain and 10, worst imaginable pain. Intravenous paracetamol was administered as rescue medication on patients demand.

Sedation was assessed by Pasero Opioid-induced Sedation Scale (POSS).[9] The scores were as follows: 1 awake and alert; 2, slightly drowsy, easily aroused; 3, frequently drowsy, arousable, drifts off to sleep during the conversation; and 4, somnolent, minimal or no response to verbal or physical stimulation.

Nausea and vomiting were assessed on a 5-point scale: 0, no nausea or vomiting; 1, mild nausea, no treatment required; 2, nausea only, antiemetic prescribed until resolution; 3, vomiting, antiemetic prescribed until resolution; and 4, nausea/vomiting that did not respond to antiemetic. Ondansetron was used as an antiemetic for the control of vomiting. Assessment of all scores was performed every 2 hours after surgery till 24 hours.

Sample size calculation

The sample size was calculated assuming the expected mean and standard deviation of the sedation score in the nalbuphine as μ_1, σ_1 (1.3, 0.3) and in the tramadol as μ_0, σ_0 (1.5,0.3), as per the pervious study by Chatrath V et al.[10] The other parameters considered for sample size calculation included were 80% power of study and 5% two sided alpha error. The required sample size was calculated using the following formula as proposed

by Kirkwood BR et al.[11]

Formula used for sample size calculation

$$N = \frac{(u+v)^2\,(\sigma_1^2+\sigma_0^2)}{(\mu_1-\mu_0)^2}$$

N = Sample size

σ_1, σ_0 = Standard deviations (σ_1 = 0.3 and σ_0 = 0.3)

u = Two sided percentage point of the normal distribution corresponding to 100% - the power = 80%, u = 0.84

v = Percentage point of the normal distribution corresponding to the (two sided) significance level for significance level = 5%, v = 1.960.

The required sample size as per the above-mentioned calculation was 35 in each group. To account for a nonparticipation rate/loss to follow up rate of a about 10%, another 4 subjects will be added to the sample size. Hence, the final required sample size was rounded off to 40 subjects in each group.

Statistical Methods

Sedation and VAS were considered as primary outcome variables. Postoperative complications and use of rescue analgesia was considered as secondary outcome variables.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Data was also represented using appropriate diagrams like a bar diagram, pie diagram and box plots.

All Quantitative variables were checked for normal distribution within each category of explanatory variables by using visual inspection of histograms and normality Q-Q plots. Shapiro-Wilk test was also conducted to assess normal distribution. Shapiro-Wilk test p - value of > 0.05 was considered as a normal distribution.

For normally distributed Quantitative parameters the mean values were compared between study groups using Independent sample t-test (2 groups). Categorical outcomes were compared between study groups using Chi-square test. p - value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.[12]

Results

A total of 80 subjects were included in the final analysis. Most participants were aged between 61 and 70 years. In the tramadol group, 30 (75%) participants were males and 10 (25%) were females. In the nalbuphine group, 28 (70%) were males and 12 (30%) were females. The age and gender were comparable between the groups. (p - value > 0.05), (Table 1).

Table 1: Comparison of gender between group (N = 80)

Age Group	Group		Chi-square	p - value
	Tramadol (N = 40)	Nalbuphine (N = 40)		
< 20	2 (5%)	2 (5%)	0.784	0.978
21–30	9 (22.5%)	6 (15%)		
31–40	7 (17.5%)	8 (20%)		
41–50	6 (15%)	7 (17.5%)		
51–60	4 (10%)	4 (10%)		
61–70	12 (30%)	13 (32.5%)		
Gender				
Male	30 (75%)	28 (70%)	0.251	0.617
Female	10 (25%)	12 (30%)		

Among the tramadol, Proximal Femoral Nailing (PFN), Intramedullary Nailing (IMNL), Anterior Cruciate Ligament **(**ACL) repair, hemiarthroplasty and plating were more common surgeries performed. In patients receiving nalbuphine,

Table 2: Comparison of procedure between group (N = 40)

Procedure	Group	
	Tramadol (N = 40)	Nalbuphine (N = 40)
Anterior Cruciate Ligament Repair	7 (17.5%)	3 (7.5%)

Procedure	Group	
	Tramadol (*N* = 40)	Nalbuphine (*N* = 40)
Dynamic Hip Screw (DHS)	1 (2.5%)	5 (12.5%)
External Fixation (Ex Fix)	0 (0%)	3 (7.5%)
Plating	4 (10%)	0 (0%)
Hemiarthroplasty	5 (12.5%)	2 (5%)
Ilizarov	2 (5%)	0 (0%)
Intramedullary Nailing (IMNL)	6 (15%)	6 (15%)
Proximal Femoral Nailing (PFN)	14 (35%)	18 (45%)
Total Hip Replacement (THR)	1 (2.5%)	3 (7.5%)

*No statistical test was applied-due to 0 subjects in the cells.

Proximal Femoral Nailing (PFN), Intramedullary Nailing (IMNL) and Dynamic Hip Screw (DHS) was more commonly performed, (Table 2).

The mean sedation score (SED) at 2 hours was 1.65 ± 0.8 in tramadol group and it was 2.8 ± 0.41 in nalbupine group. The difference in the SED at 2 hrs between the group was statistically significant (*p* - value < 0.001). The differences were insignificant at 4, 6, 8 12 and 24 hours, (Table 3).

Table 3: Comparison of sedation between the two groups at different follow-up time periods (*N* = 80)

Parameter	(Mean ± SD)		*p* - value
	Tramadol (*N* = 40)	Nalbuphine (*N* = 40)	
Sedation 2 hrs	1.65 ± 0.8	2.8 ± 0.41	< 0.001
4 hrs	2.78 ± 0.42	2.83 ± 0.38	0.582
6 hrs	2.95 ± 0.22	3 ± 0	0.156
8 hrs	3 ± 0	3.38 ± 1.33	0.079
12 hrs	3 ± 0	3 ± 0	*
24 hrs	3 ± 0	3 ± 0	*

The mean VAS at 12 hrs was 1.06 ± 0.4 in tramadol group and it was 1.26 ± 0.44 in nalbupine group. The difference in the VAS at 12 hrs between the group was statistically significant (*p* - value 0.035). The mean VAS at 24 hrs was 0.86 ± 0.41 in tramadol group and it was 1.05 ± 0.34 in nalbupine group. The difference in the VAS at 24 hrs between the nalbupine group was statistically significant (*p* - value 0.028). Whereas, at 2, 4, 6 and 8 hours, the difference was not significant, (Table 4).

Table 4: Comparison of mean of VAS between the two groups at different follow-up time periods (*N* = 80)

Parameter	(Mean ± SD)		*p* - value
	Tramadol (*N* = 40)	Nalbuphine (*N* = 40)	
VAS 2 hrs	2.5 ± 0.99	2.2 ± 0.41	0.079
4 hrs	1.83 ± 0.55	1.79 ± 0.47	0.743
6 hrs	1.66 ± 0.57	1.6 ± 0.44	0.585
8 hrs	1.41 ± 0.48	1.3 ± 0.46	0.289
12 hrs	1.06 ± 0.4	1.26 ± 0.44	0.035
24 hrs	0.86 ± 0.41	1.05 ± 0.34	0.028

Tramadol was associated with a higher incidence of vomiting and about 6 (15%) participants in tramadol group required rescue analgesic (IV

Table 5: Comparison of complications and rescue analgesic between group (*N* = 80)

Complications	Group	
	Tramadol (*N* = 40)	Nalbuphine (*N* = 40)
Vomiting	5 (12.5%)	0 (0%)
Rescue Analgesic (IV paracetamol)	6 (15%)	0 (0%)

*No statistical test was applied-due to 0 subjects in the cells.

paracetamol). One participant needed 2 doses and 5 participants needed 1 dose of rescue analgesis (Table 5).

Discussion

The postoperative pain is a concern among most of the patients undergoing orthopedic surgical procedures. Insufficient pain relief is a common concern among these patients, which may adversely affect their quality of life and functions.[5,13] Opioid analgesics such as tramadol and nalbuphine are commonly used for the management of postoperative pain. In the present study, most participants belonged to the higher age group of 61–70 years. This was in accordance to many other previous studies.[6,14]

In the present study, the mean sedation score was significantly higher in the nalbuphine group compared to the tramadol group at 2 hrs. Gupta, KL et al.[1], in their study concluded that nalbuphine is a good sedative and provides good postoperative pain relief. Saxena, D et al.[15], in their study determined tramadol to be a safe and effective adjuvant to epidural bupivacaine for prolongation of the total duration of analgesia in lower-limb surgeries. Chatrath, V et al.[10], found that the addition of nalbuphine with bupivacaine was effective for postoperative analgesia in terms of quality of analgesia and patient satisfaction score as compared to tramadol. Solanki, RN et al.[6], concluded in their study that nalbuphine produces better pain relief and hemodynamic stability in the postoperative period in patients undergoing orthopedic surgeries when compared to tramadol. However, many comparative studies conducted in the past have concluded that the mean sedation scores did not differ between the groups for lower-limb surgery unlike the current study.[5,6]

In the present study, the mean VAS score was significantly higher in the nalbuphine group at 12 hrs and 24 hrs postsurgery. Chatrath, V et al.[10], also found that the mean VAS score in the nalbuphine group was found to be significantly lesser compared to the tramadol group. The quality of surgical analgesia was excellent in 40 (100%) patients in the nalbuphine group, which was seen only in 36 (90%) patients in the tramadol group. Solanki RN et al.[6], found similar results in their study.

In the present study, the tramadol group was associated with a higher incidence of nausea and vomiting 5 participants and 6 participants needed rescue analgesics. In the study by Solanki, RN et al.[6], Vyas, V et al.[5], Chatrath, V et al.[10], it was found that tramadol resulted in early pain relief but a higher incidence of nausea and vomiting. Sharma, K et al.[16], in their study found that mild respiratory depression and sedation was reported with Nalbuphine. Nausea vomiting was significantly high with Tramadol. A number of rescue analgesic doses were also found lesser in the other comparative studies.[5,6,10]

Conclusion

Epidural nalbuphine was a better choice in providing postoperative pain relief in patients undergoing orthopedic surgical procedures under combined spinal-epidural anesthesia. Tramadol was associated with a higher incidence of nausea and vomiting.

Key Messages

Epidural nalbuphine as well as epidural tramadol provide good postoperative pain relief. The nalbuphine is a superior drug in patients undergoing orthopedic surgical procedures under combined spinal-epidural anesthesia in terms of slightly better VAS and sedation scores.

Tramadol is associated with higher incidence of postoperative complication such as nausea, vomiting and use of rescue medication as compared to nalbuphine.

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Declarations

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References

1. Gupta KL, Gupta A, Neeraj. Efficiency of nalbuphine as an adjuvant to bupivancaine in lower-limb orthopedic surgery-a prospective study. Int J Res Med Sci 2017;5(2):623–26.
2. Bogra J, Arora N, Srivastava P. Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anesthesia for cesarean section. BMC Anesthesiol 2005;5(1):5.
3. Grond S, Sablotzki A. Clinical pharmacology of tramadol. Clin Pharmacokinet. 2004;43(13):879–923.
4. Siddiqui KM, Chohan U. Tramadol *versus* nalbuphine in total intravenous anesthesia for dilatation and evacuation. J Pak Med Assoc 2007;57(2):67–70.
5. Vyas V, Kiran K, Patil S. Comparative efficacy and safety of intravenous tramadol and nalbuphine for pain relief in postoperative patients. Indian J Pain 2018;32(2): 96–101.
6. Solanki R, Gosai N, Joshi G, et al. A comparative study of intravenous nalbuphine HCl and tramadol HCl for postoperative pain relief following orthopedic surgeries. Asian Pac J Health Sci 2015;2(1):155–60.
7. Gupta SS, Gupta AD, Ahirwal SD. Comparison of efficacy of the test of visual perceptual skills-3 and the rivermead perceptual assessment battery with performance of Indian drivers on driving simulator for determining off-road perceptual skills: A pilot study. Indian J Occup Ther 2019;51(3):90–95.
8. Ahmed A, Latif N, Khan R. Postoperative analgesia for major abdominal surgery and its effectiveness in a tertiary care hospital. J Anesthesiol Clin Pharmacol 2013;29(4): 472–77.
9. McCaffery M, Pasero C. Opioid analgesics. Pain: Clinical manual. 2nd edition. Elsevier; 1999.pp.161–299.
10. Chatrath V, Attri JP, Bala A, et al. Epidural nalbuphine for postoperative analgesia in orthopedic surgery. Anesth Essays Res 2015;9(3):326–30.
11. Kirkwood BR. Essentials of medical statistics: Blackwell Scientific Publications; 1988.
12. IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.
13. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: A clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain 2016;17(2):131–57.
14. Kumar J, Sinha PK, Prasad BK, et al. Comparative study of nalbuphine and tramadol for postoperative pain relief in patients of short surgical procedures under TIVA. Int J Contemp Med Res 2017;4(4):977–79.
15. Saxena D, Sanwat Sarkar S, Dixit A, et al. Comparative study of duration of analgesia with epidural bupivacaine and bupivacaine with tramadol in lower limb surgeries. Int J Res Med Sci 2017;5(5):2003–2010.
16. Sharma K, Audichya PC, Goyal S, et al. Randomized comparison of tramadol, nalbuphine and fentanyl used as premedication in attenuation of hemodynamic response to laryngoscopy and postoperative pain in laparoscopic cholecystecyomy. Int J Med Sci Clin Invent 2016;3(7):1968–76.

Original Research Article

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Comparison of Baska Mask with I-GEL for Insertion Success Rate and Working Performance in Laparoscopic Pelvic Surgery

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Abstract

Aims: Study aimed at comparison of recent addition Supra Glottic Airway Devices I-gel and Baska mask during general anesthesia in patients undergoing elective laparoscopic pelvic surgery. *Settings and Design:* Prospective, randomized, single blind study. *Materials and Methods:* After institutional review board approval and written informed consent, 50 patients aged 18–60 years scheduled for elective laparoscopic pelvic surgery were randomly assigned into two groups either I-gel or Baska mask. After premedication and preoxygenation, patients were induced with Inj. fentanyl 2 mcg/kg and Inj. propofol 2- 2.5 mg/kg IV. Insertion of SGA was done according to group assigned. The insertion characteristics were recorded in form of number of attempt, time of insertion, manipulation required and failed insertions. Success of orogastric tube insertion was noted in both the groups. Working performance was compared in form of hemodynamic stability, oropharyngeal leak pressure, mean tidal expiratory volume and postoperative complications. *Statistical analysis used:* Data were analyzed by using unpaired *t*-test, Chi-square test. *Results:* Shorter insertion time was found with I-gel (16.80 ± 02.23) as compared to Baska mask (21.56 ± 04.20). Oropharyngeal leak pressure and mean tidal expiration volume were higher for Baska mask (25 ± 02.50;679 ± 98.17) as compared to I-gel (22.72 ± 02.13;600.08 ± 88.06). Hemodynamic parameters and postoperative complications were comparable among both the groups. *Conclusion:* Baska mask has a better working performance with higher oropharyngeal leak pressure and mean tidal expiratory volume while I-gel has lesser insertion time.

Keywords: Laparoscopic pelvic surgery; I-gel; Baska mask; Insertion time; Oropharyngeal leak pressure; Mean tidal expiratory volume.

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Introduction

The journey of the management of the airway has come a long-way since, the development of endotracheal intubation by Macewen in 1880, to the present-day usage of sophisticated supra glottic airway devices.[1] General anesthesia requires safe and open airway.[2] Till date, tracheal intubation is the gold standard method for maintaining a patent airway during anesthesia.[3] However, this maneuver requires skill, training and practice, usually requires direct laryngoscopy.[4] Laryngoscopy and endotracheal intubation produces reflex sympathetic stimulation which causes tachycardia, raised levels of plasma catecholamines, hypertension, myocardial ischemia, depression of

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myocardial contractility, ventricular arrhythmias and increase in intracranial pressure.[5] With advancement in anesthesia technique in airway management, it has been progressed from using an endotracheal tube to a supraglottic airway device because of ease and speed of insertion, improved hemodynamic stability, reduce anesthetic requirement and less postoperative complications.[6,7]

Wide variety of supraglottic airway devices available today which are employed to protect the airway in both elective as well as emergency situations.[8] A first-generation SADs is defined as being just a simple airway tube, with no specified design features for safety or performance, provide little protection from gastric regurgitation and aspiration. Second generation SADs, on the other hand, have been developed specifically for safety, with a gastric drain tube, improved pharyngeal seal and bite block. Miller, proposed in 2014 another system, based on the sealing mechanism (three generations) and on the anatomic location of sealing (base-of-tongue or perilaryngeal) (Table 1).

Laparoscopic surgery requires creation of pneumoperitoneum and appropriate positioning. The effectiveness of SAD use in gynecological surgery may be attributed to the short and elective nature of surgery, limitation of pneumoperitoneum and positioning to acceptable limits and the advantages offered by SAD in ambulatory surgery.

I-gel is a cuffless, single-use second generation supraglottic device.[9] I-gel is made up of a thermoplastic elastomer (styrene butadiene styrene ethylene)[10], a gel like material that is designed to more closely fit in the perilaryngeal anatomy without the need of inflatable cuff. I-gel has a gastric drainage tube that allow for passage of a nasogastric tube for stomach decompression, which significantly reduces risk of regurgitation and pulmonary aspiration.[11] I-gel has an intrinsic bite block to prevent compression of the airway tube and prevent misplacement and rotation.[12]

Baska mask is a novel 3rd generation SAD made up of medical grade silicon. It has noninflatable cuff, which is moulded to take shape of supraglottic airway, potentially reducing the risk of oropharyngeal tissue and nerve damage induce by cuff overinflation.[13] Baska mask has cuffless membranous bowl which inflates and deflates with each positive pressure inspiration and expiration respectively. Baska mask has an inbuilt tab that permits to increase its angulations for easy negotiation of oropharyngeal curve during placement. Baska mask has esophageal drainage inlet and side channel for aspiration of gastric content as well as integrated bite block.[14,15]

Materials and Methods

The study was done at tertiary care hospital, after obtaining approval from Institutional Review Board (IRB no.770/2018). It was registered with clinical trial registry-India under CTRI /2019/05/019242.

History of presenting complaint, past history, operative history, and drug history was taken. General examination of patients was done and vital parameters assessed. After preanesthetic check-up and necessary investigations, following patients were included and excluded from the study.

Inclusion Criteria

- Age of patient: 18–60 years.
- Gender: male/female.
- ASA Grade I–III.
- Laparoscopic Gynecological pelvic surgery for short-duration of 90–120 minutes.

Exclusion Criteria

- Age < 18 years and > 60 years.
- Risk of aspiration (nonadequately NBM, gastroesophageal reflux, BMI > 35 kg/m2, obstetrics' patient).
- Difficult Airway (mouth opening < 2 cm, mallampati class 4, limited neck extension, previous difficult intubation).
- Preoperative sore throat.
- Limited access to patient airway during surgery.

After taking written informed consent in the local language, patients were randomized using computer generated random number sequence methods in two groups:

Group A (I-gel Group).

Group B (Baska mask Group).

After shifting the patient to the preanesthetic care room, 20 G intravenous catheter is inserted on nondominant hand. Baseline parameters were recorded by multipara monitor, ECG for Heart Rate (HR), Noninvasive Blood Pressure (NIBP) for Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) and Pulse Oximetry for Oxygen Saturation (SpO_2). All patients were premedicated with Inj. ondansetron

0.08 mg/Kg IV, Inj. glycopyrrolate 0.004 mg/kg IV, Inj. midazolam 0.02 mg/kg IV and Inj. fentanyl 2 mcg/kg IV 20 minutes prior to surgery.

Patients were shifted to operation theater and were preoxygenated with 100% oxygen for 3 mins by face mask with Bains circuit. Patients were induced with Inj. propofol 2–2.5 mg/kg IV slowly till loss of eyelash reflex, jaw relaxation, absence of movements and apnea. Patients were ventilated with Bains circuit. Insertion of Supraglottic airway device was done according to group assigned to the patients either with I-gel or Baska mask. The size of supraglottic airway device was selected as per manufacturer recommendation.

Correct positioning of device was confirmed by bilateral chest movement and capnography. The time of insertion was counted from picking up the devices till establishment of manual ventilation *via* the Supraglottic airway device. If, ventilation was found to be inadequate, maneuver like neck flexion or extension, chin lift, gentle modification of the depth of the device will be applied. If, ventilation still remains inadequate device was then removed and inserted again. Maximum three failed insertion were permitted before it is considered as a failure. After insertion of device, appropriate sized of gastric tube was lubricated and placed into the stomach through the gastric channel. The correct placement of the gastric tube was confirmed by either aspiration of fluid or detection of injected air by auscultation over epigastrium. The ease of the device as well as gastric tube was graded as 1 (easy) and 2 (difficult).

Oropharyngeal leak pressure was measured by closing the adjustable pressure limiting valve against 5 l/min fresh gas flow and recording the airway pressure at equilibrium when air leak was heard in the oropharynx to a maximum airway pressure of 40 cm of H_2O. Supraglottic airway device was connected to ventilator with pressure controlled ventilation set as 17 cm H_2O[8] for 5 breaths to measure the mean tidal expire volume. Alveolar ventilation was set to maintain $EtCO_2$ in the range of 4–4.6 kpa (30 mm Hg).

Anesthesia was maintained with oxygen, nitrous oxide, IPPV, sevoflurane and intermittent dose of injection Atracurium. Hemodynamic parameters like heart rate, blood pressure as well as SpO_2 were recorded before, during and after induction with I-gel or Baska mask insertion at 1, 5, 10 (min) and after removal of the device.

At the end of surgery all the patients were ventilated with 100 % oxygen. After the fulfilment of the criteria of emergence, the SGA was removed and examined for traces of blood. Patients were asked for the pharyngolaryngeal pain and nausea before discharge from recovery.

Statistical analysis

Considering ease of insertion, attempts of I-gel and Baska mask insertion, oropharyngeal leak pressure, expired tidal volume, hemodynamic changes as the main outcome measure of interest in this study with at least 10% efficacy shown by the treatment group with permitted alpha error of 0.5 and beta error of 0.2 the power of study comes out to be 80%.

Data collected was analyzed as mean + SD and % which ever applied. Statistical analysis was done by graph pad instat 3.0 software. Intergroup comparison between two groups was done using the unpaired student *t*-test for quantitative data and Chi-square test for qualitative data ($p < 0.05$ was considered as statistical significant).

Results

The demographic and surgical data were comparable among both the groups, shown in Tables 2 and 3. I-gel was inserted successfully in 24 patients (96%) in first attempt and one patient (4%) in second attempt. Baska mask was inserted in successfully in 23 patients (92%) in first attempt and 2 patients (8%) in second attempt. There was no failure in insertion of airway in any group. One patient (4%) in I-gel Group and 2 patients (8%) in Baska mask Groups required airway manipulation for adequate ventilation (Table 4).

Table 1: Classification of SAD

Sealing mechanism	Location of sealing	
	Perilaryngeal	Base of tongue
1st generation-inflatable cuff	CLMA, PLMA	Combitube
2nd generation-preshaped	I-gel	SLIPA
3rd generation-self energizing	Baska mask	

Abbreviations: [CLMA - Classical Laryngeal Mask Airway, PLMA - ProSeal Laryngeal Mask Airway]

Table 2: Patient Characteristics

Patients characteristics	Group A Mean ± SD (*n* - 25)	Group B Mean ± SD (*n* - 25)	*p* - value
Age (years)	30.00 ± 07.20	30.00 ± 08.50	0.9293
Weight (kg)	57.28 ± 13.20	58.52 ± 11.66	0.7265
Height (cm)	157.48 ± 02.80	158.64 ± 02.70	0.1429

Table 3: Duration of surgery

Time	Group A Mean ± SD (*n* - 25)	Group B Mean ± SD (*n* - 25)	*p* - value
Duration (minutes)	75.40 ± 09.00	77.40 ± 09.02	0.4367

The mean insertion time was significantly less in I-gel as compared to Baska mask. ($p < 0.0001$), shown in Fig. 3. The Oropharyngeal leak pressure (p value 0.0017) and Mean tidal expiratory volume (p value 0.0041) were significantly higher in Baska mask group than I-gel, Figs. 4 and 5. Gastric tube could be inserted more easily and successfully in I-gel then Baska mask group but the difference was not statistically significant. (p value > 0.05). The heart rate and mean arterial pressure were comparable among both the groups, Figs. 7 and 8. Blood staining was observed in two and three cases each in the I-gel and Baska mask groups respectively. There was no incidence of Laryngobronchospasm in any of the groups, (Fig. 9).

