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Volume 6 (6 issues) will be published in 2019
pISSN: 2349-8471, eISSN: 2455-6238

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INDIAN JOURNAL OF ANESTHESIA AND ANALGESIA

July - August 2019
Volume 6 Number 4 (Part - II)

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Original Research Articles

Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(4) (Part - II): 1265-1274
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.29

Study on Comparing the Postoperative Analgesic Efficacy of Ultrasound Guided Tansverse Abdominis Plane Block with 0.25% Bupivacaine and 0.375% Ropivacaine in Laparoscopic Surgeries

P Kalyan Chakravarthy[1], Sireesha Ejjapureddi[2], Hemnath Babu Kotla[3], Jaya Chandra[4], K Ramya[5], M Ramya[6]

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Abstract

Introduction: Improvements in surgical training, as well as developments of instruments, imaging, and surgical techniques, have made laparoscopic surgery safe and feasible across different medical fields. It has its own advantages as it is minimally invasive with less postoperative pain, more rapid recovery, shorter hospital stay and earlier return to normal activity. *Aims:* The objective of the present study is to compare the efficacy of a single shot ultrasound guided Transversus Abdominis plane block with 0.375% Ropivacaine and 0.25% bupivacaine in providing post operative analgesia upto 24 hours for laparoscopic surgeries. *Materials and Methods:* It is a prospective, randomized, double blinded study in 60 adult patients including both males and females belonging to American Society of Anesthesiologist (ASA) I & II were included in the current study. *Results:* Bupivacaine and ropivacaine provided equally effective analgesia with TAP block till 24 hours after the block. There is also no significant difference in hemodynamics and sedation scores in between the groups. In both the groups the mean, duration of time taken for the pain score to be >4 (moderate pain) by numerical rating scale was around 15 hours after the block. Only seven patients (23.3%) in bupivacaine group and nine patients (30.0%) in ropivacaine group received the rescue analgesic once. Regarding the duration of analgesia both the drugs provided equally effective analgesia till the end of observation period i.e., 24 hours post operatively. *Conclusion:* Bupivacaine and Ropivacaine in laparoscopic surgeries showed that both (0.25%) bupivacaine and (0.375%) ropivacaine provided equally effective postoperative analgesia, better pain scores and required less doses of rescue analgesics in the first 24 hours duration after the block.

Keywords: Postoperative Analgesic; Tansverse Abdominis Plane; Bupivacaine; Ropivacaine.

How to cite this article:

P Kalyan Chakravarthy, Sireesha Ejjapureddi, Hemnath Babu Kotla *et al.* Study on Comparing the Postoperative Analgesic Efficacy of Ultrasound Guided Tansverse Abdominis Plane Block with 0.25% Bupivacaine and 0.375% Ropivacaine in Laparoscopic Surgeries. Indian J Anesth Analg. 2019;6(4):1265-1274.

Introduction

Laparoscopic surgery has existed since the development of diagnostic laparoscopy and it has since become a frequently applied technique for a wide field of indications. The procedure has become the gold standard for many organ systems. Significant improvements in surgical training, as

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Received on 15.04.2019, **Accepted on** 14.05.2019

well as developments of instruments, imaging, and surgical techniques, have made laparoscopic surgery safe and feasible across different medical fields. It has its own advantages as it is minimally invasive with less post-operative pain, more rapid recovery, shorter hospital stay and earlier return to normal activity. However, patients undergoing laparoscopic abdominal surgery experience moderate or even severe pain in the early post-operative period. This pain is caused by a number of mechanisms, including incision the anterior abdominal wall, pneumo peritoneum causing stretching of anterior abdominal wall.

The most traditional approach to postoperative pain relief is multimodal using nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids. Nonetheless, there are severe restrictions on the availability of opioids and other essential medications which are used to reduce nausea, vomiting, constipation, urinary retention, respiratory depression and sedation, used for the management of pain.[2] Therefore, the use of non-opioid analgesic techniques can lead to an improved quality of recovery for surgical patients. Poorly controlled acute pain after abdominal surgery is associated with a variety of unwanted postoperative consequences, including patient suffering, distress, respiratory complications, delirium, myocardial ischaemia, prolonged hospital stay and an increased likelihood of chronic pain. A number of modalities have been tried over the years to reduce the postoperative pain after laparoscopic cholecystectomy, including systemic analgesia with non- steroidal anti-inflammatory drugs (NSAIDs) and opioids, port-site local anesthetic infiltration", intravenous patient controlled analgesia, patient controlled thoracic epidural analgesia. Trans versus abdominis plane block, intraperitoneal lavage of local anesthetic agents and low pressure pneumoperitoneum".