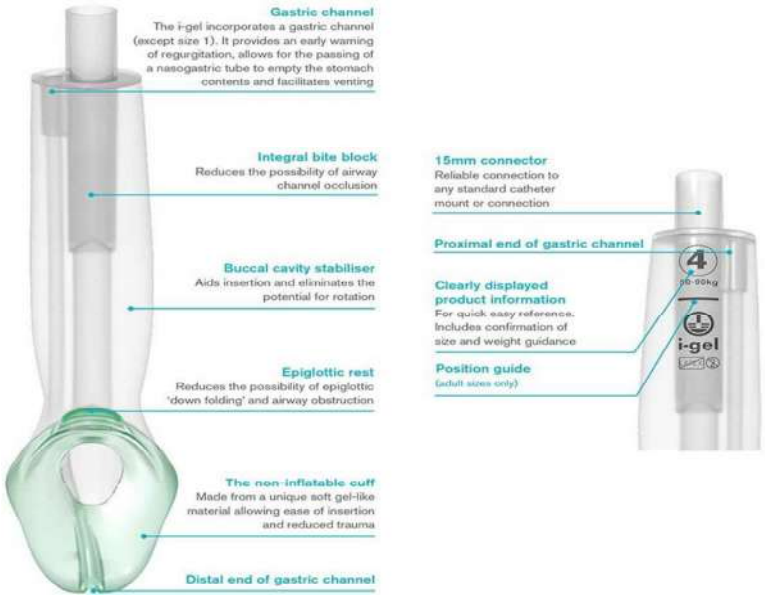

Fig. 1: I-GEL.

Table 4: Insertion characteristics of the device

Variable		Group A Mean ± SD (*n* - 25)		Group B Mean ± SD (*n* - 25)		*p* - value
		%	*N*	%	*N*	
Insertion attempts	First	24	96	23	92	0.5515
	Second	01	04	02	08	
Manipulation required after insertion to improve ventilation	Yes	01	04	02	08	0.5515
	No	24	96	23	92	
Failed insertion	Yes	00	00	00	00	
	No	25	100	25	100	

Table 5: Mean Insertion time of the device

Time	Group A Mean ± SD (*n* - 25)	Group B Mean ± SD (*n* - 25)	*p* - Value
Duration (sec)	16.80 ± 02.23	21.56 ± 04.20	< 0.0001

Table 6: Working performance of device

Variable	Group A Mean ± SD (*n* - 25)	Group B Mean ± SD (*n* - 25)	*p* - Value
Oropharyngeal leak pressure	22.72 ± 02.13	25.00 ± 02.50	0.0017
Expired tidal volume	600.08 ± 88.06	679.00 ± 98.17	0.0041
$EtCO_2$	31.84 ± 01.70	32.16 ± 01.79	0.5206

Abbreviation: [$EtCO_2$ - End Tidal CO_2]

Fig. 2: Baska Mask

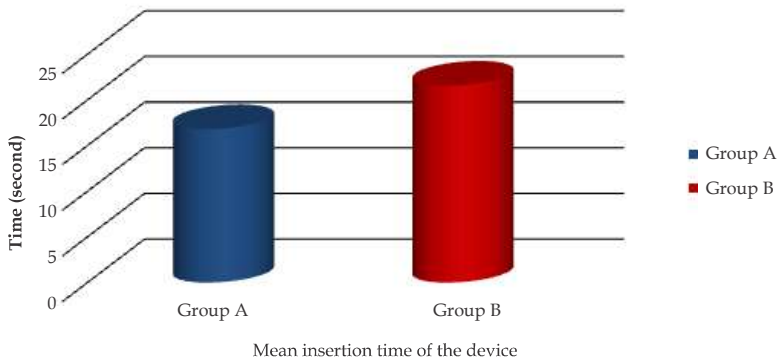

Fig. 3: Mean insertion time of device.

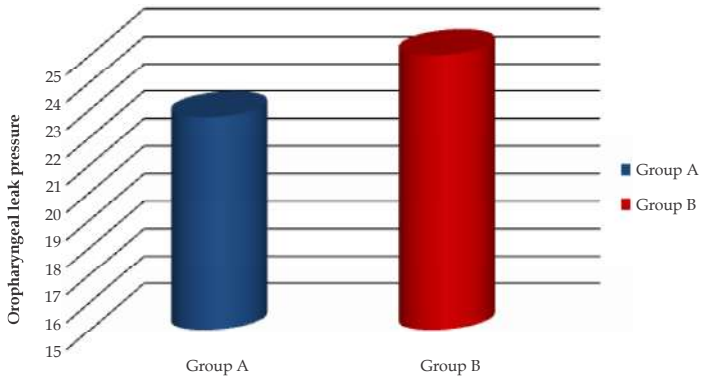

Fig. 4: Oropharyngeal Leak Pressure.

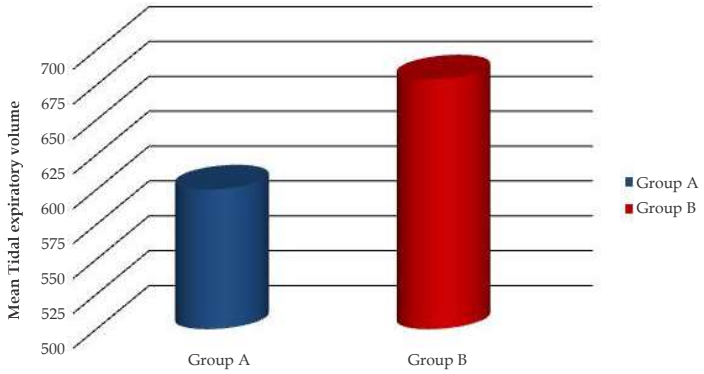

Fig. 5: Mean Tidal expiratory volume

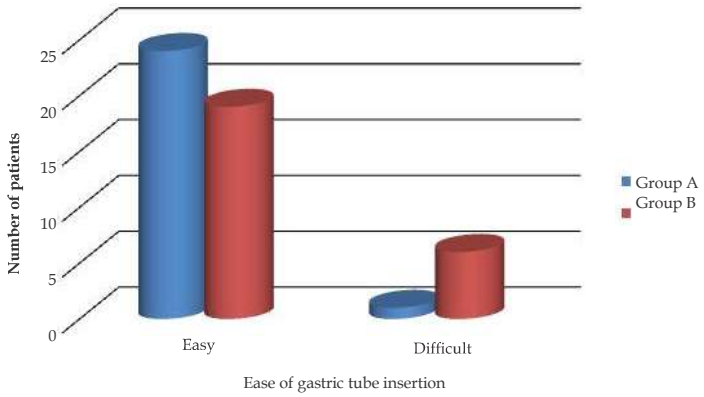

Fig. 6: Gastric tube insertion**.**

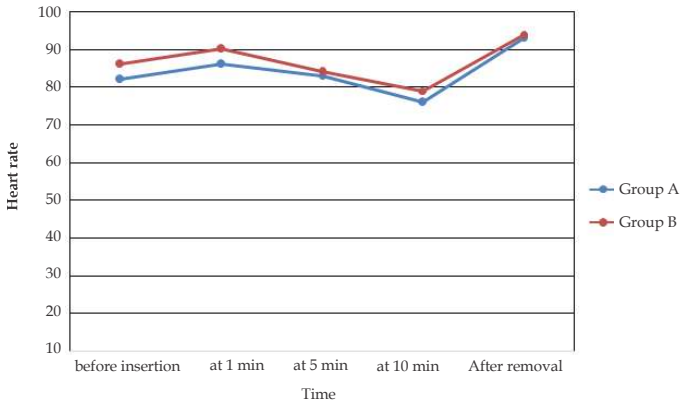

Fig. 7: Changes in Heart rate.

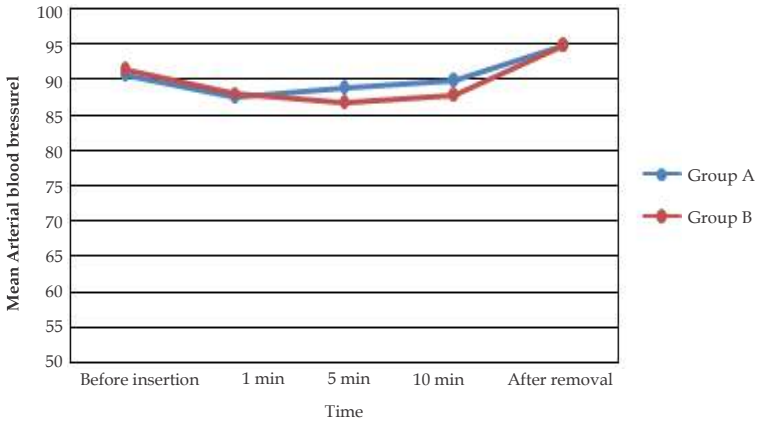

Fig. 8: Changes in mean arterial pressure.

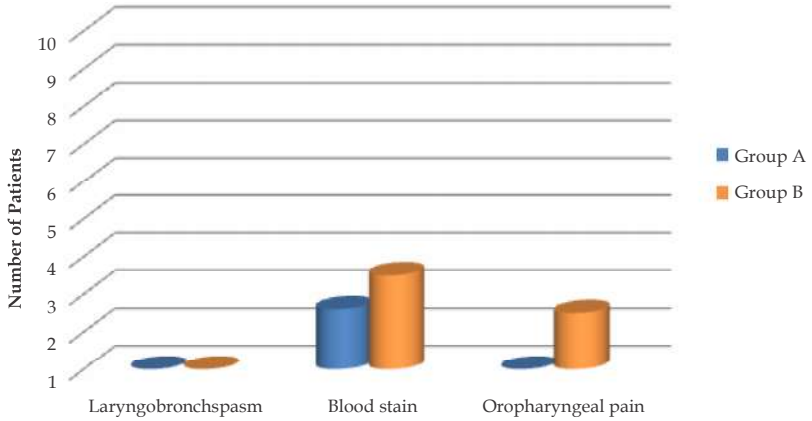

Fig. 9: Postoperative complications.

Discussion

Trend in airway management has recently been progressed from using an endotracheal tube to a supraglottic airway devices.[16] However, the use of supraglottic airway devices in laparoscopic surgery remain controversial because of increased risk of insufficient ventilation and pulmonary aspiration.[17,18] After introduction of airway devices with drainage system we can overcome many problems associated with its use.[19] Lu et al., have shown better suitability of supra glottic airway devices with drainage tube for securing airway in laparoscopic surgery.[20]

First generation supraglottic airway devices act as airway conduits whereas second generation devices have safety designs like integrated bite block, gastric drainage channel and act as airway conduit for endotracheal intubation.[21] Some of the cuffless devices like I-gel and Baska mask may reduce the risk of laryngopharyngeal trauma. First generation supraglottic airway devices develop air leak during positive pressure ventilation of 16–20 cm H_2O. But second-generation devices maintain seal pressure at 25–28 cm H_2O, which has permitted its use during complex surgeries including laparoscopic surgery, in which intraabdominal pressure is high. More recently, changes in surgical environment like shorter length of hospital stay, minimally invasive surgery and increased cost have all had some impact on the choice of airway management. Being less invasive supraglottic airway devices is good option for gynecological day care surgery. The Baska mask is a recently introduced device with self-energizing membranous cuff which provides high-oropharyngeal leak pressure which enhances the patient safety and ease of insertion when compared with the other noninflatable devices such as I-gel. Because both the Baska mask and I-gel have a noninflatable self-sealing mechanism, we decided to compare these two devices in laparoscopic surgery.

The present study shows, comparable demographic data (age, height and weight), shown in Table 2 and surgical details (type and duration of surgery) (Table 3).

In present study, first attempt insertion success rate was comparable between Group A and

Group B (Group A-96%; Group B-92% on first attempt) (p value > 0.05), this result was similar to a previously done study.[22,23] The lower success rate achieved with Baska mask may be attributed to the morphology of the device and unique expertise needed to insert the device. There was no failure after insertion and one patient in Group A and two patients in Group B required airway manipulation. (p value > 0.05), Table 4, which was similar to a previously done study.[24]

In present study, shorter insertion time was found with I-gel (16.80 ± 02.23) as compared to Baska mask (21.56 ± 04.20) (p value < 0.05), Table 5, this observation was correlated with previously done study.[22,23] This may be due to I-gel being less bulky as compared to Baska mask making it more handy device to insert and remove which is responsible for lesser insertion time.

The supraglottic airway device having separate gastric channel has the advantage of passing gastric tube through it which enable us for gastric decompression. In this study, ease of gastric tube placement was more with I-gel (24/25) then Baska mask (19/25), though the difference was not statistically significant (p value > 0.05), Fig. 6, which corelated with previously done study by El refai et al. in 2008.[25]

In present study, oropharyngeal leak pressure and mean tidal expiration volume were higher for Baska mask (25 ± 02.50;679 ± 98.17) as compared to I-gel (22.72 ± 02.13;600.08 ± 88.06) (p value < 0.05), Table 6, thereby providing greater airway protection during laparoscopic surgery. These findings were consistent with findings observed by other authors.[22,23,26] High oropharyngeal leak pressure of Baska mask may due to unique design of the cuff, a recoilable membrane that inflates and deflates with respiratory cycle. As pressure increases cuff inflates itself with positive pressure ventilation, which may improve the seal, thereby reducing the leak and provides high mean tidal expiratory volume making the ventilation more efficient.

Hemodynamic variables (heart rate and mean arterial pressure) were comparable between both the groups (p value > 0.05), Figs. 7–8. There was no statistically significant increase in heart rate and mean arterial pressure from baseline after insertion of device, this may be due to same stress response produced by both the devices, These results were comparable with previously done study.[26]

In the present study, Baska mask was associated with higher incidence of blood staining of the device (Group A-8% and Group B-12%) and oropharyngeal pain (Group A-4% and Group B-8%) in comparison to I-gel. But the difference was not statistically significant (p value > 0.05). These findings were correlated with previously done study.[26] The soft seal noninflatable supraglottic airway devices like I-gel or Baska mask has the potential advantage of minimal tissue compression which leads to lower incidence of laryngopharyngeal morbidity in form of Laryngobronchospasm, oropharyngeal pain and blood staining of device when compared to inflatable SADs.

There are several limitations to this study. First, findings may not be applicable to the patients with difficult airway. Second, we took single measurement of oropharyngeal leak pressure and did not observe it in the different positions of the patient. Third, it was an open label study as device blinding was not possible which could lead to bias. We recommend such more studies to compare the efficacy of both the devices and to support our study.

Conclusion

We conclude that, I-gel and Baska mask both are safe to use in laparoscopic pelvic surgery. Baska mask has a better working performance with higher oropharyngeal leak pressure and mean tidal expiratory volume while I-gel has lesser insertion time.

References

1. James CD. Sir William Macewen and anesthesia. Anesthesia 1974;29: 743–53.
2. Weber U, Oghuz R, Potura LA, et al. Comparison of the I-gel and the LMA-Unique laryngeal mask airway in patients with mild to moderate obesity during elective short-term surgery. Anesthesia 2011;66:481–87.
3. The European Resuscitation Council (ERC) and the American Heart
4. Association (AHA) in collaboration with the International Liaison Committee on Resuscitation (ILCOR): International Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiac Care. An International Consensus on Science. Resuscitation 2000;6:29–71.
5. Peppard SB, Dickens JH. Laryngeal injury following short-term intubation. Ann Otol Rhinol Laryngol 1983;92:327–30.
6. Gal TJ. Airway management. In: Miller RD, editor.

Textbook of anesthesia, 6th ed. Philadelphia: Elsevier; 2005.pp.1617–652.

7. Cork RC, Depa RM, Standen JR. Prospective comparison of use of the laryngeal mask and endotracheal tube for ambulatory surgery. Anes Analg 1994;79:719–27.
8. Ronald D Miller, Textbook of Miller's anesthesia, 8th edition.
9. Jayashree S. Laryngeal masks airway and its variants. Indian J Anesth 2005;49:275–80.
10. Dinsmore J, Maxwell W, Ickerigill M. Early experience with I-gel. Resuscitation 2007.
11. 7th edition. Wokingham, UK: Intersurgical Ltd; 2009. [accessed 16th feb, 2012]. I-gel User Guide. http://www.igel.com
12. Cattano D, Ferrario L, Maddukuri V, et al. A randomized clinical comparison of the Intersurgical I-gel and LMA Unique in nonobese adults during general surgery. Minerva Anesthesia 2011;77: 292–29.
13. Wharton NM, Gibbison B, Gabbott DA, et al. I-gel insertion by novices in manikins and patients. Anesthesia 2008;63: 991–95.
14. Zhang J, Zhao Z, Chen Y, et al. New insights into the mechanism of injury to the recurrent laryngeal nerve associated with the laryngeal mask airway. Medical Science Monitor 2010;16:HY7–9.
15. Alexiev V, Ochana A, Abdelrahman D, et al. Comparison of the Baska_ mask with the single-use laryngeal mask airway in low-risk female patients undergoing ambulatory surgery. Anesthesia 2013;68:1026–32.
16. Alexiev V, Salim A, Kevin LG, et al. An observational study of the Baska_ mask: A novel supraglottic airway. Anesthesia 2012;67:640–45.
17. Cork RC, Depa RM, Standen JR. Prospective comparison of use of the laryngeal mask and endotracheal tube for ambulatory surgery. Anes Analg 1994;79:719–27.
18. Abdi W, Amathieu R, Adhoum A, et al. Sparing the larynx during gynecological laparoscopy: A randomized trial comparing the LMA Supreme and the ETT. Acta Anesthesiol Scand 2010;54:141–46.
19. Teoh WH, Lee KM, Suhitharan T, et al. Comparison of the LMA Supreme vsthe I-gel in paralyzed patients 2011;66(3);226–27.
20. Ramaiah R, Das D, Bhanaker SM, et al. Extra glotticir way devices; A review. International Journal of Critical Illness and Injury Science 2014;4(1): 77–87.
21. Lu PP, Brimacombe J, Yang C, shy M(2002) Proseal versus classic laryngeal mask airway for positive pressure ventilation during laparoscopic cholecystectomy. Br j Anesthesia 2002;88:824–27.
22. Almeida G, Costa AC, Machado HS. Supraglottic airway devices; A review in a new era of Airway Management. J Anesthclin Res 2016;7;7.
23. Shanmugavelu G, Kanagarajan T. Comparing the functional analysis of I-gel with Baska mask in laparoscopic surgeries: an observational study. Int J Res Med Sci 2018;6:14403
24. Chaudhary UK, Mahajan SR, Mahajan M, et al. A comparative analysis of the Baska mask *versus* I-gel for general anesthesia in surgical patients undergoing laparoscopic cholecystectomy. Acta Med Int 2018;5:69–73.
25. Mustafa. Comparison of new generation Baska mask with I-gel and C-LMA in outpatient urological intervention. Saudi med J 2019;7:23824.
26. NAR El refai. Comparative study between Baska and I-gel in spontaneously ventilated females undergoing minor gynecological procedures 2018;69: 201–208.
27. Rehab Abdel Raof Abdel Aziz, Yasser Mohamed Osman. Department, comparison of I-gel with Baska mask airway for controled ventilation in obese patients undergoing ambulatory surgery: A Prospective Randomized Trial. Journal of Anesthesiology 2017;5;29–35.

Original Research Article

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Evaluation of Airway Blocks Vs General Anesthesia for Diagnostic Direct Laryngoscopy and Biopsy for Carcinoma Larynx: A Comparative Study

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Abstract

Aims: Evaluation of airway blocks *vs* general anesthesia for diagnostic direct laryngoscopy & biopsy for carcinoma larynx it is a comparative study. *Materials and Methods:* A total of 60 patients between the age group 50–70 years were included in the study. They were ASA Grade 3 or 4 and scheduled for Laryngeal biopsy under anesthesia. Patients were randomized in two groups, Group A received airway blocks with 2% lignocaine and Group B received general anesthesia. Group A patients received bilateral superior laryngeal nerve block, glossopharyngeal nerve block and transtracheal block. Group B patients received general anesthesia. Patients were monitored during anesthesia using continuous ECG, NIBP and Pulseoximetry. Intraoperative IV fluids were given according to the protocols. Vital data was recorded preoperatively and during direct laryngoscopy at every 5 minutes interval. *Results:* Preoperative vitals were same in both groups and statistically there was no significant difference in the data. Mean arterial pressures were raised during postoperative period. The postop analgesia was significantly higher in Group A and lasted longer as compared to Group B and patients were less agitated and calm. In Group B patients, most of them required postop nebulization as compared to Group A where no patient needed nebulization. *Conclusion:* Laryngeal biopsies done under regional airway blocks have less of hemodynamic changes and good analgesia in postop period, compared to cases done under general anesthesia.

Keywords: Laryngoscopy; Biopsy; Carcinoma larynx; Glossopharyngeal nerve block.

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Introduction

Laryngoscopy and endotracheal intubation is the commonest method of securing a definitive airway for administering anesthesia in ENT procedures like direct laryngoscopy guided biopsy in suspected carcinoma glottis and subglottis patients.[1] However, it is associated with tachycardia and hypertension.[3] Transitory hypertension and tachycardia are of no consequence in healthy individuals, but either or both may be hazardous to the patients with hypertension, myocardial insufficiency or cerebrovascular disease.[2] The choice of anesthesia becomes more of a concern in such patients because most of them are old, frail and with one or more associated systemic illness like hypertension,

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diabetes, ischemic heart disease etc. Recent developments in regional anesthesia have resulted in a number of innovative and refined options to practitioners, often allowing regional techniques to be used for patients with presumed difficult airways. However, not every surgery can be performed under regional anesthesia. In addition, even in the hands of the most skilled regional anesthesiologist, blocks are subject to a certain rate of complications or failure.[3]

In addition, there are many situations in which the anesthesiologist is called on to secure an airway in less than ideal circumstances. Expertise with regional anesthesia of airway allows intubation in awake patients with suspected difficult intubation, upper airway trauma, or cervical spine fractures. Therefore, it is essential that every regional anesthesiologist be skilled in the administration of general anesthesia and especially in the management of the difficult airway.

One major decision must be made with every procedure will the patient be intubated while under general anesthesia, or does the patient need to be awake during intubation, Intubation under general anesthesia (even with inhalational induction and spontaneous respiration) carries the inherent risk of losing control of the difficult airway.

For this reason, many anesthesiologists, on recognition of a difficult airway, elect to perform an awake intubation using either fiberoptic laryngobronchoscopy or awake direct laryngoscopy.

Direct laryngoscopy in an awake, unprepared patient can be extremely challenging. Excessive salivation and gag and cough reflexes can make intubation difficult, if not impossible, under awake conditions. In addition, the stress and discomfort may lead to undesirable elevations in the patient's sympathetic and parasympathetic outflow.[16] Several highly effective topical and regional anesthesia techniques have been developed to subdue these reflexes and facilitate intubation. Each of these techniques has the common goal of reducing sensation over the specific regions that will be encountered by the fiberoptic bronchoscope and endotracheal tube.

Materials and Methods

The present study, conducted in 60 patients aged between 50 and 70 yrs who are scheduled for elective Laryngeal Biopsy in a Carcinoma Larynx patients under Anesthesia in Government ENT Hospital, Koti attached to Osmania Medical College, Koti, Hyderabad.

After approval from the Departmental ethics committee and written informed consent from the patients, a randomized control study was conducted on 60 patients, planned for elective Direct Laryngoscopic Biopsy under anesthesia. Patients are selected between 50 and 70 years of age comprising both sexes. They are divided into 2 groups of each group containing 30 patients.

Inclusion Criteria

Patients in the age group 50 to 70 yrs, ASA Grade II, III or IV.

Exclusion Criteria

Allergic to Lignocaine**,** Emergency operative case**,** Therapeutic anticoagulation and Mouth opening less than 2 cms.

All patients were preoperatively evaluated for surgery. All investigations were conducted before the surgery. Basic Investigations conducted and all patients were asked to continue taking bronchodilators and nebulization with salbutamol, budecort the night before and in the morning before surgery. The patients were informed about the procedure in detail before commencing the operation.

On arrival in the operation theater, after confirming adequate starvation, patient's heart rate, Noninvasive blood pressure, oxygen saturation, respiratory rate and ECG were monitored. Intravenous access was secured with 20G cannula and Ringer's lactate solution at 2 ml kg^{-1} was started.

All the patients are allocated into 2 groups randomly. The patients in Group 'A' received Airway Blocks with Inj. 2% Lignocaine and without intubation. Patients in Group 'B' received general anesthesia with intubation and no airway blocks. Group A patients were given premedication with Inj. glycopyrrolate 0.04 mcg/kg IV and Inj. midazolam 1 mg IV 2 % lignocaine viscous gargling was done for nasopharyngeal and oral block. Bilateral superior laryngeal nerve block was given with Inj. 2% lignocaine. Transtracheal block is given by puncturing the cricothyroid membrane with Inj. 4% lignocaine.

Group B patients received conventional general anesthesia. Premedication with Inj. glycopyrrolate 0.04 mcg/kg and Inj. fentanyl 2 μg/kg iv given after preoxygenation for 3 minutes and induction with Inj. propofol 2 mg/kg, Inj. suxamethonium 2 mg/kg, followed by intubation with smaller size

no. 5ID MLS cuffed endotracheal tube. IPPV was given using circle absorbing system connected to anesthesia work station at a rate of 14 breaths/min and 8 ml/kg tidal volume.

Maintenance was done with 33% oxygen, 66% nitrous oxide and Inj. Inhalational agent sevoflurane 2% used. Intermittent suxamethonium IV was given. Patients were monitored during anesthesia using continuous 5 lead ECG, NIBP and Pulse oximetry. Intraoperative IV fluids were given according to the protocols.

Vital data was recorded at induction during laryngoscopy and every 5 minutes interval during intraop period. The parameters recorded were Pulse Rate, Systolic blood pressure, Diastolic blood pressure, Mean arterial pressures. In all patients the duration of surgery was around 20 ± 5 minutes.

After completion of surgery, extubation was done in Group B patients and they were transported to the postanesthesia care ward after confirming an adequate level of consciousness and intact reflexes. The patients were observed for 1 hour, in postoperative period for analgesia, hemodynamics and also pain was assessed by using VAS Score.

Statistical Analysis

The data thus collected was entered into an Excel sheet. It was further subjected to statistical analysis in MS Excel and SPSS v16. Data was expressed in frequencies and percentages when qualitative and in Mean ± SD when quantitative. Unpaired Student *t*-test was used for comparing the trends for all parameters in the two groups. A 'p' value of < 0.05 was considered significant.

Results

There was no statistical difference in demographical details in either groups.

Pulse rate was compared at different time interval intraoperatively. It was observed that, mean pulse rate at 0 min, is the period during direct laryngoscopy in Group A was 88.12/min compared to Group B 97.68/min and there was statistical significant in mean pulse rates at 0 min ($p < 0.001$).

Mean pulse rate at 5 mins in Group A was 84.1/min compared to Group B 103.28/min there was statistical significant in mean pulse rates in at 5 mins ($p < 0.001$). Mean pulse rate at 10 mins was significantly lower in Group A 83.3/min compared to Group B 101.2/min ($p < 0.001$). Mean pulse rate at 15 mins was significantly lower in Group A 82.7/min compared to Group B 101.8/min ($p < 0.001$). Mean pulse rate at 20 mins was significantly lower in Group A 83.7/min compared to Group B 102.7/min ($p < 0.001$).

Table 1: Bio-Physical Profile and preop vitals of both groups

Parameter	Group A		Group B		*t*-value	*p* - value
	Mean	SD	Mean	SD		
Age (yrs)	59.4	5.38	61.36	5.36	1.291	0.102
Preop PR (/min)	83.24	5.6	82.4	4.96	0.562	0.577
Preop MAP (mm of Hg)	73.6	5.2	74.3	4.9	0.44	0.66

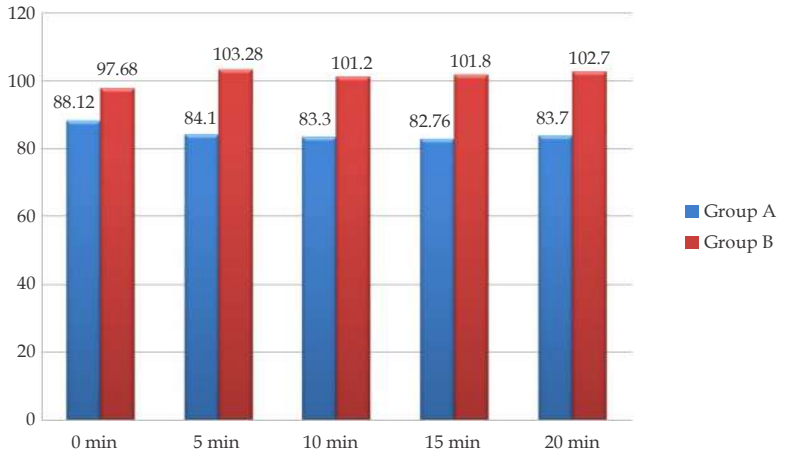

Fig. 1: Intraoperative mean Pulse rates.

Table 2: Vital data at the beginning of the procedure in both the groups

	Group A		Group B	
	PR	MAP	PR	MAP
After airway block	76	83	–	–
After intubation	–	–	82	90

Mean arterial pressure was compared at different time intervals intraoperatively. It was observed that, mean arterial pressure at 0 min in Group A was 71.72 mm Hg compare to Group B 82.7 mm Hg. There was statistical significant in MAP at 0 min ($p < 0.001$).

Mean arterial pressure at 5 mins in Group A was 70.16 mm Hg compare to Group B 80.44 mm Hg. There was statistical significant in MAP at 10 mins ($p < 0.001$). Mean arterial pressure at 10 mins was significantly lower in Group A 69.5 mm Hg compared to Group B 87.28 mm Hg ($p < 0.001$).

Mean arterial pressure at 15 mins was significantly lower in Group A 67.96 mm Hg compared to Group B 86.68 mm Hg ($p < 0.001$). Mean arterial pressure at 20 mins was significantly lower in Group A 67.16 mm Hg compared to Group B 86.76 mm Hg ($p < 0.001$).

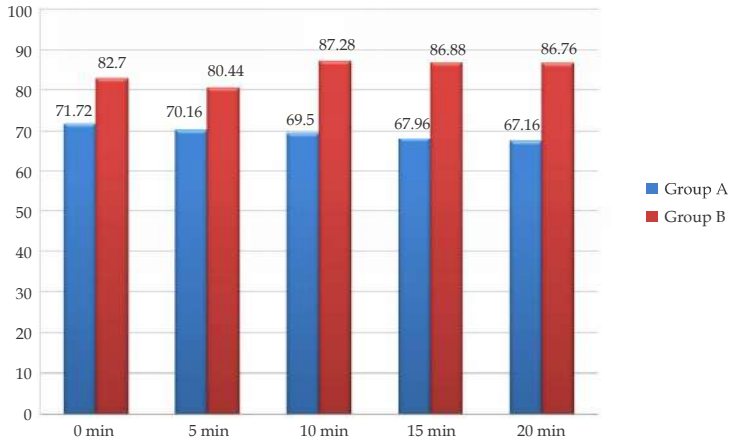

Fig. 2: MAP (in mm Hg) comparison in two groups at different time interval intraoperatively.

Pulse rate was compared at different time interval postoperatively. It was observed that, Mean pulse rate at 30 mins in Group A was 74.12 significantly lower when compared to Group B 80.44 ($p < 0.001$). At 40 mins Mean pulse rate in Group A was 72.28 significantly lower compared to Group B 80.48 ($p < 0.001$).

Mean pulse rate at 50 mins in Group A was 69.84 significantly lower than the mean pulse rate in Group B 85.3 ($p < 0.001$). Mean pulse rate at 60 mins was 67.72 significantly lower than the mean pulse rate in Group B 85.48 ($p < 0.001$).

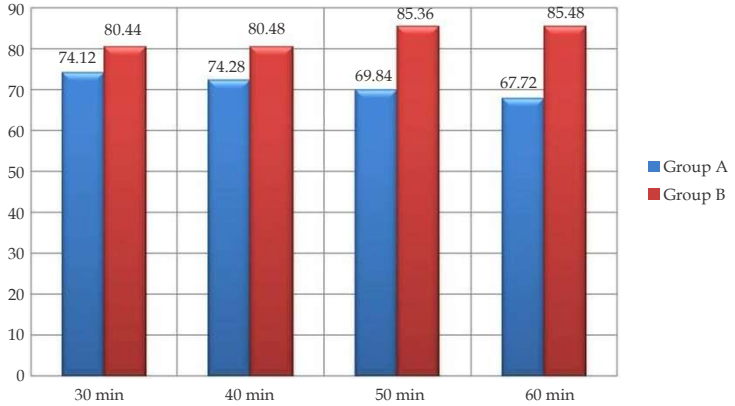

Fig. 3: Pulse rate (per min) comparison in two groups at different time interval postoperatively.

Mean Arterial pressure was compared at different time interval postoperatively. It was observed that, Mean arterial pressure at 30 mins in Group A was 67.08 significantly lower than the mean arterial pressure in Group B is 86.28 ($p < 0.001$). At 40 mins mean arterial pressure in Group A was 65.48 significantly lower than the mean arterial pressure in Group B is 86.16 ($p < 0.001$).

Mean arterial pressure at 50 mins in Group A was 64.88 significantly lower than the mean arterial pressure in Group B is 89.76 ($p < 0.001$). Mean arterial pressure at 60 mins in Group A was 64.32 significantly lower than the mean arterial pressure in Group B is 89.84 ($p < 0.001$).

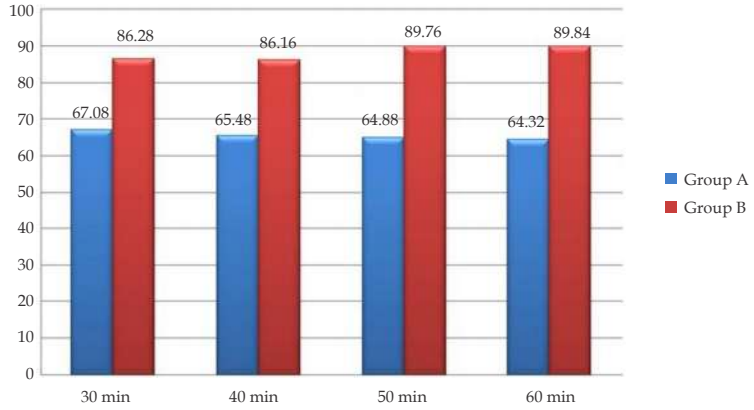

Fig. 4: Mean Arterial Pressure (mm Hg) comparison in two groups at different time interval postoperatively.

Pain scoring at different time interval postoperatively was measured using VAS score. It was observed that the mean VAS score at 30 mins in Group A was 1.16, significantly lower than Group B 2.0 ($p < 0.001$). The mean VAS score at 40 mins in Group A was 1.6, significantly lower than Group B 2.32 ($p < 0.001$).

The mean VAS score at 50 mins was significantly lower in Group A, 2.0 compared to Group B, 3.68 ($p < 0.001$). The mean VAS score at 60 mins was significantly lower in Group A, 2.4 compared to Group B, 3.76 ($p < 0.001$).

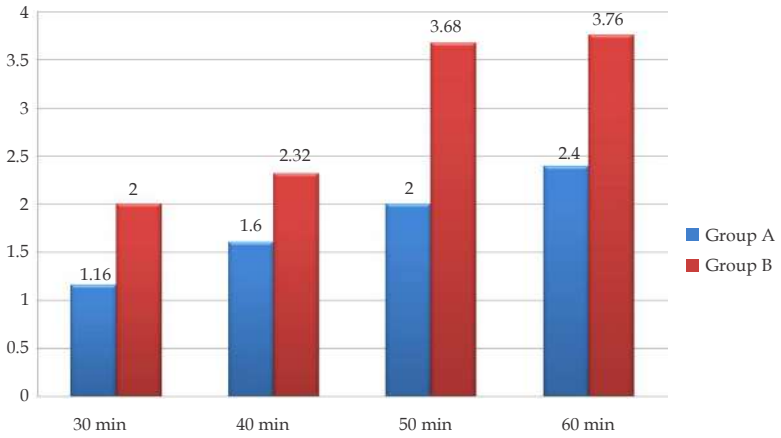

Fig. 5: Comparison of pain scoring according to VAS in two groups at different time interval postoperatively.

Discussion

There has always been a debate with regional *versus* general anesthesia in patients undergoing head and neck surgeries. It becomes a particular concern when the regional anesthesia becomes the best available option in cases like carcinoma larynx with unknown growth extent. General anesthesia with intubation may become highly difficult and challenging in face of fragile growth which may bleed at the time

of tube insertion and may completely block the airway which may render even mask ventilation difficult. The difficult airway algorithm which includes call for help in such a scenario may not be applicable in this case as we don't have much time left after paralyzing the patient. Another way is to do awake intubation which can be highly stressful for these patients and will result in a fighting patient, which will deprive the surgical procedure and may raise the blood pressure to such an extent that it may lead to intracranial hemorrhage in old patients. So, we should expertise with the regional anesthetic techniques. As with other forms of regional anesthesia, airway blocks will provide the anesthetist with additional tools with which to better treat his/her patients. These tools will prove to be useful not only in the operating room setting, but also in emergency room and intensive care areas as well, and will add to the confidence and abilities of the practitioner. There has always been a debate with regional *versus* general anesthesia in patients undergoing head and neck surgeries. It becomes a particular concern when the regional anesthesia becomes the best available option in cases like carcinoma larynx with unknown growth extent.

General anesthesia with intubation may become highly difficult and challenging in face of fragile growth which may bleed at the time of tube insertion and may completely block the airway which may render even mask ventilation difficult. The difficult airway algorithm which includes call for help in such a scenario may not be applicable in this case as we don't have much time left after paralyzing the patient.

This study was undertaken to observe the hemodynamic responses during direct laryngoscopy and biopsy in carcinoma larynx patients with airway blocks *vs* general anesthesia.

Patient with allergic to lignocaine drug, patients with coagulopathies and patients with less than 2 cms of mouth opening were excluded from study. Total 60 patients were taken and divided into two groups. Group A (n = 30) with airway blocks, Group B (n = 30) with general anesthesia. All patients received premedication 15 mins before the procedure with antisialogoguage preoperatively. In all patients average duration of surgery was around 20 ± 5 mins. Patients in Group A, didn't receive any analgesic drugs during intraoperative and postoperative period. Patients in Group B received Inj. Fentanyl 2 μ/kg intraoperatively.

Patients were selected between 50 yrs and 70 yrs of age. The Mean age was (Mean ± SD) 59.4 ± 5.38 in Group A and Mean age was 61.36 ± 5.36 in Group B. The difference was statistically insignificant (p > 0.05) i.e. (p = 0.102).

The difference in average preoperative pulse rate was statistically not significant (p = 0.577). Preoperative Mean pulse rate in Group A 83.24 ± 5.6 and in Group B 82.4 ± 4.96.

The Preoperative Mean Arterial Pressure (MAP) in Group A 73.6 ± 5.2 and in Group B 74.3 ± 4.9 and differences were observed that there are statistically insignificant (p > 0.05) i.e. (p = 0.66).

All patients were followed in the intraoperative period for hemodynamics (pulse rate & Mean arterial blood pressure). Recordings were done during direct laryngoscopy, at the intervals of 0, 5, 10, 15, & 20 mins intraoperatively and postoperatively at 10 mins interval up to 60mins.

In postoperative period pain was monitored by VAS score at the intervals of every 10 minutes. Statistical analysis of the derived parameters were carried out using unpaired "t" test and p - values less than 0.05 was considered significant.

In Group A immediately after airway block pulse rate was 76 per minute and Mean Arterial Pressure (MAP) was 83 and in Group B immediately after intubation pulse rate was 82 per minute and Mean Arterial Pressure was 90.

Intraoperatively Mean Pulse rate of Group A (88.12 ± 7.2, 84.1 ± 6.4, 83.3 ± 4.2, 82.76 ± 4.6, 83.7 ± 5.8) was compared with Group B (97.68 ± 6.7, 103.28 ± 5.5, 101.2 ± 8, 101.2 ± 7.7) at all points of time and found statistically significant (p < 0.001).

Intraoperatively Mean Arterial Pressure (MAP) levels were observed to be high in Group B than Group A. MAP intraoperatively for Group A (Mean ± SD) (71.72 ± 9.04, 70.16 ± 6.8, 69.5 ± 3.3, 67.96 ± 2.9, 67.16 ± 3.19) was compared with Group B (82.7 ± 5.7, 80.44 ± 4.6, 87.28 ± 4.54, 86.88 ± 4.3, 86.76 ± 3.5). The differences were statistically significant at all the points of time (p < 0.001).

Postoperatively Mean Pulse rate levels were observed to be lower among Group A than Group A. Mean Pulse rates for Group A (74.12 ± 4.5, 72.28 ± 3, 69.84 ± 3.03, 67.72 ± 4.08) were compared with Group B (80.44 ± 4.6, 80.48 ± 4.9, 85.36 ± 4.7, 85.48 ± 6.10) and difference was statistically significant at all intervals (p < 0.001).

Postoperatively Mean Arterial Pressure (MAP) values were observed at all times among Group B than Group A. Mean MAP values in Group A (67.08 ± 2.9, 65.48 ± 2.6, 64.88 ± 2.4, 64.32 ± 2.6) were

compared with Group B (86.28 ± 2.59, 86.16 ± 2.13, 89.76 ± 3.7, 89.84 ± 5.5) throughout the intervals postoperatively and found to be that statistically significant ($p < 0.001$).

Subjective assessment of pain was studied postoperatively by 10 cm Visual Analog Score scale. Mean Pain scores in by VAS at all points of time were less in Group A than Group B. Mean Pain scores in Group A (1.16 ± 0.68, 1.6 ± 0.81, 2 ±., 2.4 ± 0.7) were compared with Group B (2 ± 0.57, 2.32 ± 0.47, 3.68 ± 1.3, 3.76 ± 0.7) and difference was found statistically significant at all intervals of time ($p < 0.001$).

V Trivedi, B Patil studied on 100 patients divided into two groups to compare the effects of regional airway blocks *vs* general anesthesia.[4] Baseline preoperative values of pulse and blood pressure were noted and were recorded at 0, 5, 7, 9, 10 and 15 mins. Postoperative sedation and VAS scores were recorded at 0, 5, 15, 30 mins initially and then hourly. Their study showed significant hemodynamic changes in Group II with significant raise in MAP and PR during perioperative period. Whereas in Group I, there was a stability in MAP and PR perioperatively. The postop analgesia was significantly higher in Group I and lasted longer as compared to Group II, and patients were less agitated and calm as assessed by the sedation score. In Group II most of the patients required postop nebulization as compared to Group I where no patient needed nebulization.

Rastogi A et al. conducted a comparison of general anesthesia *versus* regional anesthesia with sedation in selected maxillofacial surgery concluded that regional block with sedation is a safe alternative technique for patients undergoing surgery for mandible fracture or TMJ ankylosis, with clear advantages over general anesthesia.[5]

Babitha Gupta et al. studied, topical airway anesthesia for awake fiberoptic intubation: comparison between airway nerve blocks and nebulized lignocaine by ultrasonic nebulizer.[6] Awake Fiberoptic Bronchoscope (FOB) guided intubation is the fold standard of airway management in patients with cervical spine injury concluded that the time taken for intubation was significantly lower in Group NB compared to Group L. Group L had increased number of cough/gaging episodes as compared to Group NB. Vocal cord visibility and ease of intubation were better in patients who received airway blocks and patient comfort was better in Group NB. They also concluded that Upper airway blocks provide better quality of anesthesia with lignocaine nebulization as assessed by patient recall of procedure, coughing/ gagging episodes, ease of intubation, vocal cord visibility and time taken to intubate.

Abeer Ahmed studied to evaluate the effect of bilateral block of the internal branch of Superior Laryngeal Nerve (SLN) as an adjuvant to general anesthesia during endoscopic laryngeal surgery when smaller dose of muscle relaxant is used.[7] Seventy-six patients required endoscopic laryngosurgery in whom general anesthesia was preceded by bilateral superior laryngeal nerve block either with 2% lidocaine (L-Group) or with saline (C-Group). The reaction to endotracheal tube insertion was better in L-Group as less frequent cough occurred in L-Group (one patient) compared to (8 patients) C-Group (p value < 0.05).

The maximum pressor response was observed immediately after intubation, at which the increase in MAP from baseline in C-Group (24.4%) was significantly higher than in L-Group (6.4%) ($p < 0.05$) and the increase in HR from baseline in C-Group (29.5%) was significantly higher than in L-Group (14.8%) ($p < 0.05$). The MAP and HR remain significantly higher in C-Group than that of the L-Group all through the intraoperative period. The incidence of severe cough was significantly higher in C-Group just before extubation (bucking), 5 min and 30 min postextubation. Incidence and severity of postoperative sore throat was significantly higher in C-Group in the first 4 h postoperatively.

U Bissinger, H Guggenberger et al. undertook a study to assess the practicality, success, and complication rate of Retrograde-Guided Fiberoptic Intubation (RGFI) in a larger series of patients with laryngeal carcinoma.[8] The investigation was performed prospectively with 93 consecutive patients scheduled for laryngectomy. The RGFI technique was performed with the patient under continuous mask ventilation.[9]

Such airway blocks may be highly useful in the era of fiberotic intubation now for better operating conditions and postop analgesia for the patients. Glossopharyngeal nerve block, with radiological control, was used to relieve severe pain due to oropharyngeal carcinoma by monogmery et al.[10] park et al. evaluate the glossopharyngeal nerve block for posttonsillectomy pain. But its use should be advanced to anesthesia procedures also. On the basis of above results, we advise airway blocks for ENT procedures like direct laryngoscpic biopsy for a better inraoperative hemodynamic stability and postop analgesia and securing a safe airway in predicting difficult airway patients and less

complications related to general anesthesia. But still more randomized control trials should be done.[11]

Conclusion

The study shows that laryngeal biopsies done under regional airway blocks have less of hemodynamic changes and good analgesia in postop period, compared to cases done under general anesthesia.

Hence, suggesting that regional airway blocks for anesthesia in short procedure of upper airways and also in cases of predicting difficult airway cases for securing the safe airway can be very useful alternate to the general anesthesia.

References

1. Donlon, DJ Doyle, MA Feldman. Anesthesia for eye, ear, nose and throat surgery. Miller's anesthesia, RD Miller, 6th edition., 2005, Church Hill Livingstone, USA; pp. 2542–43.
2. Faccenda KA, Finucane BT. Complications of regional anesthesia: Incidence and prevention. Drug Saf 2001;24:413–42.
3. Auroy Y, Narchi P, Messiah A. Serious complications related to regional anesthesia: Results of a prospective survey in France. Anesthesiology 1997;87:479–86.
4. V Trivedi, B Patil. Evaluation of airway blocks *versus* general anesthesia for diagnostic direct laryngoscopy and biopsy for carcinoma of the larynx: A study of 100 patients. The Internet Journal of Anesthesiology 2009; 26(1):1–8.
5. Rastogi A, Gyanesh P, Agarwal A, et al. Comparison of general anesthesia *vs* regional anesthesia with sedation in selected maxillofacial surgeries. A randomized controled study. EPUB 2013 Apr;42(3):250–54.
6. Gupta B, Kohli S, Farooque K. Topical airway anesthesia for awake fiberoptic intubation: Comparison between airway nerve blocks and nebulized lignocaine by ultrasonic nebulizer. Saudi J Anesth 2014;8(Suppl 1):S15–19.
7. Abeer Ahmed Dalia Saad Abdel Rahman Youness. Superior laryngeal nerve block as an adjuvant to General Anesthesia during endoscopic laryngeal surgeries: A randomized controlled trial. Egyptian Journal of Anesthesia 2015 April;31(2): 167–74.
8. Bissinger U. Retrograde-guided fiberoptic intubation in patients with laryngeal carcinoma. Anesth and Analg 1995;81:408–10.
9. Kundra P, Kutralam S, Ravishankar M. Local anesthesia for awake fiberoptic nasotracheal intubation. Acta Anesthesiol Scand 2000;44:511–16.
10. Montogmery W. Aspects of the management of chronic pain illustrated by ninth nerve block. British Journal of Anesthesia 1972;44(4):383–85.
11. Hee-Pyoung Park, Jung-won Hwang, Sang-Hyun Park. The effects of glossopharyngeal nerve block on postoperative pain relief after tonsillectomy: The importance of the extent of obtunded gag reflex as a clinical indicator. Anesth Analg 2007 Jul;105(1):267–71.

Original Research Article

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Effects of Adding Tramadol and Nalbuphine with Ropivacaine among Patients Undergoing Upper Limb Orthopedic Surgeries in A Tertiary Care Hospital

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Abstract

Background: Brachial plexus block is the widely-used nerve block in anesthesia for upperlimb surgeries. Ropivacaine, a newer local anesthetic with less cardiotoxicity used frequently now-a-days. Adding adjuvants increases the quality of the block and duration of analgesia. *Aims of the study:* Aim of the study is to compare the effects of adding 100 mg Tramadol and 10 mg Nalbuphine to 0.5% Ropivacaine in Supraclavicular brachial plexus block in patients undergoing upperlimb orthopedic surgeries. Also, study the block characteristics and complications during the study. *Materials and Methods:* A prospective randomized control study was conducted on, 60 ASA I/II patients of either sex at 20–50 years of age, undergoing upperlimb orthopedic surgeries. Group RT received 32 ml of drug mixture (30 ml 0.5% Ropivacaine plus 2 ml of Tramadol), whereas Group RN received 32 ml of the mixture (30 ml of 0.5% Ropivacaine plus 10 mg of Nalbuphine). Time of onset and duration of sensory and motor blocks, duration of analgesia, time for first rescue analgesia and a total number of doses of rescue analgesia were monitored and recorded. *Results:* Onset of sensory block, motor block in Group RT (8.82 ± 2.2 and 9.45 ± 0.5) was statistically faster than Group RN (11.45 ± 2.1 and 12.23 ± 1.2) respectively. The total duration of sensory and motor block was significantly more in Group RN than Group RT. The time of first rescue analgesia was significantly longer in Group RN (18.12 ± 1.2) than RT (14.32 ± 3.3). The total dose of rescue analgesia was statistically insignificant among the groups (2 *vs* 2). 5 patients in Group RT developed nausea and vomiting. ***Conclusion:*** The addition of Tramadol fastens the onset of sensory and motor blocks but the addition of Nalbuphine produces a longer duration of sensory and motor blocks with negligible complications.

Keywords: Ropivacaine; Tramadol; Nalbuphine; Brachial Plexus Block.

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Introduction

Brachial plexus block is the widely-performed nerve block for surgeries distal to shoulder. Among all approaches, the supraclavicular approach is widely used and associated with a high success rate and fewer complications. Here nerves blocked at the level of trunks. They provide adequate anesthesia and through this, we can avoid unwanted effects of anesthetic drugs

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and hemodynamic effects of laryngoscopy and intubation.[1,2] Action of local anesthetics is short-lived so there are so many additives that can increase the duration of anesthesia and decrease the need for postoperative analgesia.Clonidine, Dexmedetomidine, opioids, dexamethasone, midazolam and magnesium sulfate. Due to its easy availability, among opioids, tramadol has been widely used as an adjuvant to local anesthetics. Another opioid Nalbuphine is gaining popularity now-a-days. It is an agonist-antagonist opioid (agonist at kappa receptors and antagonist at mu-receptor). Nalbuphine has equal potency as morphine in analgesia[3] Ropivacaine has been used in brachial plexus blocks as bupivacaine provides prolonged motor blockade and has cardiovascular toxicity. There are very few studies have been done on ropivacaine.[4] As far as our knowledge there was no previous study has compared these two drugs in supraclavicular brachial plexus block. So, in this prospective study, we are comparing the effects of adding tramadol and nalbuphine to 0.5% ropivacaine on block characteristics and the requirement of postoperative analgesia.[5]

Materials and Methods

After getting institutional ethical committee approval and informed written consent from the patients, Totally of 60 ASA I and II patients in the age group of 20–50 years who were posted for elective upperlimb procedures were selected for the study. Those patients with allergic to any of the study drugs, respiratory, liver, renal diseases, coagulopathy, obese patients and infection at the local site were excluded from the study. Obviously, whoever not willing to participate and patients with failed blocks were excluded. The patients have divided into Two Groups (n = 30) *Group RT:* Receives 30 ml of 0.5% Ropivacaine with 100 mg of Tramadol – the total volume of 32 ml. *Group RN:* Receives 30 ml of 0.5% Ropivacaine with 10 mg of Nalbuphine (1 ml drug with 1 ml normal saline) – the total volume of 32 ml. Patients were divided into two groups based on a computer-generated random number table. All patients were educated about the Numerical Rating Scale for postoperative pain[11] during preoperative visits. (0 = no pain, 1–3 = mild pain, 4–6 = moderate pain and 7–10 = severe pain). All patients were given 6 hours fasting and Tablet Ranitidine 150 mg and tablet alprazolam 0.5 mg night before surgery. After arrival into OR all patients attached with standard ASA monitors (Pulse oximeter, NIBP, ECG, RR, and temperature). Baseline vitals have been documented. IV cannula of 18 G was secured on the contralateral limb and started with a lactated ringer solution at the rate of 100 ml per hour. Under strict aseptic precautions with proper painting and draping with head turned to 45-degree opposite side, supraclavicular brachial plexus block was performed with electrical nerve stimulator B BRAUN with Stimuplex 5 cm insulated 22 G needle. Landmark was 2 cm above the midclavicular point and just lateral to the scalenus anterior muscle. The set frequency was 1 Hz and the starting current was 2 mA. The needle was directed caudally and posteromedial direction, Once motor response on the forearm and hand the frequency decreases gradually to 0.5 mA. if response persists study drug was given per their group allocation after negative aspiration of blood. Drug solution preparation and performance of block were done by different anesthesiologists who were not involved in the study. The injected area was gently massaged to improve the uniform spread of the drug. After the block, the onset of the block was tested every 2 minutes until a complete block occurs or till 30 minutes. Sensory block was assessed with cold sensation method over distribution of median, radial, ulnar and musculocutaneous nerves. Onset defined as the time interval between the injection of a drug to achieve a sensory loss of Grade 2. The time interval between the injection of a drug to the requirement of the first analgesia was defined as the duration of sensory block. Motor block was assessed with the Modified Bromage Scale. Onset defined as the duration between the injection of a drug to a motor block of Grade 3. The duration of motor block was the time interval between the injection of a drug to complete motor recovery in the forearm and hand. Throughout the procedure heart rate, blood pressure was monitored and documented. Any incidents of bradycardia (HR < 60 bpm), tachycardia (HR > 100), hypotension (decrease in MAP > 20% of baseline), hypertensive episodes (increase in MAP > 20% of baseline) were documented. Other complications like nausea, vomiting, sedation, pneumothorax, hematoma, local anesthetic toxicity and respiratory depression were also documented. Sedation was assessed with a Ramsay sedation scale. Time to first rescue analgesia was time between injection of the block to the numerical rating scale of more than 4. Injection Paracetamol infusion was given at the dose of 15 mg/kg. Patients were asked for pain by using a numerical rating scale every hourly till 6 hours, 2nd hourly

till 12 hours and then every 4 hourly for the next 12 hours. The total analgesic requirement was also documented.

Statistical Analysis

Time to first rescue analgesia was taken as a primary variable to measure the sample size. Based on the pilot study over 8 patients, with ropivacaine, we found the time to first rescue analgesia was 320 minutes. It was calculated that a minimum of 26 patients needed in each group with a confidence interval of 95%, 5% alpha error and power of the study was 80%. We took a sample size of 30 in each group to avoid any loss or exclusion of patients during the study. Statistical analysis was done by using SSPS software *version* 17.0. All data were documented as mean and standard deviations. Student's *t*-test was used to analyze demographic data. Onset, duration of sensory and motor block was analyzed by using the Chi-square test. The value is considered statistically significant when the p - value is < 0.05.

Results

Table 1 shows, Patients on both RTand RN Groups were compared based on Age, Sex, Weight, ASA status and duration of surgery, ($p > 0.05$).

Table 1: Patients Characteristics (Values; Mean ± SD)

Sl. No	Characteristics	Group RT	Group RN	*p* - value
1	Age (years)	35.23 ± 4.41	37.21 ± 3.34	0.231
2	Sex (M/F)	17/13	16/14	0.062
3	Weight (Kgs)	70.01 ± 2.1	68 ± 3.4	0.143
4	ASA (I/II)	20/10	19/11	0.235
5	Duration of surgery (Mins)	92.2 ± 2.2	91.4 ± 3.3	0.324

Table 2 shows, the Onset of sensory block, motor block in Group RT (8.82 ± 2.2 and 9.45 ± 0.5) was statistically faster than Group RN (11.45 ± 2.1 and 12.23 ± 1.2). The total duration of sensory and motor block was significantly more in Group RN than Group RT. The time of first rescue analgesia was significantly longer in Group RN (18.12 ± 1.2) than RT (14.32 ± 3.3). The total dose of rescue analgesia was statistically insignificant among the groups (2 *vs* 2).

Table 2: Characteristics of the block

Sl. No	Block characteristics	Group RT	Group RN	*p* - value
1	Onset of sensory block (mins)	8.82 ± 2.2*	11.45 ± 2.1	< 0.05
2	Onset of motor block (mins)	9.45 ± 0.5*	12.23 ± 1.2	< 0.05
3	Duration of sensory block (hrs)	13.21 ± 2.1	16.31 ± 2.3*	< 0.05
4	Duration of motor block (hrs)	11.31 ± 0.3	14.32 ± 2.1*	< 0.05
5	Duration of analgesia (hrs)	14.32 ± 3.3	18.12 ± 1.2*	< 0.05
6	Time to first rescue analgesic (hrs)	15.12 ± 2.1	19.13 ± 1.3*	< 0.05
7	Total number of a dose of rescue analgesia in 24 hours	2	2	0.1342

Table 3 shows, 5 patients in RT developed nausea and vomiting. No other patients in either group developed any complications. Sedation scores were comparable to both the groups.

Table 3: Complications

Sl. No	Complications	Group RT	Group RN	*p* - value
1	Nausea	5	0	< 0.05
2	Vomiting	5	0	< 0.05
3	Sedation (3 and above)	0	0	–
4	Pneumothorax	0	0	–
5	Hematoma	0	0	–
6	Local Anesthetic Toxicity	0	0	–
7	Respiratory Depression	0	0	–
8	Bradycardia	0	0	–
9	Hypotension	0	0	–

Figs. 1 and 2, throughout the procedure, hemodynamic variables were comparable in both groups. None of the patients developed bradycardia or hypotension.

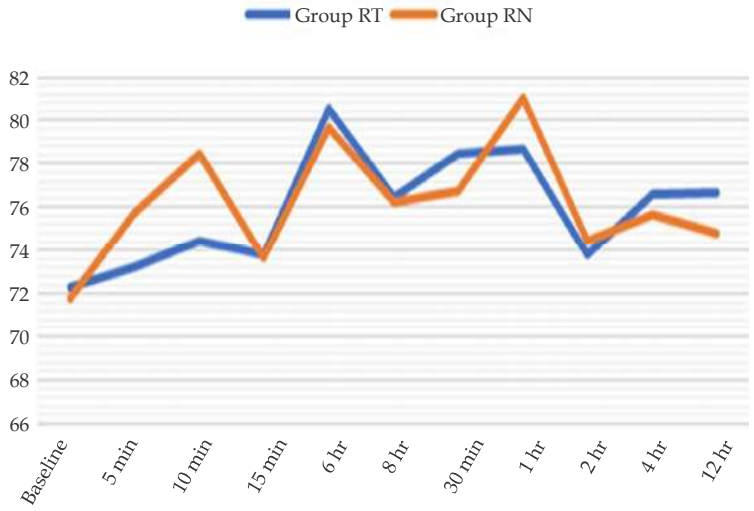

Fig. 1: Changes in mean heart rate.

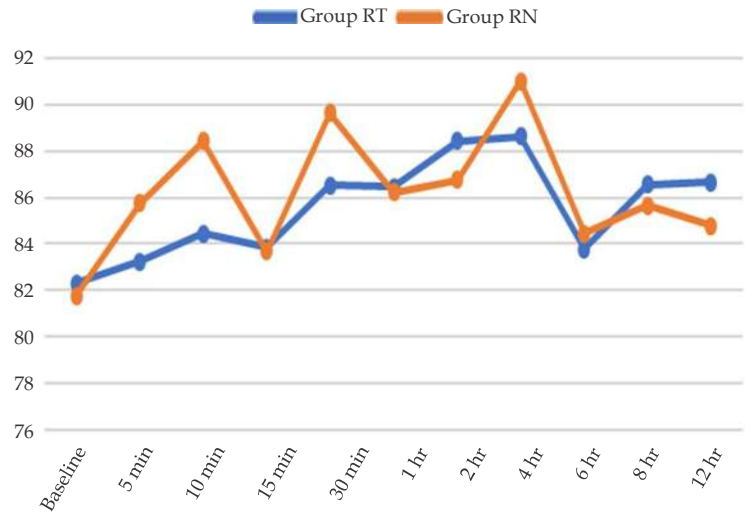

Fig. 2: Changes in mean arterial pressure.

Discussion

Supraclavicular brachial plexus block is a widely used block for upperlimb surgeries. Local anesthetics used in the brachial plexus block provide adequate analgesia and relaxation for the surgery and it also prevents the need for laryngoscopy and endotracheal intubation. Thereby reduces the stress on the patient's cardiovascular system and it reduces surgical stress. It also avoids the drug's exposure to multiple systems.[6] Only local anesthetics do not produce longer analgesia so, there are some adjuvants that can increase the duration of analgesia and quality of the plexus block. It reduces the postoperative pain and need for analgesics. In our study, we compared Inj. Tramadol and Inj. Nalbuphine with 0.5% Ropivacaine in a supraclavicular brachial block in patients posted for upper limb orthopedic surgeries. Since, there was no direct comparison of these two drugs we could not provide direct references.[7] In our study, we monitored the onset and duration of sensory and motor blocks. The total duration of analgesia, time for first rescue analgesia and the total number of doses of rescue analgesia (Inj. Paracetamol 15 mg/kg). complications if any were also noted. Percentage of Ropivacaine, Doses

of Tramadol and Nalbuphine were selected from previous studies.[8] According to our study onset of the block both sensory and motor block was significantly faster in the tramadol group than the nalbuphine group. Sensory block onset was faster than motor onset. the onset of sensory and motor block was more in the nalbuphine group[9] Das A et al. compared plain ropivacaine and ropivacaine with nalbuphine, in this study addition of nalbuphine didn't add any advantage in the onset of the block with 0.5% ropivacaine. The duration of sensory and motor block was significantly higher in the nalbuphine group than the tramadol group.[10] Krebs EE et al. compared but orphanol and tramadol with levobupivacaine, they found that 2 mg of but orphanol provides longer duration of sensory and motor block when compared to 100 mg tramadol with minimal side effects[11] Kothari D et al. found that addition of nalbuphine prolongs the duration of sensory and motor blocks when used along with 0.5% Ropivacaine except for Eledjam JJ et al. who used 0.75% instead of 0.5% which was the concentration of Ropivacaine in our study. Duration of analgesia (14.32 ± 3.3 *vs* 18.12 ± 1.2) and time for the first rescue analgesia (15.12 ± 2.1 *vs* 19.13 ± 1.3) were significantly higher with nalbuphine group than tramadol group. The total number of doses of rescue analgesia was similar in both groups. 5 patients in the Tramadol group developed nausea and vomiting which was statistically significant. There was no pneumothorax, hemothorax, local anesthetic toxicity, respiratory depression, bradycardia, hypotension and over sedation.[12,13]

Conclusion

Even though adding 100 mg Tramadol hastens the onset of supraclavicular brachial plexus block produced by 0.5% Ropivacaine, adding 10 mg of nalbuphine produces a better quality of the block and prolonged analgesia with fewer side-effects.

Financial support: Nil.

Conflicts of interest: Ethical committee clearance was given by the institution**.**

References

1. Brattwall M, Jildenstål P, Warrén Stomberg M, et al. Upper extremity nerve block: How can benefit, duration, and safety be improved? An update [*version* 1; referees: 3 approved] F1000Research2016, 5 (F1000 Faculty Rev):907
2. Neal JM, Gerancher JC, Hebl JR. Upper extremity regional anesthesia: Essentials of our current understanding. Reg Anesth Pain Med 2009;34:134–70.
3. Kalika P, Arun JM. Evaluation of clonidine as an adjuvant to brachial plexus block and its comparison with tramadol. J Anesthesiol Clin Pharmacol 2017;33:197–202.
4. Kathuria S, Gupta S, Dhawan I. Dexmedetomidine as an adjuvant to ropivacaine in supraclavicular brachial plexus block. Saudi J Anesth 2015;9:148–54.
5. Saryazdi H, Yazdani A, Sajedi P et al.) Comparative evaluation of adding different opiates (Morphine, Meperidine, Buprenorphine, or Fentanyl) to lidocaine in duration and quality of axillary brachial plexus block. Advanced Biomedical Research 2015;4:232–37.
6. Kim YJ, Lee GY, Kim DY, et al. Dexamethasone Added to Levobupivacaine Improves Postoperative Analgesia in Ultrasound-Guided Interscalene Brachial Plexus Blockade for Arthroscopic Shoulder Surgery. Korean Journal of Anesthesiology, 2012;62:130–134.
7. Jarbo K, Batra YK, Panda NB. Brachial plexus block with midazolam and bupivacaine improves analgesia. Can J Anesth 2005;52:822–26.
8. Gunduz A, Bilir A, Gulec S. Magnesium added to prilocaine prolongs the duration of axillary plexus block. Reg Anesth Pain Med 2006;31:233–36.
9. Nagpal V, Rana S, Singh J, et al. Comparative study of systemically and perineurally administered tramadol as an adjunct for supraclavicular brachial plexus block. J Anesthesiol Clin Pharmacol 2015;31:191–95.
10. Das A, Roy Basunia S, Mukherjee A, et al. Perineural nalbuphine in ambulatory upper limb surgery: A comparison of effects of levobupivacaine with and without nalbuphine as an adjuvant in supraclavicular brachial plexus block. A prospective, double-blinded, randomized controlled study. Anesth Essays Res 2017;11:40–46.
11. Krebs EE, Carey TS, Weinberger M. Accuracy of the pain numeric rating scale as a screening test in primary care. J Gen Intern Med 2007;22:1453–458.
12. Kothari D. Supraclavicular brachial plexus block: A new approach. Indian J Anesth 2003;47:287–88.
13. Eledjam JJ, Deschodt J, Viel EJ, et al. Brachial plexus block with bupivacaine: Effects of added alpha-adrenergic agonists. Comparison between clonidine and epinephrine. Can J Anesth 1991;38:870–75.

Original Research Article

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A Comparative Study of Intrathecal Clonidine with Hyperbaric Bupivacaine Administered As A Mixture and Sequentially in Cesarean Section

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Abstract

Context: Adjuvants and hyperbaric bupivacaine are mixed in a single syringe before injecting the drugs intrathecally. Their densities may be altered by mixing them in a single syringe, thus affecting their spread. Administering local anesthetic and the adjuvant separately minimizes the effect of changes in densities. *Aims:* To compare efficacy of intrathecal clonidine with hyperbaric bupivacaine administered as a mixture and sequentially and to assess the onset and duration of sensory and motor blockade and postoperative analgesia. *Settings and Design:* Group M received mixture of clonidine (75 mcg) and hyperbaric bupivacaine 0.5% (10 mg) and Group S received clonidine (75 mcg) followed by hyperbaric bupivacaine 0.5% (10 mg) through separate syringes. *Materials and Methods:* 60 full term parturients of elective cesarean section were divided into two groups based on the technique of intrathecal drug administration. *Statistical analysis used:* Quantitative data was analyzed by student's '*t*' test and qualitative data was analyzed by Chi-square test. *Results:* Duration of analgesia was significantly longer in Group S (474.33 ± 20.79 min) than in Group M (337 ± 18.22 min). The time to achieve highest sensory block and complete motor block was significantly less in Group S. *Conclusions:* When clonidine and hyperbaric bupivacaine were administered in a sequential manner, block characteristics improved significantly compared to the administration of the mixture of the two drugs.

Keywords: Bupivacaine; Clonidine; Postoperative analgesia; Spinal anesthesia.

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Introduction

Subarachanoid block is a widely used method providing a fast onset and Effective sensory and motor blockade. It has definitive advantages like profound analgesia which can be produced in a large part of the body by relatively simple injection of small amount of local anesthestic agent. Spinal anesthesia has been widely used for Cesarean Section (CS) deliveries because of greater maternal safety, fetal benefits, higher parental Satisfaction, and consumer demand.[1] Bupivacaine is the local anesthetic most commonly used. In order to extend intraoperative analgesia into postoperative period a number of spinal adjuvants like opioids are added to improve the block quality and provide postoperative

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pain relief, examples include morphine, fentanyl, diamorphine or buprenorphine.[2] Central neuraxial opioids, intrathecal as well as epidural, offer the benefit of analgesia but however, the related side-effects include sense of dizziness, nausea, vomiting, pruritus, urinary retention and even cases of respiratory depression have been reported.[3] Clonidione, a selective partial agonist for alpha-2 adrenoreceptors, is an attractive alternative to commonly used opioids, and is known to increase both sensory and motor block of LA.[4,5] Several studies have shown that clonidine also has antihyperalgesic effect and thus, reduces the postoperative analgesic requirement.[6] Commonly, adjuvants are mixed with LA in a single syringe before injecting the drugs intrathecally. Mixing of these drugs changes the density of both drugs, thus affecting their spread in the Cerebrospinal Fluid (CSF).[7] Density is known to influence the spread of LA, but the effect of adjuvant solution density on its movement in the CSF has not been studied extensively.[8,9]

Therefore, we hypothesized that if we administer LA and the adjuvants separately, it may minimize the effect of the changes in densities and their actions. We compared block characteristics, intraoperative hemodynamics and postoperative pain relief in patients undergoing CS under Subarachnoid Block (SAB), after administering Hyperbaric Bupivacaine (HB) and clonidine as a mixture in single syringe and sequentially in two syringes.

The main objectives of the study are:

1. To compare efficacy and safety of intrathecal clonidine with hyperbaric bupivacaine administered as a mixture and sequentially.
2. To assess the onset and level of blockage.
3. Duration of sensory and motor blockade and postoperative analgesia.

Materials and Methods

This clinical study was conducted on 60 ASA Grade 1 and 2 patients aged 18–40 years undergoing elective cesarean section at our institute from November 2018 to November 2019.

Patients were divided into two groups of 30 patients each.

Group M (Mixture group) patients received intrathecal mixture of 0.5% hyperbaric bupivacaine 10 mg and clonidine 75 mcg;

Group S (Sequential group) patients received intrathecal clonidine 75 mcg followed by 0.5% hyperbaric bupivacaine 10 mg.

Inclusion Criteria

1. ASA Grade 1 and 2 patients;
2. Age group of 18–40 Years.

Exclusion Criteria

1. Patients belonging to ASA Grade 3 and 4;
2. Patient's on opioids and α_2 agonist like clonidine;
3. Patients allergic to any of the drugs mentioned above;
4. Patients with other comorbidities.

Methods of Study

Preanesthetic check up was carried out preoperatively with a detailed history, general physical examination, systemic examination and laboratory investigations. Airway assessment and spinal column examination were done.

Procedure

Patient was shifted to the OT table; IV access was obtained on the forearm with 18 gauge IV cannula and lactated Ringer's solution 500 ml was infused intravenously before the block. The monitors connected to the patient included noninvasive BP, pulse oximeter and ECG. Baseline PR, BP and RR, SpO_2 were recorded. Under strict aseptic precautions, lumbar puncture was performed in left lateral or sitting position by midline approach using disposable Quince spinal needle (25 G) at L3-L4 intervertebral space, after free flow of CSF study drugs were injected according to group. Patients were monitored continuously using non invasive blood pressure, pulse oximeter and electrocardiogram. After spinal anesthesia, Oxygen (4L/min) was given by facemask. Lactated Ringer's solution (10 ml/kg/hr) was given.

Results

A total of 60 ASA Grade 1 and 2 patients aged 18–40 years posted for elective cesarean section was selected and were divided into two groups of 30 patients each:

Group M (Mixture group) patients received

intrathecal mixture of 0.5% hyperbaric bupivacaine 10 mg + clonidine 75 mcg.

Group S (Sequential Group) patients received intrathecal clonidine 75 mcg followed by 0.5% hyperbaric bupivacaine 10 mg separately.

The mean time for onset of sensory block in Group M was 126.4 ± 5.51 seconds and Group S was 120.2 ± 5.55 seconds. The onset of sensory block in Group S was faster compared to Group M and is highly significant with $p < 0.001$. The mean time for onset of motor block in Group M was 242 ± 38.92 seconds and Group S was 168 ± 40.36 seconds.

Table 1: Onset time of sensory and motor block

	Group M	Group S	*p* - value	Result
Sensory block onset	126.4 ± 5.51	120.2 ± 5.55	< 0.001	HS
Motor block onset	242 ± 38.92	168 ± 40.36	< 0.001	HS

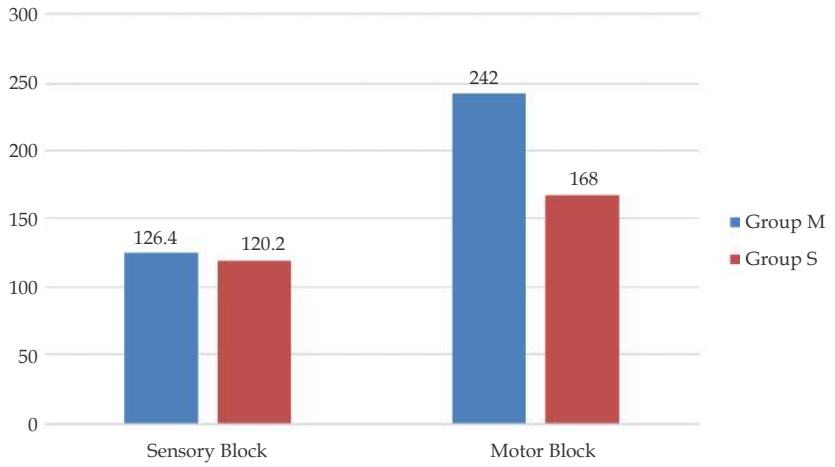

Fig. 1: Onset time of sensory and motor block.

The mean time for peak sensory block in Group M was 467.33 ± 32.92 seconds and 424.833 ± 41.26 seconds in Group S with $p < 0.001$, which was statistically highly significant.

Table 2: Time to peak sensory block

	Group M	Group S	*p* - value	Result
Peak sensory block (secs)	467.33 ± 32.92	424.83 ± 41.26	< 0.001	HS

Ten percent of patients attained T8 level blockade, 43% patients attained T6 level blockade and 47% patients attained T4 level blockade in Group M where as in Group S 3% patients attained T8 level, 33% patients attained T6 level and 63% attained T4 level blockade. Group S achieved higher level of sensory block.

Table 3: Highest level of sensory block

	Group M (*n* %)	Group S (*n* %)
T4	14 (46.67)	19 (63.33)
T6	13 (43.33)	10 (33.33)
T8	3 (10)	1 (3.33)

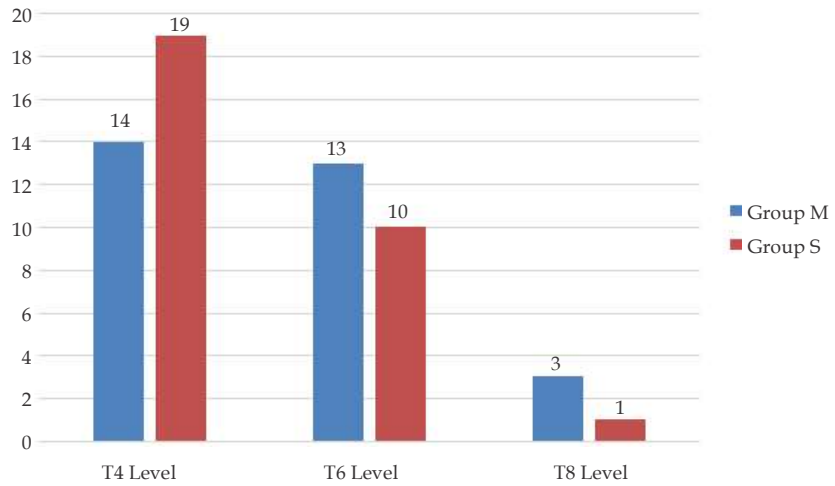

Fig. 2: Highest level of sensory block.

Mean duration of complete analgesia, effective analgesia in Group S higher than Group M which was statistically highly significant ($p < 0.001$). The time for first request for rescue analgesic postoperatively in Group M was earlier than in Group S which was statistically highly significant ($p < 0.001$).

Table 4: Duration of Analgesia

	Group M	Group S	*p* - value	Result
Duration of complete analgesia (minutes)	262.67 ± 85.14	387.67 ± 63	< 0.001	HS
Duration of effective analgesia (minutes)	371.33 ± 108.9	560.33 ± 78.32	< 0.001	HS
Time to first pain medication (minutes)	426.53 ± 94.91	604.00 ± 97.23	< 0.001	HS

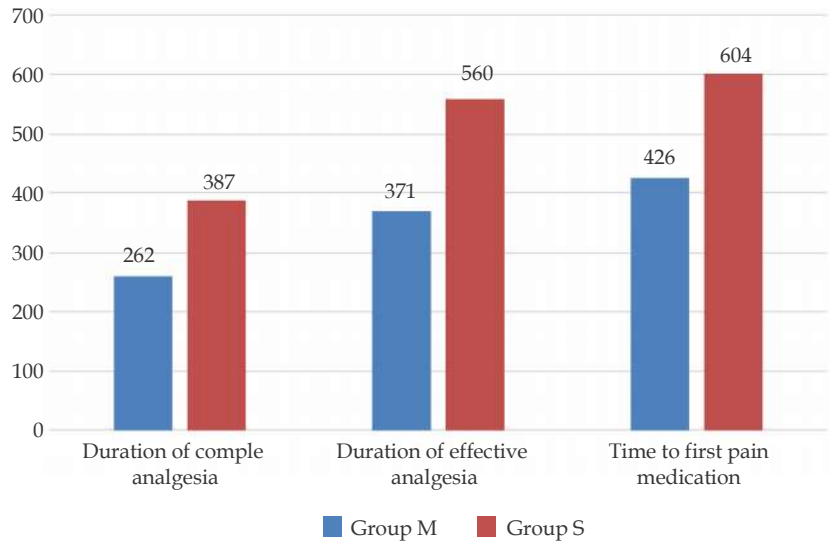

Fig. 3: Duration of analgesia

In our study, in Group M 10% patients had hypotension whereas in Group S 13.3% patients had hypotension. There was no bradycardia, mouth dryness and respiratory distress in either groups.

Table 5: Perioperative Complications

Cases	Hypotension	Vasopressor used	Bradycardia	Respiratory distress	Mouth dryness
Group M	3	1	0	0	0
Group S	4	2	0	0	0

VAS at the end of three hours was 0.7 ± 0.75 and 0.17 ± 0.38 ($p < 0.001$), at the end of six hours it was 2.9 ± 0.89 and 1.3 ± 0.3 ($p < 0.001$) and at the end of twelve hours it was 5.27 ± 0.58 and 4.2 ± 0.41 ($p < 0.001$) respectively in Group M and Group S. VAS was statistically significant at 3,6, and 12 hours in both groups but Group S had better pain relief (lower VAS) in the postoperative period than in Group M.

Table 6: Visual analog scale (VAS) score

Time (Hrs)	Group M	Group S	*p* - value	Result
3	0.7 ± 0.75	0.17 ± 0.38	0.001	HS
6	2.9 ± 0.89	1.3 ± 0.6	< 0.001	HS
12	5.27 ± 0.58	4.2 ± 0.41	< 0.001	HS

Discussion

The present study was carried out to compare efficacy and safety of intrathecal clonidine with hyperbaric bupivacaine administered as a mixture and sequentially during spinal anesthesia in patient posted for elective cesarean section. Our study design, consisted of 60 patients aged between 18 and 40 years, ASA physical status I/II were randomly divided into two groups after taking informed consent. The study has demonstrated that the sequential administration of bupivacaine with clonidine in spinal anesthesia significantly decreases the onset time, prolongs the duration of sensory, motor blockade and postoperative analgesia than in mixture group.

Onset of sensory and motor blockade

In our study, there was statistically highly significant difference with regard to onset of sensory and motor block between the groups with faster onset in Group S than Group M.

Gurudatta et al.[10], concluded that the mean time for onset of sensory blockade was faster in Group BC (Clonidine Group) compared to Group B (Bupivacaine Group) and the mean time for onset of motor blockade was also faster in BC Group compared to Group B.

Jyoti Pushkar et al.[11], in their study found rapid onset of both sensory & motor block, delayed sensory block regression & motor block resolution as well as prolonged postoperative analgesia in Sequential Group compared to Mixed Group.

Sachan et al.[12], observed that the mean onset time of sensory and motor block was similar in both groups.

Time for peak sensory level and highest sensory level blockade

In our study, the mean time to achieve peak sensory level in Group S was faster compared to Group M was (467.33 ± 32.92 seconds *vs* 424.83 ± 41.26 seconds).

In Group S, more percentage of patients attained T4 level block (63.33%) when compared to Group M (46.67%).

Desai et al.[7] in their comparative study observed that the time to reach highest level of block was less when morphine and fentanyl were administered sequentially with hyperbaric bupivacaine than given as a mixture.

In the study of Jyoti Pushkar et al.[11] the mean time to reach maximal sensory height and complete the motor block were less in Group S compared to Group M.

In the study of Sachan et al.[12] time to reach maximum sensory block height and maximum motor block was significantly less in Group B (sequential drugs) than Group M (mixed drugs).

Duration of analgesia

The duration of complete analgesia and effective analgesia was longer in Group S compared to Group M. The time for first request of rescue analgesic postoperatively was considerably prolonged in Group S by 160–175 minutes compared to Group M,

thereby, reducing the requirement of analgesics in the early postoperative period. The quality of analgesia was better as the VAS was lower in Group S than in Group M.

In the study of Jyoti Pushkar et al.[11] the mean time taken for sensory block to regress to T10 level was significantly longer in Group B (240.67 ± 18.47 min) than in Group M (153.83 ± 13.11 min). Similarly, the mean duration of analgesia lasted significantly longer in Group B (474.33 ± 20.79 min) than in Group M (337 ± 18.22 min), depicting significant prolongation of analgesic effect in the group receiving drugs in a sequential fashion.

Desai et al.[7], in their comparative study observed that dextrose in a HB solution slowed the movement of morphine molecules in the CSF, reducing the exposure of supraspinal centers to morphine. Clonidine also being hypobaric drug acting on both spinal and supraspinal receptors, might exhibit similar properties.

Dobrydnjov et al.[13] observed that the quality of intraoperative analgesia was better in Clonidine Group when compared to Bupivacaine Group.

Postoperative analgesia

In our study VAS scores were statistically significant at 3, 6, and 12 hours in both groups but Group S had better pain relief (lower VAS) in the postoperative period than Group M.

BS Sethi et al.[14] in their study found that the duration of effective analgesia was significantly prolonged with addition of clonidine (614 mins) compared to bupivacaine alone (223 mins).

No patient in the Clonidine Group required additional intraoperative analgesics compared with 17.6% in the Bupivacaine Group alone. There was improved patient comfort and reduced need for intramuscular and intravenous analgesia in the immediate postoperative period.

Side-effects

In our study, in Group M 10% patients had hypotension, where as in group S13.33% patients had hypotension. Hypotention was managed by intravenous fluids and vasopressors. There was no bradycardia, mouth dryness, urinary retention or respiratory depression in either groups. Sachan et al.[12] observed hypotension in 13% patients in Group M and 16% in Group B and none of the patients had bradycardia.

In the study of Jyoti Pushkar et al.[11] one patient in Group M & two in Group S had bradycardia. They observed hypotension in 13.24% in Group M & 16.63% in Group S. Dobrydnjov et al.[13] in their study concluded that small dose of intrathecal clonidine is not usually associated with systemic side-effects such as bradycardia, hypotension or sedation.

Conclusion

On the basis of the present clinical comparative study, we can conclude that sequential administration of clonidine 75 mcg with 0.5% hyperbaric bupivacaine 10 mg in spinal anesthesia posted for elective cesarean section decreases the onset time of sensory and motor block and prolongs the duration of analgesia with no significant postoperative complications when compared to the administration of drugs as mixture with no difference in neonatal outcome.

Key Messages: It is an old age practice to mix adjuvants with hyperbaric bupivacaine in a single syringe before injecting the drugs intrathecally but administering local anesthetic and the adjuvant separately improved block characteristics like duration of analgesia and the time to achieve highest sensory block and complete motor block significantly.

References

1. Hawkins JL, Koonin LM, Palmer SK, et al. Anesthesia-related deaths during obstetric delivery in the United States, 1979–1990. Anesthesiology 1997;86:277–84.
2. Poonam S Ghodki, Shalini P Sardesai. Evaluation of the effect of intrathecal clonidine to decrease shoulder pain in laparoscopy under spinal anesthesia. Indian J Anesth 2010;54(3)231–34.
3. Gustafsson LL, Schildt B, Jackobson K. Adverse effects of extradural and intrathecal opiates: Report of a nation-wide survey in Sweden Br J Anesth 1982;54:479–86.
4. Gecaj-Gashi A, Terziqi H, Pervorfi T, et al. Intrathecal clonidine added to small-dose bupivacaine prolongs postoperative analgesia in patients undergoing transurethral surgery. Can Urol Assoc J 2012;6:25–29.
5. Thakur A, Bhardwaj M, Kaur K, et al. Intrathecal clonidine as an adjuvant to hyperbaric bupivacaine in patients undergoing inguinal herniorrhaphy: A randomized double-blinded study. J Anesthesiol Clin Pharmacol 2013;29: 66–70.
6. Lavand'homme PM, Roelants F, Waterloos

H, et al. An evaluation of the postoperative antihyperalgesic and analgesic effects of intrathecal clonidine administered during elective cesarean delivery. Anesth Analg 2008;107: 948–55.

7. Desai S, Lim Y, Tan CH, et al. A randomized controlled trial of hyperbaric bupivacaine with opioids, injected as either a mixture or sequentially, for spinal anesthesia for cesarean section. Anesth Intensive Care 2010;38: 280–84.
8. Hocking G, Wildsmith JA. Intrathecal drug spread. Br J Anesth 2004;93: 568–78.
9. Imbelloni LE, Moreira AD, Gaspar FC, et al. Assessment of the densities of local anesthetics and their combination with adjuvants: An experimental study. Rev Bras Anestesiol 2009;59:154–65.
10. Gurudatta, G Svenkatesh et al. A Prospective randomized controlled study of the effect of intrathecal clonidine with hyperbaric bupivacaine 0.5% for lower abdominal surgeries. Karnataka Anesthesia J 2008;9:120–80.
11. Pushkar Deshpande Jyoti, S Ghodki Poonam, Sardesai Shalini. Comparative clinical study between premixed and sequential administration of intrathecal clonidine with hyperbaric bupivacaine in lower limb orthopedic surgeries. Indian Journal of Applied Research 2015 March;5(3).
12. Sachan P, Kumar N, Sharma JP. Intrathecal clonidine with hyperbaric bupivacaine administered as a mixture and sequentially in cesarean section: A randomized controlled study. Indian J Anesth 2014;58:287–92.
13. Dobrydnjov I, Axelsson K, Thorn SE. Clonidine combined with small-dose bupivacaine during spinal anesthesia for inguinal herniorrhaphy: A randomized double-blinded study. Anesth Analg 2003;96:1496–503(s).
14. Sethi BS, Samuel M, Sreevastava D. Efficacy of analgesic effects of low-dose intrathecal clonidine as adjuvant to bupivacaine. Indian J Anesth 2007;51(5): 415–19.

Original Research Article

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Efficacy of Propofol-ketamine Over Propofol-butorphanol in Surgical Procedures less than 60 Minutes

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Abstract

Context: Propofol due to its favorable pharmacokinetic profile is widely used in TIVA. Propofol, when used alone causes decrease in cardiac index and mean arterial pressure and lacks analgesic property. To overcome these disadvantages, many adjuvant drugs are added. *Aim:* To compare two drug regimens: Propofol-ketamine and propofol-butorphanol in surgical procedures less than 60 minutes. *Settings and Design:* Hospital based comparative study was carried out at Department of Anesthesiology, SVS Medical College, Mahabubnagar. *Methods:* Sixty patients aged 18–60 years of both sexes belonging to ASA I and ASA II Grades were randomly allotted to one of two groups of 30 each. Group K received ketamine 1 mg/kg and propofol 1.5 mg/kg as inducing agent and Group B received butorphanol 20 µg/kg and propofol 1.5 mg/kg. In both the groups, anesthesia was maintained with propofol 9 mg/kg/hr *via* infusion pump. Heart rate, SBP, DBP were monitored as baseline, induction and in postinduction period after 10, 20, 30, 40 minutes. Occurrence of pain on injection with propofol was noted. Postoperative sedation was assessed using Ramsay Hunt sedation score and incidence of PONV was noted in both groups. *Statistical Analysis:* The data was analyzed using *t*-test and *p* - value of < 0.05 was considered statistically significant. *Results:* In Group B, there was significant variation in heart rate, SBP and DBP at everytime interval from baseline to end of surgery whereas there was no statistically significant change in hemodynamic parameter throughout surgery in Group K. The incidence of sedation postoperatively in Group K was 36.7% whereas in group B it was 46.7%. It was found that in Group B patients 23.3% of them had pain as compared with 56.7% in Group K showing pain. There was no statistically significant difference in two groups regarding incidence of PONV. *Conclusion:* Data and their analysis suggest that combination of Propofol-ketamine, offered better hemodynamic stability over propofol-butorphanol.

Keywords: Anesthesia technique; TIVA; Hemodynamic stability; PONV; Propofol; Ketamine; Butorphanol.

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Introduction

Total Intravenous Anesthesia (TIVA) as currently practiced uses several types of drugs, each performing a specific role. There is a perceived wisdom that they should all have rapid clearance rate and little delay between change in infusion rates, plasma levels and pharmacological actions. This allows for rapid induction, good plane of surgical stage of anesthesia and at the end of surgery,

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smooth emergence and early recovery. There is growing interest in TIVA for the induction and maintenance of anesthesia, because of increasing availability of infusion pumps with the necessary features. Total intravenous anesthesia overcomes some of the disadvantages of traditional inhalation anesthesia in the following ways:[1]

1. The components of TIVA can be regulated independently as the need for each component changes during surgery. Both somatic and autonomic responses to varying degrees of surgical stimulation can be controlled.
2. Use of precision vaporizers can be avoided.
3. Operation theatres remain unpolluted by trace concentrations of nitrous oxide or volatile anesthetic agents. Although the evidence is unclear or controversial, inhalation of these gases may cause bone marrow depression, an increase incidence of miscarriages in pregnant operating room personnel and a decrease in the alertness of the anesthesiologist's.

Virtually all intravenous anesthetic agents like Thiopentone, Methohexitone, Etomidate, Buprenorphine, Morphine etc., have been tried for TIVA but they have been abandoned because of their own drawbacks.[2]

Propofol is a newer intravenous anesthetic agent, having favorable pharmacokinetic profile. It has already achieved considerable popularity for induction and maintenance of anesthesia for short-duration surgeries. Propofol is pleasant for most patients. It has a high clearance rate and rapid decline in blood concentration, making it eminently suitable for infusion. When Propofol infusion is discontinued there is rapid recovery from anaesthetic state. Ketamine which is water soluble intravenous anesthetic belongs to phencyclidine group of drugs. It is the only intravenous anesthetic which has hypnotic, analgesic and amnesic properties, and cheaper than Fentanyl and Butorphanol.[3]

Neither Propofol nor Ketamine are suitable as sole anesthetic agents. The most common adjuvant is an opioid analgesic and this is sufficient to provide complete anesthesia. Propofol produces a reduction in both cardiac index and mean arterial pressure, in contrast, Ketamine increases the same.[4]

Butorphanol, a synthetic opioid is used along with Propofol to provide analgesia. Butorphanol provides good analgesia but is associated with adverse effects like cardio depressant action, dizziness and sedation.[5]

Hence, in this study we compared two drug regimens, i.e. Propofol-Ketamine and Propofol-Butorphanol for TIVA technique in patients undergoing short surgical procedures of less than 60 minutes.

Materials and Methods

Source of Data

Sixty patients of SVS Medical College, Mahbubnagar, scheduled to undergo Elective short surgical procedures [less than 1 hour], with physical status ASAI and ASAII, in the age group 18–60 years, of both sexes were randomly selected.

The study was carried out with the approval of hospital research and ethics committee, after obtaining informed consent from patient. Those patients who required muscle relaxation and patients with anticipated difficult mask ventilation, patient with psychiatric disorders, on thyroid medication, hypertensive and with cardiac disease were not included in the study.

Study Design

Randomized, prospective, controlled study.

Inclusion criteria

1. 18–0 years of age;
2. ASA Class I and II ;
3. Patients coming for elective surgeries.

Exclusion criteria

1. Age < 18 years and > 60 years;
2. Patients with psychiatric disorders, thyroid disorders, cardiac disease, hypertension;
3. Anticipated difficult airway;
4. ASA class III and IV.

Design

The study included 60 patients randomly allocated into two groups:

Group K: 30 patients received Propofol-Ketamine combination;

Group B: 30 patients received Propofol-Butorphanol combination.

Preanesthetic evaluation included detailed history and physical examination to rule out cardiorespiratory disease and to know contraindications to drugs and techniques used.

Hemoglobin percentage, bleeding and clotting

time, HIV, HbSAg, RFT, serum electrolytes, chest *X*-ray, random blood sugars were done for each case. No special investigations were done for the study purpose.

All the patients were premedicated with injection Midazolam IV (0.01 mg/kg) 30 minutes before surgery. On arrival to the operation room an infusion line with 18-gauge cannula was started. Each patient was connected to NIBP, Pulse oximeter and ECG monitor.

Methods of collection of data

Anesthesia was induced with Propofol-Ketamine in Group K and with Propofol-Butorphanol in Group B with appropriate dosage according to body weight. Reading was collected from ECG, NIBP and pulse oximeter at regular intervals. Pain on injection with Propofol was noted while injecting Propofol, patients were continuously observed for vocal response, facial grimace, arm withdrawal or tears suggesting pain. Sedation was assessed in postoperative period using standard sedation score; Ramsay hunt sedation scoring was used. Incidence of PONV was noted.

Statistical analysis

The data was analyzed using *t*-test and *p* - value of < 0.05 was considered statistically significant.

Results

The present study was conducted on 60 patients undergoing elective short surgical procedure under TIVA belonging to American Society of Anesthesiology Grade I, Grade II physical statutes.

In this study, patients between age group of 18–60 year of both sexes were included.

Table 1 shows, age distribution in study groups. The mean age of the patients in two groups was similar at 39.833 years and 39.333 years and the difference was statistically not found to be significant.

Table 1: Age distribution in study groups

Group	Number	Mean	Standard deviation	*p* - value
Group K	30	39.833	10.75	0.1257
Group B	30	39.333	10.67	

Table 2 shows, sex Distribution in study groups. In Ketamine Group, out of 30 patients, 14 (46.7%) were females and 16 (53.3%) were male patients. In Butorphanol Group, out of 30 patients 15 (50%) were female and 15 (50%) were male patients. There was no statistically significant difference between the 2 groups.

Table 2: Sex Distribution in study groups

Sex	Group K	Group B	Total	Chi-square	*p* - value
Female	14 (46.7%)	15 (50%)	29 (48.3%)		
Male	16 (53.3%)	15 (50%)	31 (51.7%)		

Table 3 shows, intergroup comparison of changes in Systolic Blood Pressure (SBP) Period. The basal SBP in Ketamine group was 132.814.29 mm of Hg and in Butorphanol group was 135.67 13.30 mm of Hg. Both the groups were comparable statistically. On arrival, SBP in Ketamine group was 134.2014.41 mm of Hg and in Butorphanol group was 140.4711.78 mm of Hg. Both the groups were comparable statistically. SBP at induction in Ketamine group was 135.9313.58 and in Butorphanol group was 119.8713.85 mm of Hg. The difference in SBP in 2 groups was statistically highly significant with *p* - value of 0.0001. SBP at 10 minutes in Ketamine group was 133.6311.96 mm of Hg and in Butorphanol group it was 115.9023.58 mm of Hg. The difference in SBP in 2 groups was statistically highly significant. SBP at 20 minutes in Ketamine group was 135.0712.41 mm of Hg and in Butorphanol group was 122.9011.28 of mm of Hg. The difference in SBP in 2 groups was statistically highly significant. SBP at 30 minutes in Ketamine group was 133.4511.98 and in Butorphanol group was127.7617.17. The difference in SBP in 2 groups was statistically highly significant (*p* - 0.0005). SBP at 40 min in Ketamine group was 133.0011.14 mmof Hg and in Butorphanol group was 126.6014.35 mm of Hg. The difference in SBP in 2 groups was statistically highly significant.

Table 3: Intergroup comparison of changes in Systolic Blood Pressure (SBP) Period

Period	Group	N	Minimum	Maximum	Mean	SD	T value	*p* - value
Baseline	K	30	110	160	132.8	14.29	0.804	0.425
	B	30	110	158	135.7	13.31		
Arrival	K	30	110	160	134.2	14.41	1.843	0.07
	B	30	110	160	140.47	11.78		
Induction	K	30	100	168	135.9	13.58	4.536	0.0001
	B	30	100	142	119.87	13.85		
10 min	K	30	110	156	133.63	11.96	3.673	0.0001
	B	30	11	140	115.9	23.58		
20 min	K	30	110	154	135.07	12.41	3.943	0.0001
	B	29	106	140	122.9	11.28		
30 min	K	29	110	156	133.45	11.98	2.855	0.005
	B	25	70	156	127.76	17.17		
40 min	K	22	116	150	133.00	11.14	1.603	0.113
	B	20	106	150	126.6	14.35		

Table 4 shows, intergroup comparison of changes in Diastolic Blood Pressure (DBP). The baseline DBP in Ketamine group was 82.27.09 and in Butorphanol group was 80.575.894. Both the groups were comparable statistically. DBP on arrival in Ketamine group was 81.476.66 mm of Hg and in Butorphanol group was 82.536.146 mm of Hg. Both the groups were comparable statistically. On induction DBP in Ketamine group was 80.676.97 mm of Hg and in Butorphanol group was 68.937.31 mm of Hg. The difference was statistically significant. DBP at 10 minutes in Ketamine group was 78.935.21 and in Butorphanol group was 69.305.82 mm of Hg. The difference in DBP was statistically highly significant. DBP at 20 min in Ketamine group was 80.136.84 and in Butorphanol group was 71.525.44 mm of Hg. The difference in 2 groups was significant statistically. DBP at 30 min in Ketamine group was 78.146.04 mm of Hg and in Butorphanol was 74.2412.52 mm of Hg. The difference was not significant statistically. DBP at 40 min interval in Ketamine group was 77.645.33 and in Butorphanol group was 73.96.09 and it was statistically significant.

Table 4: Intergroup comparison of changes in Diastolic Blood Pressure (DBP)

Period	Group	N	Minimum	Maximum	Mean	SD	*t*-value	*p* - value
Baseline	K	30	70	94	82.2	7.09	0.97	0.33
	B	30	70	96	80.57	5.89		
Arrival	K	30	70	94	81.47	6.66	0.645	0.522
	B	30	70	96	82.53	6.14		
Induction	K	30	68	96	80.67	6.97	6.361	0.0001
	B	30	60	86	68.93	7.31		
10 min	K	30	70	90	78.93	5.21	6.78	0.0001
	B	30	60	80	69.3	5.82		
20 min	K	30	68	102	80.13	6.84	5.36	0.0001
	B	29	64	80	71.52	5.44		
30 min	K	29	68	90	78.14	6.04	1.42	0.143
	B	25	64	130	74.24	12.52		
40 min	K	22	70	90	77.64	5.33	2.215	0.031
	B	20	66	92	73.60	6.09		

Table 5 shows, intergroup comparison of HR at various time intervals. Base line heart rate in Ketamine group was 76.73 4.94 and in Butorphanol group was 74.204.96, both the groups were comparable statistically. On arrival in Ketamine group the mean heart rate was 77.804.85 and in Butorphanol group it was 79.007.62. Both the groups were comparable statistically. Mean heart rate at

induction in Ketamine group was 78.134.72 and in Butorphanol group, it was 73.008.12, the differences were significant statistically. At 10 min the mean heart rate was 77.474.81 in Ketamine group and it was 70.836.59 in Butorphanol group. Difference in both the groups was statistically significant. The mean heart rate at 20 minutes in Ketamine group was 78.807.25 and in Butorphanol group was 71.074.64; there was a significant difference when compared. At 30 minutes, the mean heart rate in Ketamine group was 78.835.91 and in Butorphanol group was 69.683.94. The difference was statistically significant. At 40 minutes, the mean heart rate in Ketamine group was 81.138.13 and in Butorphanol group was 70.405.21 this difference was highly significant.

Table 5: Intergroup comparison of HR at various time intervals

Period	Group	N	Minimum	Maximum	Mean	SD	*t*-value	*p* - value
Baseline	K	30	70	86	76.73	4.94	1.72	0.62
	B	30	64	86	74.2	4.96		
Arrival	K	30	70	88	77.8	4.82	0.727	0.47
	B	30	66	94	79.0	7.62		
Induction	K	30	70	88	78.13	4.72	2.991	0.004
	B	30	60	92	73.0	8.12		
10 min	K	30	70	86	77.47	4.81	4.452	0.0001
	B	30	60	84	70.83	6.59		
20 min	K	30	70	100	78.8	7.25	4.858	0.0001
	B	29	60	78	71.07	4.64		
30 min	K	29	68	90	78.83	5.91	4.452	0.0001
	B	64	62	78	69.68	3.94		
40 min	K	22	68	96	81.13	8.13	5.061	0.0001
	B	20	60	84	70.4	5.215		

Table 6 shows, comparison of Pain on injection with Propofol. In Group K, out of 30 subjects studied, 17 patients experienced pain on injection with Propofol (56.7%). In Group B, out of 30 subjects studied, 7 patients experienced pain on injection with Propofol (23.3%). There was a statistically significant difference between the two groups.

Table 6: Comparison of Pain on injection with Propofol

Pain on injection	Group K		Group B		Total	
	Number	%	Number	%	Number	%
Absent	13	43.3	23	76.7	36	60
Present	17	56.7	7	23.3	24	40
Total	30	100.0	30	100.0	60	100

p = 0.008, HS

Table 7 shows, comparison of Postoperative sedation. In Group K, out of 30 patients studied, 11 (36.7%) had postoperative sedation, whereas in Group B 17 (56.7%) had postoperative sedation. Though there was no statistically significant difference on comparison among 2 groups, it can be clearly inferred that prevalence of sedation was high in Group B.

Table 7: Comparison of Postoperative sedation

Postoperative sedation	Group K		Group B		Total	
	Number	%	Number	%	Number	%
Absent	19	63.3	13	43.3	32	53.3
Present	11	36.7	17	56.7	28	46.7
Total	30	100.0	30	100.0	60	100.0

p = 0.121, NS

Table 8 shows, incidence of postoperative nausea and vomiting. In Group K, out of 30 subjects studied, 6 subjects complained of PONV in postoperative period (20%). In Group B, 8 subjects complained of PONV (26.7%). The two groups (23.3%) when compared, the incidence of PONV was not significant statistically.

Table 8: Incidence of Postoperative nausea and vomiting

Postoperative nausea and vomiting	Group K		Group B		Total	
	Number	%	Number	%	Number	%
Absent	24	80	22	73.3	46	76.7
Present	6	20	8	26.7	14	23.3
Total	30	100	30	100	60	100

$p = 0.542$, NS

Discussion

Total intravenous anesthesia has been a subject of interest for all anesthesiologists, as this is now well-established as an appropriate alternative to the traditional approach of volatile anesthetics alone; indeed sometimes it is the preferred alternative.

The availability of drugs with short blood-brain equilibration times enables the clinician to use intravenous anesthetics and analgesics where controllability is easy and rapid. The advent of continuous infusion system has made administering TIVA all the more popular and convenient. But, even today, we are still without any one intravenous drug that can alone provide all the requirements of anesthesia (i.e. unconsciousness, analgesia and muscle relaxation). Hence, there is need to administer several different agents to produce the desired results. This in turn leads to important and significant drug interactions.[6]

We studied two drug regimens; Propofol-Ketamine, (Group K) and Propofol-Butorphanol, (Group B) for TIVA technique. In the present study, with Group K, there was no statistically significant change in heart rate, systolic blood pressure and diastolic blood pressure during postinduction and maintenance of anesthesia throughout the procedure when compared to Group B.

A similar study was done by Dunnihoo M et al.[7] using Propofol-Ketamine on cardiovascular response and wake up time. They showed that this combination maintained better hemodynamic stability and there was no significant change in heart rate and arterial blood pressure throughout the procedure.

In another study conducted by Furuya A et al.[8] investigated for arterial pressure changes during the induction of anesthesia with Propofol by adding intravenous Ketamine in 12 patients. Authors concluded that administration of Ketamine before induction with Propofol preserved hemodynamic stability in terms of blood pressure and heart rate compared with induction with Propofol alone.

The advantages of Ketamine in terms of better hemodynamically intraoperatively, when combined with Propofol have been studied by numeros investigators. Hernandez C et al.[9] compared three techniques for intravenous anesthesia (Propofol-Ketamine and Propofol-Fentanyl). They found that Propofol-Ketamine are most stable hemodynamically.

In the present study in Group B, basal, postinduction and intraoperative hemodynamic variables like heart rate, systolic blood pressure and diastolic blood pressure were monitored. We found that there was statistically significant decrease in heart rate after induction and during maintenance phase of anesthesia. A significant decrease in systolic blood pressure and diastolic blood pressure were also observed after induction and during maintenance of anesthesia with Propofol-Butorphanol.

A study was conducted by Mayer M et al.[10] where they compared the hemodynamic and analgesic effects of Propofol-Ketamine with Propofol-Fentanyl an opioid similar to Butorphanol. They found that distinct decrease in mean arterial blood pressure and heart rate after induction and maintenance of anesthesia with Propofol-Fentanyl were seen. Saha K et al.[11] conducted a randomized double-blind study to evaluate the efficiency of combination of Propofol-Ketamine and Propofol-Fentanyl in 60 patients undergoing minor surgery. They showed that significant decrease in heart rate after induction and maintenance of anesthesia with Propofol and Fentanyl. A significant decrease in systolic blood pressure was also observed.

Propofol, a modern intravenous hypnotic, produces a reduction in both cardiac index (CI) and Mean Arterial Pressure (MAP). Ketamine, a potent analgesic in contrast causes an increase in mean arterial blood pressure and cardiac index. The aim of present study was to investigate whether the combination of Propofol-Ketamine or Propofol-Butorphanol can give better hemodynamic stability during induction and maintenance of anesthesia. The present study concluded that, the single-dose of Ketamine during induction of anesthesia was enough to neutralize the cardio-depressant effect of Propofol. During the maintenance of anesthesia, there was better hemodynamic stability in Ketamine group than in Butorphanol group. Butorphanol intensified the fall in arterial blood pressure after Propofol induction and patients in this group were more sedated.

A difference in incidence of sedation in two groups was noted. In Ketamine group, the incidence was 36.7% where as in Butorphanol group, the incidence was 56.7%.

A study, conducted by Rosendo MF et al.[12] showed the effect of Ketamine and Propofol in terms of respiration, postoperative mood, perception and cognition. They concluded that, a mixture of Propofol and Ketamine provided hemodynamic stability during anesthesia and produced a positive mood state during recovery period without side-effect. The combination also appeared to prompt early recovery of cognitive function. This may be due to the fact that Propofol inhibits NMDA receptors in Hippocampus neurons, which may have contributed to the positive effect on mood. Sedative effects of Propofol are partially antagonized by arousal effect of Ketamine.[13]

Pain on injection with Propofol is attenuated by various methods like injection of Propofol in carrier fluid, large vein, and use of antiemetics, analgesics and anesthetic drugs.

Of the 2 groups studied, Butorphanol group enabled to abolish the pain on injection with Propofol. Incidence of pain was 23.3% in group B, where as in Ketamine group it was 56.7%. This is consistent with study done by Agarwal A et al.[14] where they found that effective method of attenuating Propofol induced pain is with pretreatment by Butorphanol.

One major disadvantage of TIVA is PONV, which is the rate limiting factor in patient discharged from postoperative ward. In the present study, the incidence of PONV in Group K was 20.0% where as in Group B it was 23.3%. The difference between the 2 groups was statistically insignificant.

Conclusion

The present study is conducted to evaluate and compare two drug regimens; i.e. Propofol-Ketamine and Propofol-Butorphanol for TIVA technique in patients undergoing short surgical procedures. Propofol-Ketamine (Group K) combination has the advantage of offering better hemodynamic stability and postoperative recovery in terms of sedation when compared to Propofol-Butorphanol combination. Attenuation of pain on injection was the only advantage with the Propofol–Butorphanol (Group B) combination. Incidence of PONV is similar in both the groups.

Key Messages: Combination of Propofol-ketamine can be used for total intravenous anesthesia in short surgical procedures of duration of less than 60 minutes.

Support: Nil

Conflicts of interest: Nil

References

1. Robert FJ. Total intravenous anesthesia. Anesthesiology 1996;84:149–51.
2. Sandin R, Nordstrom O. Awareness during total intravenous anesthesia. Br J Anesth 1993;71:782–87.
3. Vasanth S, Radhakrishnan A, Keshavan VH. Effect site concentration of propofol at induction and recovery of anesthesia: A correlative dose-response study. Indian J Anesth 2018;62:54–60.
4. Scheepstra GL, Booij LH, Rutten CL, et al. Propofol for induction and maintenance of anesthesia: Comparison between younger and older patients. Br J Anesth 1989:62: 54–60.
5. Cheng KI, Chu KS, Fang YR, et al. Total intravenous anesthesia using Propofol and Ketamine for ambulatory gynecologic laparoscopy. Kaohsiungc J Med Sci 1999;15(9):536–41.
6. Michel Foehn ER. Adult and pediatric anesthesia/ sedation for gastrointestinal procedures outside of the operating room. Curr Opin Anesth 2015;28(4):469–77.
7. Dunnihoo M, Wuest A, Meyer M, et al. The effects of total intravenous anesthesia using propofol, ketamine, and vecuronium on cardiovascular response and wake up time. Am Assoc Nurse Anesthetists J 1994;62(3):261–63.

8. Furuya A, Matsukawa T, Ozaki M, et al. Intravenous ketamine attenuates arterial pressure changes during the induction of anesthesia with propofol. Eur J Anesthesiol 2001;18(2):88–92.
9. Hernandez C, Parramon F, Garcia-Velasco P, et al. Comparative study of 3 techniques for total intravenous anesthesia: Midazolam-ketamine, propofol-ketamine, and propofol-fentanyl. Rev Esp Anestesiol Reanim 1999;46:154–58.
10. Mayer M, Ochmann O, Doenicke A, et al. The effect of Propofol-Ketamine anesthesia on hemodynamics and analgesia in comparison with Propofol-Fentanyl]. [Article in German]. Anesthesist 1990;39(12):609–619.
11. Saha K, Saigopal M, Sundar R. Comparative evaluation of propofol ketamine and propofol fentanyl in minor surgery. Indian J Anesth 2001;45:100–103.
12. Rosendo MF, Laura CD, Merritt TM, et al. The effects of small-dose ketamine on propofol sedation: Respiration, postoperative mood, perception, cognition and pain. Anesth Analg 2001;92(6):1465–469.
13. Kaur J. Dose sparing of induction dose of Propofol by Fentanyl and Butorphanol: A comparison based on entropy analysis. Saudi J Anesth 2013;7:128–33.
14. Agarwal A, Raza M, Dhiraaj S, et al. Pain during injection of propofol: The effect of prior administration of butorphanol. Anesth Analg 2004;99(1):117–19.

Original Research Article

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Comparison of Conventional Dose *versus* Low-dose Infusion of Dexmedetomidine on Hemodynamic Stress Response: A Prospective Institutional Based Study

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Abstract

Background: Laparoscopic cholecystectomy is one of the most common practiced surgeries for gall bladder disease. Dexmedetomidine is a α2 agonist with sedative, sympatholytic and analgesic properties and hence, it can be a very useful adjuvant in anaesthesia as stress response buster, sedative and analgesic. *Materials and Methods:* The present study was conducted on 90 patients with American Society of Anesthesiologists physical status I to III scheduled for laparoscopic cholecystectomy of both genders. Patients were divided into 3 Group. Group I (Control) patients received normal saline 0.9% infusion, Group II patients received dexmedetomidine infusion 1 mcg/kg/h and Group III patients received dexmedetomidine infusion 0.4 mcg/kg/h. parameters such as duration of anesthesia, duration of surgery, change in heart rate, MAP etc. was compared in both groups. *Results:* ASA I was 25 in Group I, 26 in Group II and 23 in Group III, ASA Grade II was 5 in Group I, 4 in Group II and 7 in Group III. The difference was nonsignificant ($p > 0.05$). Mean duration of anesthesia in Group I was 92.1 minute, in Group II was 98.4 minutes and in Group III was 85.2 minutes, mean duration of surgery in Group I was 77.4 minutes, in Group II was 92.3 minutes and in Group III was 75.1 minutes. The difference was nonsignificant ($p > 0.05$). The mean PR (beats/min) before starting in Group I was 88.3, in Group II was 91.4 and in Group III was 90.3. After 15 minutes was 87.2 in Group I, 82.3 in Group II and 80.4 in Group III. 1 minute after induction was 87.3, 82.5 and 80.6 in groups. MAP before staring was 99.3 mm Hg, 99.2 and 101.4 mm Hg in all groups, after 15 minutes was 98.4, 95.2 and 98.9 in all groups, 1 minute after induction was 98.2, 89.5 and 89.9 in all groups respectively. The difference was nonsignificant ($p > 0.05$). *Conclusion:* Low dose dexmedetomidine infusion in the dose of 0.4 mcg/kg/h effectively attenuates haemodynamic stress response without any adverse events.

Keywords: Dexmedetomidine; Stress Response; Laparoscopic Cholecystectomy.

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Introduction

Laparoscopic cholecystectomy (LC) is most commonly performed procedure for gall bladder disease, it requires small limited incisions, very short hospital stay, faster recovery times; less health care costs which further reduces the hospital stay.1 LC is also associated with stress response induced by surgery; laryngoscopy, tracheal intubation and extubation involve sympathetic stimulation. The

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pneumoperitoneum (PP) and CO_2 insufflation, required in laparoscopic surgeries, lead to increase in plasma nor- epinephrine, epinephrine levels and plasma renin activity.[2] All these changes lead to increase in heart rate, blood pressure, systemic and pulmonary vascular resistance.[1]

Many drugs, namely, alpha-2 adrenergic receptors agonists, high-doses of opioids, and β-blockers have been tried in the past to decrease stress responses during laparoscopic surgery. By reducing the sympathoadrenal and cardiovascular responses caused by noxious surgical stimuli, the alpha-2 agonists inhibit the stress responses mediated by the sympathetic nervous system. Alpha-2 adrenoceptors› activation results in sympatholysis, inhibition of renin release, and decrease in insulin release from the pancreas.[3]

Dexmedetomidine, introduced in 1999 for human use, is a selective α_2 agonist with 8 times more affinity for α_2 adrenergic receptors compared to clonidine and possesses all the properties of α_2 agonist without respiratory depression.[3] Intravenous use of dexmedetomidine in the perioperative period had been found to decrease serum catecholamine levels by 90%, to blunt the hemodynamic response to laryngoscopy, tracheal intubation, pneumoperitoneum and extubation, to provide sedation without respiratory depression and to decrease postoperative analgesic requirements. Dexmedetomidine is a selective and potent α_2-adrenergic agonist. The α_2/α_1 selectivity of dexmedetomidine is 1600 times higher than that of clonidine.[4]

The present study was conducted to compare conventional dose *versus* low-dose infusion of dexmedetomidine on hemodynamic stress response.

Materials and Methods

The present study was conducted in the department of General Surgery and Anesthesiology, Indira Gandhi Madical College and Hospital. Shimla, HP. It comprized of 90 patients with American Society of Anesthesiologists physical status I to III scheduled for laparoscopic cholecystectomy of both genders. All patients were informed regarding the study and written consent was obtained.

Patient information such as name, age, gender etc. was recorded. Patients were divided into 3 group. Group I (Control) patients received normal saline 0.9% infusion, Group II patients received dexmedetomidine infusion 1 mcg/kg/h and Group III patients received dexmedetomidine infusion 0.4 mcg/kg/h. parameters such as duration of anesthesia, duration of surgery, change in heart rate, MAP etc. was compared among the groups. Results thus obtained were subjected to statistical analysis. p - value less than 0.05 was considered significant.

Results

Table 1 shows, that Group I (Control) patients received normal saline 0.9% infusion, Group II patients received dexmedetomidine infusion 1 mcg/kg/h and Group III patients received dexmedetomidine infusion 0.4 mcg/kg/h.

Table 1: Distribution of patients

Groups	Group I	Group II	Group III
Agent	Normal saline 0.9%	Dexmedetomidine infusion 1 mcg/kg/h	Dexmedetomidine infusion 0.4 mcg/kg/h
Number	30	30	30

Table 2 shows, that ASA I was 25 in Group I, 26 in Group II and 23 in Group III, ASA Grade II was 5 in Group I, 4 in Group II and 7 in Group III. The difference was nonsignificant ($p > 0.05$). Mean duration of anesthesia in Group I was 92.1 minute, in Group II was 98.4 minutes and in Group III was 85.2 minutes, mean duration of

Table 2: Comparison of parameters

Parameters	Group I	Group II	Group III	*p* - value
ASA I	25.0	26.0	23	0.12
ASA II	5.0	4.0	7.0	0.06
Duration of anes (min)	92.1	98.4	85.2	0.09
Duration of surg (min)	77.4	92.3	75.1	0.08

surgery in Group I was 77.4 minutes, in Group II was 92.3 minutes and in Group III was 75.1 minutes. The difference was nonsignificant ($p > 0.05$).

Table 3 and Fig. 1 shows, that mean PA (beats/min) before starting in Group I was 88.3, in Group II was 91.4 and in Group III was 90.3. After 15 minutes was 87.2 in Group I, 82.3 in Group II and 80.4 in Group III. 1 minute after induction was 87.3, 82.5 and 80.6 in Groups. MAP before staring was 99.3 mm Hg, 99.2 and 101.4 mm Hg in all groups, after 15 minutes was 98.4, 95.2 and 98.9 in all groups, 1 minute after induction was 98.2, 89.5 and 89.9 in all groups respectively. The difference was nonsignificant ($p > 0.05$).

Table 3: Changes in PR and MAP in groups

Parameters	Group I	Group II	Group III	*p* - value
PR before starting	88.3±3.56	91.4±4.32	90.3±5.32	0.1
After 15 minutes	87.2±2.34	82.3±3.42	80.4±4.68	0.71
1 minute after induction	87.3±3.45	82.5±4.98	80.6±2.43	0.62
10 minutes after insufflation	85.54±2.53	85.0±4.65	79.01±4.67	0.76
30 minutes after insufflation	89.02±4.32	86.05±9.34	85.87±4.89	0.43
5 minutes after desufflation	80.35±4.34	76.23±4.56	75.34±4.89	0.67
MAP before starting	99.3±6.54	99.2±4.78	101.4±9.54	0.14
After 15 minutes	98.4±3.56	95.2±6.54	98.9±7.3	0.87
1 minute after induction	98.2±8.54	89.5±8.54	89.9±3.2	0.58
10 minutes after insufflation	100.1±5.56	92.43±4.34	88.43±3.56	0.36
30 minutes after insufflation	90.34±6.78	96.87±6.45	93.87±3.23	0.37
5 minutes after desufflation	85.43±4.32	82.98±5.45	79.45±7.34	0.56

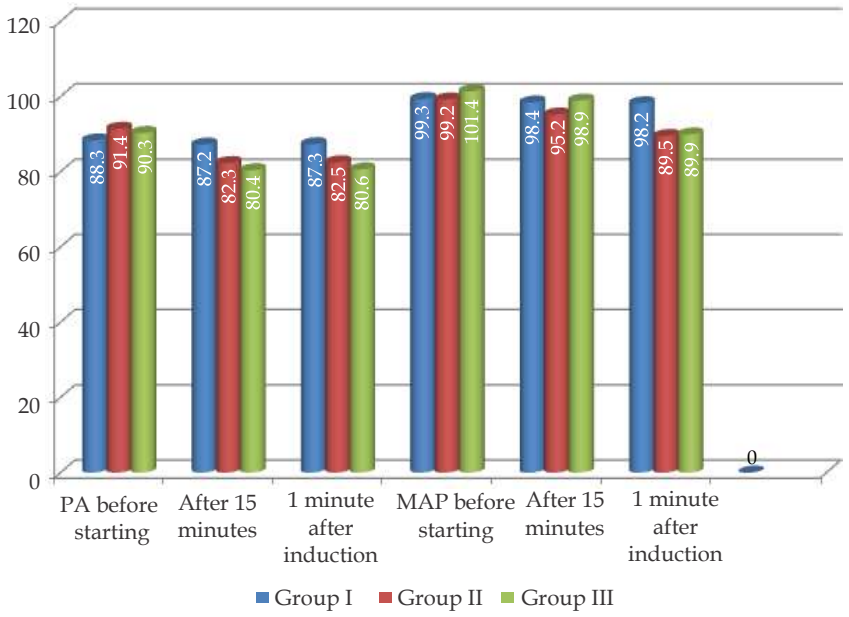

Fig 1: Changes in PR and MAP in groups

Discussion

There has been limited research on evaluating the stress responses during laparoscopic cholecystectomy. There have been evidences that prolonged laparoscopic procedures have been found to be associated with increased stress responses. Dexmedetomidine decreases renin release thereby imparting hemodynamic stability. Cortisol levels have been shown to be decreased by dexmedetomidine.[5]

Perioperative period is a stressful period, and dexmedetomidine is a useful drug to decrease stress responses.[6] Dexmedetomidine has been used by previous researchers as loading dose of 1 mcg/kg over 10 min, followed by maintenance infusion at 0.2–0.7 mcg/kg/h. Our study involves the use of dexmedetomidine in two different doses among

two groups - 1 mcg/kg over 10 min, followed by maintenance infusion at 1 mcg/kg/h or other one being 1 mcg/kg as loading dose followed by maintenance infusion of 0.4 mcg/kg/h. Renal functions in the form of serum creatinine, BUN, and urine output were within normal range in our set of patients.[7] Metabolites of dexmedetomidine biotransformation are excreted in the urine (about 95%). The pharmacokinetics of dexmedetomidine in participants with severe renal impairment (creatinine clearance < 30 ml/min) is not altered relative to healthy controls. Intraoperative use of dexmedetomidine infusion has showed insignificant difference with renal functions on percutaneous nephrolithotomy.[8] The present study was conducted to compare conventional dose *versus* low-dose infusion of dexmedetomidine on hemodynamic stress response.

However, with higher dose infusion of dexmedetomidine, high incidence of adverse cardiac effects have been observed.[9] A biphasic response on blood pressure occurs with a bolus dose.[10] Initially, there occurs hypertension followed by fall in blood pressure. This response is seen often more in young and healthy patients.[9] Stimulation of α2 B receptors in vascular smooth muscles is said to be responsible for this. Low dose infusion of 0.25-0.5 mcg/kg/h results in a monophasic response of 10-15% fall in mean arterial blood pressure and PR.[10] Apart from providing stress response attenuation, the added effects of dexmedetomidine are sedation and analgesia. Sedation produced by α2 agonists is unique in the sense that the patients can be easily aroused to co-operate during procedures and also respond to the verbal commands and then can return to sleep like state when not stimulated.[9]

Manne et al.[11] found that in group NS significant haemodynamic stress response was seen following laryngoscopy, tracheal intubation, creation of pneumoperitoneum and extubation. In dexmedetomidine groups, the haemodynamic response was significantly attenuated. The results, however, were statistically better in Dex 0.4 group compared with Dex 0.2 group. Post-operative 24 hour analgesic requirements were much less in dexmedetomidine groups. No significant side effects were noted.

Conclusion

Low dose dexmedetomidine infusion in the dose of 0.4 mcg/kg/h effectively attenuates haemodynamic stress response without any adverse events.

References

1. Black TE. Anaesthesia for Laparoscopic assisted surgery. In: Wylie Churchill- Davidson's A Practice of Anaesthesia; Healy TEJ, Knight PR (eds). 7thedition, 2003.p.1391-96.
2. Isik B, Arslan M, Özsoylar O, Akçabay M. The effects of α2:α1 adrenergic receptor agonist dexmedetomidine on hemodynamic response in direct laryngoscopy. Open Otorhinolaryngol J., 2007;1:5-11.
3. Hayden P, Cowman S. Anesthesia for laparoscopic surgery. Contin Educ Anesth Crit Care Pain 2011;11:177–80.
4. Bajwa S, Kulshrestha A. Dexmedetomidine: An adjuvant making large inroads into clinical practice. Ann Med Health Sci Res 2013;3:475–83.
5. Sekhon V, Menon P, Arora S, et al. Nephrectomy in children: Comparison of stress response to laparoscopic and open methods. J Indian Assoc Pediatr Surg 2013;18:53–57.
6. Matsumoto ED, Margulis V, Tunc L, et al. Cytokine response to surgical stress: Comparison of pure laparoscopic, handassisted laparoscopic, and open nephrectomy. J Endourol 2005;19:1140–145.
7. Panchgar V, Shetti AN, Sunitha HB, et al. The effectiveness of intravenous dexmedetomidine on perioperative hemodynamics, analgesic requirement, and side-effects profile in patients undergoing laparoscopic surgery under general anesthesia. Anesth Essays Res 2017;11:72-77.
8. Selimuzzaman S, Begum N, Islam N, et al. Effects of surgical stress on serum cortisol level: A comparative study between elective and emergency surgery. J Bangladesh Soc Physiol 2007;2:28-33.
9. Tufanogullari B, White PF, Peixoto MP, Kianpour D, Lacour T, Griffin J, et al. Dexmedetomidine infusion during laparoscopic bariatric surgery: The effect on recovery outcome variables. Anesth Analg2008;106:1741-8.
10. Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology 1992;77:1134-42.
11. Manne GR, Upadhyay MR, Swadia V. Effects of low-dose dexmedetomidine infusion on hemodynamic. Indian j anaesth 2014 Nov-Dec; 58(6):726–31.

Original Research Article

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A Comparative Study of Efficacy of Dexmedetomidine and Fentanyl As an Adjuvant to Inrathecal Bupivacaine for Lower Limb and Lower Abdominal Surgeries

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Abstract

Background: Many adjuvants have been tried to improve the duration of spinal anesthesia and quality of analgesia both intraoperatively and postoperatively to overcome the disadvantages of spinal anesthesia. *Aims:* The aim of this study was to evaluate the onset and duration of sensory and motor block, hemodynamic effect, postoperative analgesia and adverse effects of dexmeditomedine or fentanyl given with hyperbaric bupivacaine for spinal anesthesia. *Materials and Methods:* 120 patients were divided into two groups of sixty each undergoing lower limb and lower abdominal surgeries with ASA Grade 1 and 2. Patients were randomly allocated to receive either *Group BD*: 0.5% Hyperbaric Bupivacaine 15 mg + 5 μg Dexmedetomidine; *Group BF*: 0.5% Hyperbaric Bupivacaine 15 mg + 25 μg Fentanyl intrathecally. *Results:* Patients in dexmedetomidine group showed a significantly prolonged duration of motor and sensory block than patients in fentanyl group. *Conclusions:* Addition of dexmedetomidine potentiates bupivacaine spinal anesthesia by increasing significantly the duration of motor and sensory blockage with hemodynamic stability and reduced rescue analgesics as compared to fentanyl.

Keywords: Bupivacaine; Spinal anesthesia; Dexmedetomidine; Fentanyl.

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Introduction

Spinal anesthesia is a popular and common technique for lower abdominal surgeries. It is simple to perform, offers rapid onset of action, relatively less side-effects and early patient's discharge has made this the choice of many surgical procedures.[1]

However, postoperative pain control is a major problem because spinal anesthesia using only local anesthetics is associated with relatively short duration of action and thus early analgesic intervention is needed in the postoperative period. A number of adjuvants such as clonidine, midazolam, fentanyl and others have been used with local anesthetics' in spinal anaesthesia to avoid intra operative visceral and somatic pain and prolong the effect of spinal anaesthesia.[2,3]

The addition of Fentanyl to hyperbaric bupivacaine improves the quality of intraoperative and early postoperative subarachnoid block.[5] The addition of opioids to local anesthetic solutions have disadvantages such pruritis and respiratory depression.

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Dexmedetomidine, a highly selective α_2 agonist with a relative high ratio of α_2/α_1 activity (1620:1) possesses all these properties but lack respiratory depression, which makes it a safe adjuvant.[4]

Materials and Methods

This study was conducted after approval from ethical committee of institution. Written informed consent was taken from all patients.

The study population of 120 patients, age and sex matched was randomly divided by computer generated slip in to two groups with 60 patients in each group:

Group D: received 0.5% Bupivacaine 15 mg + Dexmedetomidine 5 mcg.

Group F: received 0.5% Bupivacaine 15 mg + Fentanyl 25 mcg.

Inclusion criteria: were adult patients aged between 18 and 60 years belonging to ASA Grade 1 and 2, of both sex undergoing lower limb and lower abdominal surgeries.

Exclusion criteria: were Patient refusal, infection at the site of injection, hypersensitivity to drugs, bleeding diathesis, heart blocks, peripheral neuropathy and patients with cardiac, pulmonary, hepatic or renal disorder.

Patients were shifted to OT table; IV access was obtained on the forearm with 18 Gauge IV cannula and Lactated Ringer's solution 500 ml infused intravenously before the block. The monitors were connected to the patient which include noninvasive blood pressure, pulse oximeter. Baseline PR, BP, RR and SpO_2 were recorded.

Under strict aseptic precautions, lumbar puncture was performed by using disposable Quincke spinal needle (25 G) at L3-L4 intervertebral space and study drug was injected after confirming CSF free flow. Patients were monitored continuously using noninvasive blood pressure, pulse oximeter and electrocardiogram.

Hypotension defined as a decrease of systolic blood pressure by more than 30% from base line, was treated with IV doses of ephedrine 5 mg and IV fluid as required. Bradycardia was defined as < 50 beats/min, treated with IV atropine 0.6 mg. Incidence of adverse effects noted. Sensory testing was assessed by loss of pin prick sensation to hypodermic needle and dermatome levels were tested every 2 minute until the highest level has stabilized. Testing was then conducted every 10 minutes until the point of two segment regression of the block was observed and continued till the recovery of S2 dermatome. Postoperatively pain score was recorded by Visual analog pain scale at 3, 6 and 12 hours. Injection diclofenac was given intramuscularly as rescue analgesia when VAS was > 4.

The data obtained were entered in a Microsoft Excel sheet, and statistical analysis was performed using statistical package for the social sciences (Verson 17). Results are presented as drawings, Mean ± SD, counts and percentages. Results were compared using Independent *t*-test, Mann Whitney *U*-test and Friedman test with Dunn's post hoc test. For all tests, significant was achieved at $p < 0.05$.

Results

The groups were comparable with age, sex, height, weight has shown in Table 1, which shows no significant difference. The meantime for onset of sensory block in Group BF was 3.1 ± 0.75 minutes and in Group BD was 3.25 ± 0.95 min. The onset of sensory block in both groups was statistically not significant. The meantime for onset of motor block in Group BF was 5.38 ± 1.1 min. and in Group BD was 5.9 ± 1.32 min. There was no statistically significant difference in two groups with regard to onset of motor block. The time for two segment regression was considerably slower in Group BD with 132.27 + 9.5 min compared to Group BF which was 97.57 + 8.8 min. The difference was statistically significant.

Table 1: Demographic profile

Variables	Group I (BF)		Group II (BD)		Mann Whitney *U*-test/*t*-test	*p* - value	Remark
	Mean	SD	Mean	SD			
Age	37.29 (35)	11.85	37.37 (35, 5)	11.984	$U = 1752$	$p = 0.928$	NS
Sex Male/Female	41:19	–	41:19	–	–	–	–
Height	5.58 (5.6)	0.28	5.50 (5.5)	0.29	$U = 993$	$p = 0.151$	NS
Weight	59.71 (59)	7.9	59.82 (60)	9.369	$t = 0.0633$	$p = 0.949$	NS

NS: Not Significant.

The mean duration of sensory block (time for complete sensory recovery) in Group BF was 209.98 + 12.3 min and in Group BD was 300.15 + 18.53 min. There was statistically significant difference in duration of sensory recovery, (Table 2).

The mean duration of motor recovery in Group BF was 186.5 ± 13.22 min. and in Group BD was 272.92 ± 23.32 min. There was highly significant difference between two groups regarding motor recovery, Table 2. The mean duration of complete analgesia in Group BF 174.63 ± 23.79 min. and in Group BD was 291.78 ± 52.12 min. There was statistically significant difference in both groups with regards to duration of complete analgesia. The mean duration of effective analgesia in Group BF was 211.25 ± 21.43 min and in Group BD was 351.3 ± 36.3 min.

Table 2: Recovery parameters

Recovery parameters	Group BF	Group BD	Mann Whitney *U*-test	*p* - value
Time to two segment regression	97.57 (100) 8.81	132.27 (132) 9.51	15.50	$p < 0.001$ HS
Time to complete sensory recovery	209.98 (210.0) 12.30	300.15 (304) 18.53	0.500	$p < 0.001$ HS
Time to complete motor recovery	186.5 (184.5) 13.22	272.92 (277) 23.32	3.00	$p < 0.001$ HS

There is highly significant difference in between two groups with regard to effective analgesia. In Group BF first rescue analgesia was given after 228 minutes and in Group BD 381 minutes which is highly significant. At any interval the two groups did not differ significantly with respect to heart rate, Fig. 1. In Group BD five patients had bradycardia which was treated by 0.6 mg Atropine successfully. In Group BF no incidence of bradycardia. In BF Group 8.3% patients had nausea, 5% patients had vomiting, 3.33% patients had bradycardia, 3.3% patients had hypotension. In BD Group 3.3% patients had nausea, 8.33% patients had bradycardia, 11.6% patients had hypotension.

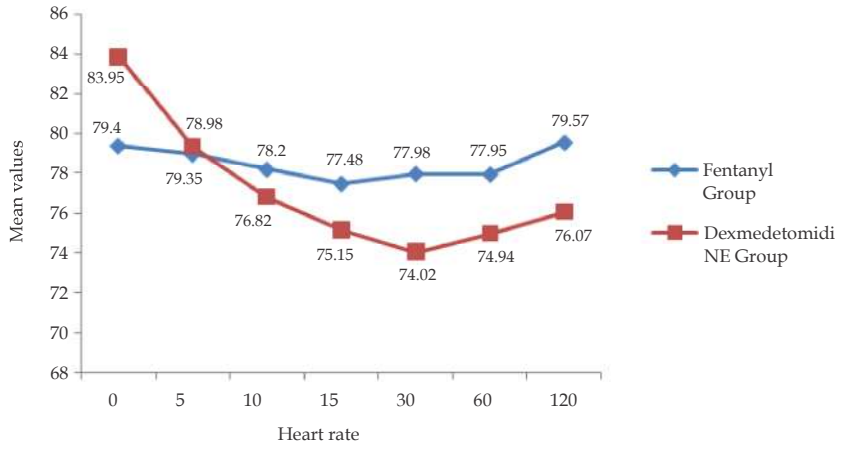

Fig. 1: Heart rate

Discussion

The analgesic effect of α_2 agonist is mediated through stimulation of α_{2C} and α_{2A} receptor in dorsal horn, thus directly suppressing pain transmission by reducing the release of pronociceptive transmitters, substance *p* and glutamate, and hyperpolarization of interneurons.[6]

Local anesthetic agents act by blocking sodium channels. The prolongation of effect may result from synergism between local anesthetic and α_2-adrenoceptor agonist, while the prolongation of the motor block of spinal anesthetics may result from the binding of α_2-adrenoceptor agonists to motor neurons in the dorsal horn[7]. Fentanyl is a lipophilic μ-receptor agonist opioid. Intrathecally, fentanyl exerts its effect by combining with opioid receptors

in the dorsal horn of spinal cord and may have a supraspinal spread and action.[8]

In our study, the intrathecal dose of Dexmedetomidine selected was based on previous study conducted by Rajni Gupta et al.[9] Our study showed, the addition of 5 mcg Dexmedetomidine with hyperbaric bupivacaine significantly increased duration of both sensory and motor block. Rajni Gupta et al.[9] had studied the effect of addition of 5 mcg Dexmedetomidine or 25 mcg Fentanyl intrathecal to 12.5 mg hyperbaric Bupivacaine for lower abdominal surgeries concluded that duration of sensory block, motor block, analgesia and time to rescue analgesic was significantly longer in Dexmedetomidine as compared to Fentanyl group, our results correlate with this study. Al-Ghanem *et al.* had studied the effect of addition of 5 μg Dexmedetomidine or 25 μg fentanyl intrathecal to 10 mg isobaric bupivacaine in vaginal hysterectomy and concluded that 5 μg Dexmedetomidine produces more prolonged motor and sensory block as compared with 25 µg fentanyl.[10] In our study, in the Dexmedetomidine group we found longer duration of both sensory and motor blockade, stable hemodynamic condition, and good patient satisfaction.

In our study, there was significant difference with respect to change in mean systolic blood pressure in both groups. But with regard to diastolic blood pressure there is statistically significant difference in reduction of mean diastolic blood pressure but not clinically (to become clinically significant, reduction in blood pressure should be more than 30%).

On the basis of the present, clinical comparative study, we can conclude that the addition of 5 mcg Dexmedetomidine to intrathecal hyperbaric bupivacaine for lower limb and lower abdominal surgeries appears to be an attractive choice as compared to 25 mcg Fentanyl. It provides a longer duration of both sensory and motor blockade, good quality of both Intraoperative and postoperative analgesia with minimal side-effects and better hemodynamic stability.

References

1. Paul G Barasch, Bruce F Collen. Clinical Anesthesia, 6th edition. Lippincort; Williams and Wilkins: 2006. pp.700–706.
2. Elia N, Culebras X, Mazza C, et al. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trials. Regional Anesthesia and Pain Medicine. 2008 Mar 1;33(2):159–67.
3. Boussofara M, Carlès M, Raucoules-Aimé M, et al. Effects of intrathecal midazolam on postoperative analgesia when added to a bupivacaine-clonidine mixture. Reg Anesth Pain Med 2006 Nov–Dec;31(6):501–05.
4. Grewal A. Dexmedetomidine: New avenues. Journal of anesthesiology Clinical Pharmacology 2011 [cited 2020 Mar 6];27:297–302.
5. Hunt CO, Naulty JS, Bader AM, et al. Perioperative analgesia with subarachnoid fentanyl-bupivacaine for cesarean delivery. Anesthesiology 1989 Oct;71(4):535–40.
6. Ishii H, Kohno T, Yamakura T, et al. Action of dexmedetomidine on the substantia gelatinosa neurons of the rat spinal cord. Eur J Neurosci 2008;27(12):3182–90. doi:10.1111 /j.1460-9568.2008.06260.
7. Harada Y, Nishioka K, Kitahata LM, et al. Visceral antinociceptive effects of spinal clonidine combined with morphine, enkephalin, or U50, 488H. Anesthesiology 1995;83:344–52.
8. Kalso E, Poyhia R, Rosenberg P. Spinal antinociception by dexmedetomidine, a highly selective α_2-adrenergic agonist. Pharmacol Toxicol 1991;68:140–43.
9. Gupta R, Verma R, Bogra J, et al. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anesthesiol Clin Pharmacol 2011;27(3):339–43. doi:10.4103/0970-9185.83678
10. Al-Ghanem SM, Massad IM, Al-Mustafa MM, et al. Effect of adding dexmedetomidine *versus* fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedures: A double blind controlled study. American Journal of Applied Sciences. 2009;6(5):882–87.

Original Research Article

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Efficacy of Tramadol and Butorphanol As Postoperative Rescue Analgesia: A Comparative Study

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Abstract

Aim: To compare the efficacy of butorphanol and tramadol in mitigating postoperative pain as rescue analgesia while observing its effect on hemodynamic stability. *Setting and Design:* This prospective, double-blinded randomized controlled study was conducted at the postoperative recovery area. *Materials and Methods:* Hundred patients of 18–60 years of age, American Society of Anesthesiologists physical status Class I and II of both sex who underwent elective laparoscopic cholecystectomy, were enrolled in this study after approval from the Institutional Ethics Committee. Patients were randomly allocated into two groups (50 patients each); Group B received injection butorphanol 1 mg and Group T received injection tramadol 100 mg intravenously in the postoperative recovery room when patient complains of pain and Visual Analog Scale (VAS) more than 4. Parameters assessed were pain intensity by Visual analog score at 10, 20, 30, 40 and 60 minutes, relief of pain is described as VAS less than 4 after 30 minutes, sedation score after 30 minutes and side-effects. *Statistical Analysis Used:* Student's *t*-test and Chi-square test were used for statistical analysis. *Results:* Pain intensity was also significantly low with butorphanol than tramadol upto 40 minutes. Relief of pain is 100% with injection butorphanol. More patients were found to be alert in tramadol group as compared with butorphanol. *Conclusions:* Intravenous butorphanol (1 mg) provides superior pain relief than intravenous tramadol (100 mg) when used as rescue analgesia for postoperative pain with lesser incidence of nausea and vomiting.

Keywords: Postoperative, Rescue analgesia, Tramadol, Butorphanol.

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Introduction

The international association for the study of pain (IASP) has defined pain in 1979 as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage". One of the most common symptoms for which a patient seeks medical advice is pain. Relief of pain is by far the most frequent indication of surgical intervention. But the surgeon in his mission often induces pain more severe than the original complaint.

Postoperative pain forms acute categories of nonmalignant pain. Though pain may be protective, defensive or diagnostic, it produces or precipitates many psychological and systemic

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side effects. Management of postoperative pain is done in two phases: one of which, is the preventive aspect (preemptive analgesia) and the other is therapeutic aspect (rescue analgesia). Postoperative pain relief can be achieved by several methods, including the use of systemic opioids and regional anesthesia with intrathecal or epidural opioids or local anesthesia. Opioids are very effective as postoperative analgesics, influencing emotional aspects of pain as well as reducing the actual pain threshold.[1] The analgesic effects of opioids arise from their ability to inhibit directly the ascending transmission of nociceptive information from the spinal cord dorsal horn and to activate pain control circuits that descend from the midbrain, through the Rostral Ventromedial Medulla (RVM) to the spinal cord dorsal horn. Pain in the perioperative setting or thereafter plays a significant role in delaying an otherwise successful recovery.[2]

Tramadol is a synthetic 4-phenyl-piperidine analog of codeine with a dual mechanism of action. Tramadol stimulates the μ-receptor and to a lesser extent the δ and κ-opioid receptors. It also activates spinal inhibition of pain by decreasing the reuptake of norepinephrine and serotonin as well as presynaptic stimulation of 5-hydroxytryptamine release.[3] Tramadol is also α_7 nicotinic acetylcholine receptor antagonist.[4] Tramadol is one fifth to one tenth as potent as morphine.[4] Tramadol is metabolized by hepatic P450 enzyme systems to the major metabolite O-desmethyltramadol, which also exerts modest stereoselective analgesic effects.[5] The primary O-demethylated metabolite of tramadol is two to four times as potent as the parent drug and may account for part of the analgesic effect.

Butorphanol is an agonist at κ-receptors. Its activity at μ-receptors is either antagonistic or partially agonistic.[6] Butorphanol has minimal affinity for σ receptors, so the incidence of dysphoria is low. The elimination half-time of butorphanol is 2.5 to 3.5 hours.[7] The analgesic activity of butorphanol is dose related and is five to eight times as potent as morphine.[8]

Thus, this study was conducted to compare the efficacy of butorphanol and tramadol in mitigating postoperative pain as rescue analgesia while observing its effect on hemodynamic stability and the presence of adverse drug reactions.

Materials and Methods

After obtaining approval from institutional ethical committee and informed written consent from all the patients, this prospective randomized, double blinded experimental study was conducted on 100 patients undergoing elective laparoscopic cholecystectomy under general anesthesia.

Inclusion criteria: were patients of age 18–60 years, ASA I or II and both sex posted for laparoscopic cholecystectomy under general anesthesia.

Exclusion criteria: were ASA III and IV, uncooperative patient, patient not giving consent, history of drug abuse, patients with coagulation disorders, pregnancy and lactation.

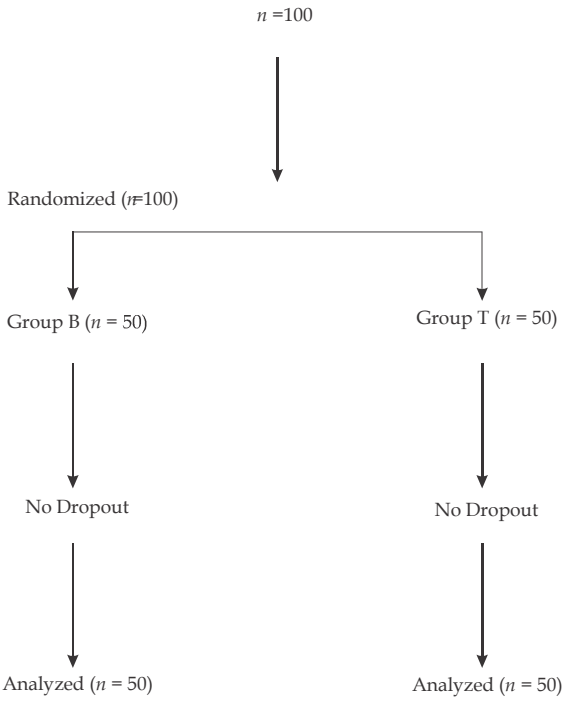

Fig. 1: Consort flow diagram of participants through each stage of randomized trial

Materials

Drugs

Drugs used in study are as follows:

(a) Injection of tramadol hydrochloride (100 mg);

(b) Injection of butorphanol tartarate (1 mg);

(c) All emergency drugs were kept ready at recovery room for safety in case of any adverse reaction occurs.

Visual Analog Scale (VAS)

Intensity of pain in postoperative period was assessed by Visual analog scale in which a score of "0" as "no pain" and a score of "10" as worst pain.

Patients with VAS of 4 or more were given rescue analgesia.

Methodology

During preoperative visit, patient's detailed history, general physical examination and clinical examination was carried out. Basic investigations like complete blood count, random blood sugar, blood urea, serum creatinine, Electrocardiogram and chest *X*-ray were carried out. The patients were explained about the anesthesia technique & research study and informed written consent was taken. They were taught how to assess intensity by using visual analog scale postoperatively. Patients were randomly allocated into two groups (50 patients each) by computer generated randomization into Group B receiving injection butorphanol 1 mg and Group T receiving injection 100 mg intravenously as rescue analgesia. Patients and the anesthetic technician who prepared the drug for study were blinded. Drugs were prepared in identical 2 ml syringes and administered according to the randomization list.

Patients were prescribed tablet lorazepam 1 mg on the night before surgery and advised nil per orally for 8 hours. On the day of surgery, intravenous cannulation (IV) was done with an 18 guage cannula. In the operation theater, baseline heart rate, blood pressure, oxygen saturation, electrocardiograph were recorded. All patients were premedicated with injection midazolam (0.05 mg. kg^{-1}) and glycopyrrolate (0.2 mg) IV. Anesthesia technique was standardized for all the cases. Injection fentanyl 2 mcg. kg^{-1} was used as analgesia. They were induced with injection propofol 2 mg. kg^{-1} IV. Intubation was facilitated by using injection vecuronium 0.1 mg. kg^{-1} IV. Anesthesia was maintained with nitrous oxide (66%) and isoflurane (1–2%) in oxygen. End tidal carbon dioxide was maintained between 35 and 40 mm Hg. Hemodynamic response to laparoscopy was attenuated by additional doses of injection fentanyl. Intraoperative muscle relaxation was maintained with intermittent doses of injection vecuronium. Reversal of neuromuscular blockade was performed with injection neostigmine 0.05 mg. kg^{-1} IV and glycopyrrolate 0.1 mg. kg^{-1} IV.

In the recovery room when patients complaint of pain and VAS score 4 or more, Group T received injection tramadol hydrochloride 100 mg intravenously and Group B received injection butorphanol tartarate 1mg intravenously as rescue analgesia.

Following clinical parameters were assessed:

I. Pain intensity by Visual analog score at 10, 20, 30, 40 and 60 minutes.

II. Relief of pain is described as VAS less than 4 after 30 minutes.

III. Sedation score after 30 minutes.

0. Alert;
1. Drowsy but arousable by verbal command;
2. Drowsy but not arousable by verbal command;
3. Arousable by deep pain;
4. Unarousable;

IV. Side-effects like Nausea and vomiting, respiratory depression (Respiratory rate < 10), bradycardia, hypotension and any allergic reaction

V. Heart rate, Systolic blood pressure, Diastolic blood pressure, SpO_2 and Respiratory rate before administration of rescue analgesia and 30 minutes after its administration.

If, patients still complains of pain after 30 minutes or VAS > 4, Injection diclofenac 75 mg in 100 ml normal saline was infused over 20 minutes. Hypotension was said to be significant if, MAP was less by 30% of prerescue analgesia value & was treated with intravenous fluids & vasopressor drugs. Simultaneously 100% oxygen was administered through face mask. Bradycardia was considered when PR was below 50 beats per minute and treated with injection atropine sulphate IV 6 mg increments. Nausea and vomiting–in these cases hypotension was first ruled out & then injection ondanstren 4 mg was given.

Sample size

Keeping power of study at 90%, confidence interval of 95%, to detect a 20 % difference in VAS score, the sample size of 27 was required in each group; however 50 patients were included in each group.

Statistical analysis

Data were expressed as mean, standard deviation & percentage. Parametric data were analyzed by unpaired student *t*-test. Nonparametric data were analyzed by Chi-square test. Analysis was performed using statistical software Statistical Product for Social Sciences (SPSS version 20.0 for Windows, Chicago, SPSS Inc.). Results were considered to be statistically significant if when p - value was < 0.05.

Results

All hundred patients were successfully enrolled in the study without anydropouts. The butorphanol and tramadol group were comparable with respect to age, sex, height, weight, ASA grading I:II, has shown in Table 1. Visual Analog Scale (VAS) score was assessed every 10 minutes interval after the intravenous dose of either butorphanol (1 mg) or tramadol (100 mg) as rescue analgesia, Table 2.

VAS score was significantly high in tramadol group as compared to butorphanol group after 10 minutes ($p < 0.05$) of injection. Pain intensity was also significantly low in Group B at 20, 30, 40 minutes. But VAS score was not statistically significant between the groups at 60 minutes. ($p = 0.4314$) Relief of pain is described as VAS score less than 4 after 30 minutes of administering rescue analgesia.

The Table 3 shows, 100% pain relief in patient's receiving injection butorphanol than injection tramadol (100% *vs* 31 %). More patients were found to be alert in tramadol group (48%) as compared with butorphanol (14%) as in Table 4. 58% patients in Group B were drowsy but arousable by verbal commands. None of the patients in the study showed sedation score 4. Sedation score was significantly high in patients receiving butorphanol ($p < 0.05$), Table 4.

The Table 5 shows, 38% of patients in tramadol group had nausea and vomiting as compared with 4% in butorphanol which is highly significant statistically < 0.001. None of the patients in the study had respiratory depression, bradycardia or hypotension.

Table 6 shows, pulse rate was significantly low in patients receiving butorphanol as compared to tramadol ($p < 0.05$) after 30 minutes of rescue analgesia. It shows patients comfort. No significant change in systolic and diastolic blood pressure, oxygen saturation and mean respiratory rate was seen between the Group B and Group T before and 30 minutes after rescue Analgesia, (Tables 7–9).

Table 1: Demographic profile

Characteristics	Group B ($n = 50$)	Group T ($n = 50$)	p - value
Age (Yrs)	43.2 ± 11.3	39.14 ± 11.8	0.082
Sex (Male : Female)	16:34	13:37	0.509
Height (Meters)	1.6 ± 0.074	1.6 ± 0.072	0.655
Weight (kilogram)	61.6 ± 8.6	61.7 ± 7.7	0.932
ASA I: II	32 : 18	34 : 16	

ASA = American Society of Anesthesiology, Data are expressed as mean ± standard deviation. *P* - value < 0.05 denotes statistical significance.

Table 2: Visual analog scale score

Time duration after rescue analgesia	Group B ($n = 50$)	Group T ($n = 50$)	p - value
At 10 minutes	1.9 ± 0.27	3.8 ± 1.3	0.0001
At 20 minutes	1.8 ± 0.38	3.74 ± 1.17	0.0001
At 30 minutes	1.6 ± 0.47	2.9 ± 0.4	0.0001
At 40 minutes	2.2 ± 0.46	2.4 ± 0.45	0.03
At 60 minutes	2.7 ± 0.69	2.8 ± 0.57	0.4314

Data are expressed as mean ± standard deviation . *P* - value < 0.05 denotes statistical significance.

Table 3: Relief of pain

Relief of pain	Group B ($n = 50$)	Group T ($n = 50$)	p - value
Yes	50 (100%)	31 (62%)	0.0009
No	0	19 (38%)	
Total	50	50	

Data are expressed as patients number or percentage.

Table 4: Sedation score

Score	0 (%)	1 (%)	2 (%)	3 (%)	4 (%)	Total
Group B	7 (14)	29 (58)	10 (20)	4 (8)	0	50
Group T	24 (48)	20 (40)	6 (12)	0	0	50

0: Alert, 1: Drowsy but arousable by verbal commands,
2: Drowsy but not arousable by verbal commands,
3: Arousable by deep pain,
4: Not arousable.

Table 5: Side-effects

Side-effects	Group B (n = 50)	Group T (n = 50)	p - value
Nausea & Vomiting	2 (4%)	19 (38%)	0.0003
Respiratory depression	0	0	
Bradycardia	0	0	
Hypotension	0	0	

Data are expressed as patients number and percentage.

Table 6: Pulse rate

Pulse rate	Group B (n = 50)	Group T (n = 50)	p - value
Before rescue analgesia	98.5 ± 4.9	97.8 ± 4.7	0.482
30 minutes after rescue analgesia	81.02 ± 4.7	89.9 ± 3.9	0.000

Data are expressed as mean ± standard deviation. p - value < 0.05 denotes statistical significance.

Table 7: Blood pressure

Blood pressure		Group B (n = 50)	Group T (n = 50)	p - value
Systolic	Before rescue analgesia	126.76 ± 15.3	123.32 ± 13.82	0.24
	30 Minutes after rescue analgesia	117.52 ± 11.92	117.48 ± 12.56	0.98
Diastolic	Before rescue analgesia	75.16 ± 7.06	73.96 7 ± .25	0.40
	30 Minutes after rescue analgesia	70.14 ± 5.2	71.04 ± 6.05	0.42

Data are expressed as mean ± standard deviation . p - value < 0.05 denotes statistical significance. Blood pressure in mm of Hg.

Table 8: Pulse oximetry (SpO_2)

SpO_2	Group B (n = 50)	Group T (n = 50)	p - value
Before rescue analgesia	98 ± 0.008	98 ± 0.008	1.00
30 Minutes after rescue analgesia	98 ± 0.07	98 ± 0.06	1.00

Data are expressed as mean ± standard deviation. p - value < 0.05 denotes statistical significance. SpO_2 in percentage.

Table 9: Respiratory rate

Respiratory rate (per minute)	Group B (n = 50)	Group T (n = 50)	p - value
Before rescue analgesia	13.5 ± 0.735	13.4 ± 0.808	0.51
30 Minutes after rescue analgesia	13.4 ± 0.782	13.32 ± 0.843	0.62

Data are expressed as mean ± standard deviation. p - value < 0.05 denotes statistical significance.

Discussion

Postoperative pain may result in psychological, physiological, neuroendocrine, respiratory and cardiovascular problems ultimately increasing the risk of postoperative morbidity and mortality Effective control of postoperative pain remains one of the most important & pressing issues in the field of anesthesia. Opioids are being widely used either alone or in combination with NSAIDS for postoperative analgesia.

Thus, the present study "efficacy of tramadol and butorphanol as postoperative rescue analgesia - A comparative study"was taken up with 100 patients of 18–60 years. The main aim of postoperative pain relief is to provide subjective comfort, in addition to inhibiting nociceptive impulse caused by trauma and to blunt autonomic as well as somatic reflexes to pain. Subsequently, this might enhance restoration of function by allowing the patient to breath, cough and to be easily ambulant.

Butorphanol is used to treat moderate to severe pain. It is an agonist at κ-receptor, but it is a weak antagonist at the μ-receptor. Several clinical studies with the injectable form of butorphanol have shown effectiveness in relieving moderate-to-severe postoperative pain.[9]

Tramadol, a weak opioid which acts on μ-receptor has been most commonly used for management of postoperative pain.[10] Tramadol has been chosen as a reference substance, as its effects are well-documented. Since, the study used identical protocols, the results obtained were comparable, combine analysis of trial was valid.

In our study, comparing the mean differences in VAS scores in two groups, it was clear that there was a greater reduction in VAS score of butorphanol group compared to tramadol group 10 minutes after injection ($p < 0.05$). But there was no difference in pain intensity 60 minutes after the injection of study drugs ($p = 0.43$). Sung et al.[1] conducted a retrospective study to compare butorphanol with morphine for use in a balanced anesthesia technique with nitrous oxide, oxygen, and neuromuscular relaxants. Neru et al.[11] have compared butorphanol and tramadol for analgesic efficacy and safety. The onset of analgesia is rapid with butorphanol as studied by Andrews.[12] The results of Galloway et al.[13] and Del Pizzo[14] were comparable with our results.

In our study, we found that relief of pain is described as VAS score less than 4 thirty minutes after injection of study drugs, was better with butorphanol as compared to tramadol ($p < 0.001$). In a comparative Study of analgesic efficacy of tramadol and butorphanol in mandibular third molar surgery four patients reported no pain and also had not taken any rescue medications in butorphanol group compared to tramadol group.[15]

From a double-blind, randomized trial conducted on postoperative patients, it appears that butorphanol tartrate provided substantial relief from moderate to severe postsurgical pain.[16,17]

Patients who received the lowest dose of butorphanol (1 mg) experienced their peak response at about 30 minutes, and the remaining treatment groups obtained maximum relief at about 60 minutes after medication.[18]

Sedation was high with butorphanol but the patients were arousable as compared to tramadol group where most of the patients were alert. None of the cases had sedation score of 4.

A side from drowsiness, the incidence of side-effects with butorphanol was negligible in a study conducted by Dobkin et al.[19] Authors have found less sedation after tramadol administration compared with equianalgesic doses of morphine.[20]

Incidence of nausea and vomiting was high with tramadol (38%) than butorphanol (4%) which is found to be highly significant ($p < 0.001$) Butorphanol does not increase the incidence of postoperative nausea and vomiting as observed by Onake and Yamamoto.[21] Nausea and vomiting were more frequent with tramadol 28% and 18% *versus* 81% and 51% than with pethidine in a study Ahluwalia et al.[22] Ofoegbu[23] found that with IM tramadol the incidence of nausea and vomiting was 19%. No other side-effects like bradycardia, hypotension, respiratory depression or allergic reaction was seen.

There was a reduction in pulse rate overall but reduction was more seen in Group B (from 98.5 to 81.02) than Group T (from 98.2 to 85.5) after giving rescue analgesia. The difference in mean pulse rate was found to be statistically significant in both groups implying decrease of pain intensity after 30 minutes was more with butorphanol.

No significant difference was seen between the groups with respect to systolic and diastolic blood pressure, oxygen saturation and respiratory rate. Patients in butorphanol group were hemodynamically more stable throughout the postoperative period which is consistent with previous report by gupta et al.[24]

Conclusion

Our study concluded that intravenous butorphanol (1 mg) provides superior pain relief than intravenous tramadol (100 mg) when used as rescue analgesia for postoperative pain with lesser incidence of nausea and vomiting. Though sedation is more with butorphanol but patients are arousable.

Source of Support: NIL

References

1. Thakore Bhoomika, Jacqueline D'Mello Jacqueline, Saksena Shalini, et al. Comparison of fentanyl and butorphanol for postoperative pain relief with intravenous patient controlled analgesia. Acute Pain 2009;11:93–99
2. Shahid M, Manjula BP, Sunil BV. A comparative study of intravenous paracetamol and intravenous tramadol for postoperative analgesia in laparotomies. Anesth Essays Res 2015;9:314–19.
3. Scott LJ, Perry CM. Tramadol: A review of its use in perioperative pain. Drugs 2000 July;60(1):139–76.
4. Minami K, Ogata J, Uezono Y. What is the main mechanism of tramadol? Naunyn Schmiedebergs Arch. Pharmacol 2015 Oct; (10): 999–1007.
5. Baraka A, Jabbour S, Ghabash M, et al. Can J Anesth 1993 Apr;40(4):308–313.
6. Miller's anesthesia 8th edition, opioid analgesics, p. 904.
7. Rosow CE. Butorphanol in perspective. Acute Care 1988; 12 Suppl 1:2–7.
8. Ameer B, Salter FJ. Drug therapy reviews: Evaluation of butorphanol tartrate. Am J Hosp Pharm 1979 Dec;36(12):1683–691.
9. Bowdle TA, Greichen SL, Bjurstrom RL, et al. Butorphanol improves CO_2 responses and ventilation after fentanyl anesthesia. AnesthAnalg 1987 Jun;66(6):517–22.
10. Putland AJ, McCluskey A. The analgesic efficacy of tramadol *versus* ketorolac in daycase laparoscopic sterilization. Anesthesia 1999 Apr;54(4):382–85.
11. Neru G, Anand S, Gulati S, et al. Comparison of tramadol and butorphanol for analgesic efficacy and safety. JK Sci 2008;10:132–34.
12. Andrews IC. Butorphanol and pentazocine. A double blind intramuscular comparison in patients with moderate to severe postoperative pain. Curr Ther Res 1977;22:647.
13. Galloway FM, Hrdlicka J, Losada M, et al. Comparison of analgesia by intravenous butorphanol and meperidine in patients with postoperative pain. Can Anesth Soc J 1977;24:90–102.
14. Del Pizzo A. A double blind study of effects of butorphanol compared with morphine in balanced anesthesia. Can Anesth Soc J 1978;25:392–97.
15. Hassan SS, Ahmed A, Rai M, et al. Analgesic efficacy of tramadol and butorphanol in mandibular third molar surgery: A comparative study. J Contemp Dent Pract 2012;13(3):364–70.
16. Sung YF, Weinstein MS, Ghani GA. Balanced anesthesia; A comparison of butorphanol and morphine. South Med J 1984;77:180–82.
17. Popio K, Kenneth A. Hemodynamic and respiratory effects of morphine and butorphanol. Clin Pharmacol Ther 1978;23(3):281–87.
18. Nagashima H, Karamanian A. Respiratory and circulatory effects of intravenous butorphanol and morphine. Clin Pharmacol Ther 1976;19:738–45.
19. Dobkin AB, Eamkaow S, Zak S et al. Butorphanol: A double-blind evaluation in postoperative patients with moderate or severe pain. Can Anesth Soc J 1974;21:600–610.
20. Lehmann KA, Jung C, Hoeckel W. Tramadol and pethidine zur postoperative schmerztherapie eine randomisierte dopple blind studie under den bedingunum der in intraverosen on demand analgesia. Schmerzther Pain Douler 1995;6:88-100.
21. Onake M, Yamamoto H. Comparison of analgesics used during balanced anesthesia on the incidence of PONV. Masui 2004;53:161–66.
22. Ahluwalia P, Rehman F, Ahluwalia A. comparison of butorphanol tartrate and tramadol hydrochloride for postoperative pain relief following abdominal surgery: A prospective, randomized, double-blind study. Int J Sci Stud 2015;3(9):120–24.
23. Ofoegbu RO. Report on a clinical trial with tramadol in the prevention of postoperative pain. Curr Ther Res 1984;36:436–44.
24. Gupta N, Anand S, Gulati S, et al. Comparison of tramadol and butorphanol for analgesic efficacy and safety. JK Science 2008;10(3):124–26.

Case Reports

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Perioperative Positioning Concerns and Airway Management in Pediatric Meningomyelocele Surgery: A Novel Innovation

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Abstract

Meningomyelocele surgeries are common in pediatric anesthesia and forms a congenital neural tube defect (herniation of meninges and neural elements through a skull defect). One of the main problems which occur during induction of these children is the difficulty in positioning for airway management and the need to prevent sac compression or rupture. We hereby describe a novel way of positioning of these children over an elevated platform, with the occipital meningomyelocele resting in the padded hollow of an adult soft silicon head rest (used during prone positioning surgeries). After successful induction and airway securing over this, the same elevated platform was used for the definitive surgical procedure. This innovative positioning adjunct not only supports the herniated sac in supine position, but also eases the intubation process in these difficult airway cases and obviates the risk of latex allergy.

Keywords: Meningomyelocele; Positioning; Silicon gel pad; Pediatric airway; Neural compression.

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Introduction

Meningomyelocele is the most common congenital primary neural tube defect and occurs approximately in 0.5–1 of every 1000 live births.[1] Meningomyelocele is the herniation of part of meninges and neural elements in a sac through the skull defect, in contrary to meningocele, which does not contain neural elements. It is most commonly seen in the occipital region.

The child presents with cystic mass on the back, comprising neural placode, arachnoid, dura, nerve roots and cerebrospinal fluid.[2] Sensory and motor deficits can occur below the level of lesion. The major perioperative goals[3] of the anesthesiologist are to avoid neural compression and premature rupture of the sac; to manage difficult airway due to problems in supine positioning and restricted neck extension; general concerns of pediatric anesthesia; risk of latex sensitization and allergy; temperature control and pain management. The occurrence of associated congenital abnormalities adds to the perioperative woes of the anesthesiologists in these patients.

We, hereby report the anesthetic management of a series of pediatric occipital meningomyeloceles posted for definitive surgery, along with an innovative positioning adjunct for the sac in supine position. This sac support has not been reported before in literature.

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Case Reports

We, hereby report four infants between the age of 1 and 9 months who presented with congenital occipital meningomyelocele and scheduled for excision and repair. After a thorough preoperative evaluation, including neurological assessment, all the infants were assessed for associated congenital anomalies. All children had normal routine investigations, with no evidence of raised intracranial pressure, meningeal irritation, or any neurological deficit.

Anesthesia Management

On the day of surgery, operating room and table was prewarmed. Anesthesia machine monitors and suction apparatus were checked for proper functioning. Difficult airway cart with equipment prepared. Since, the risk of latex allergy is high in these patients, measures were taken to avoid equipment made of latex. A brief preanesthetic evaluation was repeated on the day of surgery and adequate NPO status was ensured in all the patients.

In all our 4 cases, we used a silicone gel support for supine positioning of the patients. This silicone gel support, shown in Fig. 1,2, was actually an adult head rest used during spine surgeries for prone positioning of the patients. The silicone gel head support measured around 25 × 20 × 13 cms and there was no risk of latex allergy. Before positioning the patients, the gel support was prepadded with warm saline gauzes to prevent desiccation of the neural sac which would rest on its hollow.

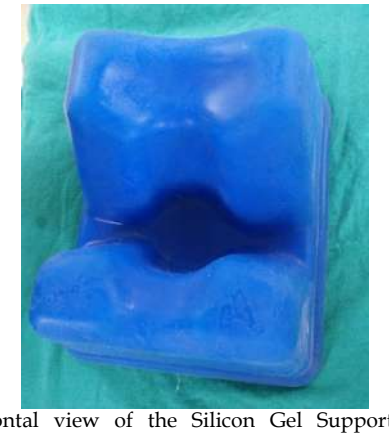
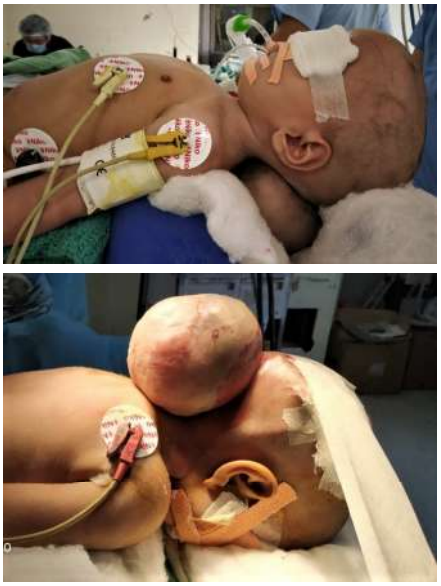


Fig 1: Frontal view of the Silicon Gel Support used for positioning.

Fig. 2: Picture showing the adult silicon head support gel used in pediatric occipital meningomyelocele

The patients were placed in supine position with the encephalocele sac hanging freely in the central hollow space between the edges of the adult silicone gel head support. The head of the infant rested on the proximal part and shoulder rested on the distal part of the silicon support, Fig. 3. Rest of the body was supported on an elevated platform made by uniformly folded towels and cotton rolls, all on same level as the silicon head support.



Figs. 3 and 4: Pictures showing the infant positioned on the silicon gel support - Figure 3 in SUPINE position after induction and Figure 4 in PRONE position for meningomyelocele surgery.

After proper supine positioning, monitors were attached. General anesthesia was given and successful airway management was possible in all the patients without any difficulty. There was no risk of latex allergy or sac compression/rupture. The same padded silicone gel support was used as head support during prone positioning of the patient for sac excision, Fig. 4. The body was supported on an equally elevated, padded platform of same height.

Discussion

Meningomyelocele is the hernial protrusion of part of meninges and neural elements in a sac from the congenital bonydefect. It results due to failure of neural tube closure at fourth week of gestation. Children present with varying degrees of sensory and motor deficits. The prognosis depends on the size of the defect, the amount of sac herniated through the defect and the associated congenital anomalies.[4]

The major anesthetic challenges in patients with occipital meningomyelocele include avoidance of neural compression, prevention of sac rupture, difficult airway considerations, circumventing latex allergy and the meticulous postoperative care.

Securing a definitive airway in pediatric population is difficult and feared due to variations in airway anatomy. Associated craniofacial disorders like occipital meningomyelocele will hamper neck extension and supine positioning of the patient. This adds on to the potential difficulty of laryngoscopy and intubation in the pediatric population. The most important challenge is to optimally position these patients with occipital mass for laryngoscopy without neural compression and rupture of the sac.[5]

Different maneuvers for airway management have been proposed by various authors. Laryngoscopy in different positions, taking help of assistants, using platforms made by towels, using adjuncts like horse shoe devices and modification of table surfaces has been noted in literatures and has recorded varying rates of success and complications.

Quezado[6] and colleagues have described a simple foam-cushion device for laryngoscopy. Intubation and laryngoscopy were attempted in lateral position. Laryngoscopy in lateral position needs more expertise and required more than one assistant for supporting the child.[7] Failure rates are relatively high.

One method described an assistant manually supporting the child's head beyond the edge of the table with the rest of the body lying on the table.[8] In another study, the child's body was fully lifted off the table, followed by laryngoscopy and intubation. Although conventional supine positioning can be achieved, head was not quite stable and there was requirement of more assistants to support the patient to prevent in advertent sac rupture.

Mowafi[9] described the platform method in which the baby was placed on a platform made of blankets and the sac was protected in a traditional dough-nut shaped support. Karim et al.[10], used an adjustable horses hoe headrest for supine positioning during laryngoscopy. It provided a stable head positioning during laryngoscopy without sac compression. But this method needed special attachments to the operating table, difficult adjustments which can be done by trained personnel and also acts as hindrance during laryngoscopy.

In our cases, we utilized the silicone gel support as an adjunct for laryngoscopy and intubation. This was an adult head rest used for prone positioning of patients during spine surgeries/ posterior fossa surgeries. This silicone gel support is easily available in operation theaters. Using this simple silicone gel support, successful airway management was possible in all the cases. There was no risk of sac compression and rupture andno risk of latex allergy. Single anesthesiologist is suffice to optimally position the patient and secure a definitive airway without any difficulty. The support was also utilized for subsequent prone positioning during surgery.

Conclusion

Positioning for successful airway management in neonates and infants with occipital meningomyelocele is a great challenge.[11] Silicone gel supports form an important adjunct for positioning in meningomyelocele patients. This report was based on our experience with a series of 4 cases and we recommend the silicone gel head support as an adjunct for successful airway management of occipital meningomyelocele. It obviates the need for cumbersome positioning of these children, along with preservation of sac and neural structures. Further, large scale randomized controlled trials need to be done using this silicon head support to cement our observations for a successful meningomyelocele surgery.

References

1. Sahni M, Ohri A. Meningomyelocele. [Updated 2019 Sep 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 10th August.
2. Copp AJ, Adzick NS, Chitty LS, et al. Spina bifida. Nat Rev Dis Primers 2015;1:15007.
3. Mahajan C, Rath GP, Dash HH, et al. Perioperative management of children with encephalocele: An institutional experience. Journal of neurosurgical anesthesiology 2011;23(4):352–56.

4. Shaer CM, Chescheir N, Schulkin J. Myelomeningocele: A review of the epidemiology, genetics, risk-factors for conception, prenatal diagnosis, and prognosis for affected individuals. Obstetrical and gynecological survey. 2007;62(7):471–79.
5. Yildirim Z, Avci E, Torun F, et al. Airway management for occipital encephalocele in neonatal patients: A review of 17 cases. Journal of Neurosciences in Rural Practice 2011;2(2):159–61.
6. Quezado Z, Finkel JC. Airway management in neonates with occipital encephalocele: Easy does it. Anesthesia and Analgesia 2008;107(4):1446.
7. Pahuja HD, Deshmukh SR, Lande SA, et al. Anesthetic management of neonate with giant occipital meningoencephalocele: Case report. Egyptian Journal of Anesthesia 2015;31(4):331–34.
8. Neeta S, Upadya M, Pachala SS. Anesthetic management of a newborn with occipital meningocele for magnetic resonance imaging. Anesthesia, essays and researches 2015;9(2):238–40.
9. Mowafi HA, Sheikh BY, Al-Ghamdi AA. Positioning for anesthetic induction of neonates with encephalocele. The Internet Journal of Anesthesiology 2001;5(3).
10. Karim R, Muhammad H, Yunus M, et al. Adjustable horseshoe headrest as a positioning adjunct in Airway Management for a giant occipital encephalocele. The Open Anesthesia Journal 2017;11(1).
11. Manhas Y, Chinnan NK, Singh AK. Neonatal airway management in occipital encephalocele. AnesthAnalg 2006;103(6):1632.

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[1] Flink H, Tegelberg Å, Thörn M, Lagerlöf F. Effect of oral iron supplementation on unstimulated salivary flow rate: A randomized, double-blind, placebo-controlled trial. J Oral Pathol Med 2006; 35: 540–7.

[2] Twetman S, Axelsson S, Dahlgren H, Holm AK, Källestål C, Lagerlöf F, et al. Caries-preventive effect of fluoride toothpaste: A systematic review. Acta Odontol Scand 2003; 61: 347–55.

Article in supplement or special issue

[3] Fleischer W, Reimer K. Povidone-iodine antisepsis. State of the art. Dermatology 1997; 195 Suppl 2: 3–9.

Corporate (collective) author

[4] American Academy of Periodontology. Sonic and ultrasonic scalers in periodontics. J Periodontol 2000; 71: 1792–801.

Unpublished article

[5] Garoushi S, Lassila LV, Tezvergil A, Vallittu PK. Static and fatigue compression test for particulate filler composite resin with fiber-reinforced composite substructure. Dent Mater 2006.

Personal author(s)

[6] Hosmer D, Lemeshow S. Applied logistic regression, 2nd edn. New York: Wiley-Interscience; 2000.

Chapter in book

[7] Nauntofte B, Tenovuo J, Lagerlöf F. Secretion and composition of saliva. In: Fejerskov O,

Kidd EAM, editors. Dental caries: The disease and its clinical management. Oxford: Blackwell Munksgaard; 2003. pp 7–27.

No author given

[8] World Health Organization. Oral health surveys - basic methods, 4th edn. Geneva: World Health Organization; 1997.

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[9] National Statistics Online—Trends in suicide by method in England and Wales, 1979–2001. www.statistics.gov.uk/downloads/theme_health/HSQ 20.pdf (accessed Jan 24, 2005): 7–18. Only verified references against the original documents should be cited. Authors are responsible for the accuracy and completeness of their references and for correct text citation. The number of reference should be kept limited to 20 in case of major communications and 10 for short communications.

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