Introduced 10 years ago in Ireland, where there was a lack of facilities and staff for acute postoperative pain treatment, it became increasingly popular worldwide because of its relative simplicity and efficacy. TAP block significantly reduces pain associated with lower abdominal surgery, regardless of whether it is used as the primary anaesthetic or for pain control after general or spinal anesthesia. With the advent of Ultrasound imaging and the promise of improved localization and efficacy, TAP blocks have once again been brought to the forefront and have gained importance as an analgesic modality. In the past few years, there have been increasing numbers of reports describing the use of TAP blocks for pain relief for adult and paediatric abdominal surgical procedures. Furthermore, the extent of morbidity arising from complications remains unknown. Any new intervention should include an assessment of the degree of patient satisfaction with tolerability of the procedure. TAP blocks are believed to provide improved postoperative analgesia and reduced requirements for medications for pain relief and a systematic review on this topic is timely. With most of the studies concentrating on the analgesic modality as such, we decided to compare the analgesic efficacy of two local anesthetics viz. Bupivacaine and Ropivacaine for lower abdominal laparoscopic surgeries.

Materials and Methods

The study was approved by the hospital ethics committee of hospital and informed consent was obtained from the study groups.

It is a prospective, randomized, double blinded study.

A total of 60 adult patients including both males and females belonging to American Society of Anesthesiologist (ASA) I & II were included in the current study.

Inclusion Criteria: ASA physical status I/II patients in Laparoscopic surgeries as Laparoscopic appendicectomy, laparoscopic myomectomy, Laparoscopic assisted vaginal hysterectomy.

Laparoscopic sterilization, Laparoscopic ovarian cystectomy, Laparoscopic sleeve gastrectomy, Baraitric surgeries. Diagnostic laparoscopy and Hysterolaparoscopy.

Exclusion Criteria: Known hypersensitivity for study drugs, Surgeries where epidural analgesia is used for postoperative pain relief.

Patients were allocated randomly to the two groups, Group-1 (bupivacaine) and Group-2 (ropivacaine) using a computer generated random numbers table when they were received in the preoperative area. An anesthesiologist not involved in the study prepared the syringes containing either bupivacaine or ropivacaine.

Group-l (n=30): received 20 ml Inj.Bupivacaine 0.25% on each side of the abdomen.

Group-2 (n=30): received 20 ml Inj.Ropivacaine 0.375% on each side of the abdomen.

After randomization, Group 1 received 20 ml 0.25% bupivacaine (10 ml of 0.5% bupivacaine+ 110 ml of sterile water) and Group 2 received 20 ml

0.375% ropivacaine (10 ml of 0.75% ropivacaine + l0 ml of sterile water) on each side.

The following monitoring methods were used are Six channel ECG connected- Leads II & V5 were monitored, Non invasive blood pressure monitor, Pulse oximetry and base-line heart rate, mean blood pressures, and oxygen saturation were recorded.

Technique of Tranversus abdominis plane (tap) block.

All surgeones were performed under general anesthesia, endotracheal intubation and controlled ventilation. Anesthesia was induced with inj. Propofol 2 mg/kg iv, Inj.Fentanyl 1-2 mcg/kg, lnj. Midazolam l mg iv, endotracheal intubation was facilitated with lnj.Vecuronium 0.1 mg/kg iv and maintained with oxygen and nitrous oxide (50:50) sevoflurane one MAC and intermittent doses of vecuronium. lnj.ketorolac 30 mg IM is given twice daily first dose being 30 mins prior to performing the block.

- At the end of the surgical procedure and before extubation the TAP block is performed under ultrasound guidance. The anaesthesiologist performing the block was blinded from the local anaesthetic drug that was being used. After skin preparation with the antiseptic, the USG probe (Sonosite, Bothell, WA) transducer with a frequency of 5-10 mHz is covered with a sterile sleeve.

The transducer probe placed in the anterior axillary line between the iliac crest below and the costal margin above, the following structures can be seen from superficial to deep-skin, subcutaneous tissue, the external oblique muscle, internal oblique muscle, the transverses abdominis muscle, peritoneum and bowel loops. Once the transversus abdominis plane is identified between the internal oblique and transversus muscles; a 23G spinal needle is inserted, the needle tip was visualised using the ultrasound probe and 20 ml of the study drug is injected after negative aspiration of blood while looking for the local spread of the drug in the plane between internal oblique and transversus muscle using USG. Block is repeated on the opposite side. After the block, neuromuscular blockade is adequately reversed with lnj.Neostigmine and Inj. glycopyrolate and the patient is extubated and shifted to post anesthesia care unit (PACU).

Parameters observed. The heart rate mean arterial pressure and oxygen saturation, pain score using numerical rating scale and sedation score using Ramsay sedation score were monitored at every fifteen minute interval for the first hour and at the end of second hour in the post anesthesia care unit.

For the first 24 hour period in the ward the pain scores and sedation scores were noted at 4th hour, 8th hour, 12th and 24th hour. The time of Requirement of rescue analgesia and the number of rescue analgesic doses were also recorded.

Pain score is assessed using numerical rating scale (Fig. 1).

The Ramsay sedation score is used to monitor sedation

Ramsay Sedation Score[3]

1 = anxious and agitated

2 = cooperative and tranquil

3 = drowsy but responsive to command

4 = asleep but responsive to a glabellar tap

5 = asleep with a sluggish response to tactile Stimulation

6 = asleep and no response

Excessive sedation was defined as a score greater than 4/6. When the Pain score >4 as per numerical rating scale rescue analgesic Inj. Tramadol 50 mg iv was given to a maximum of three doses in 24 hours.

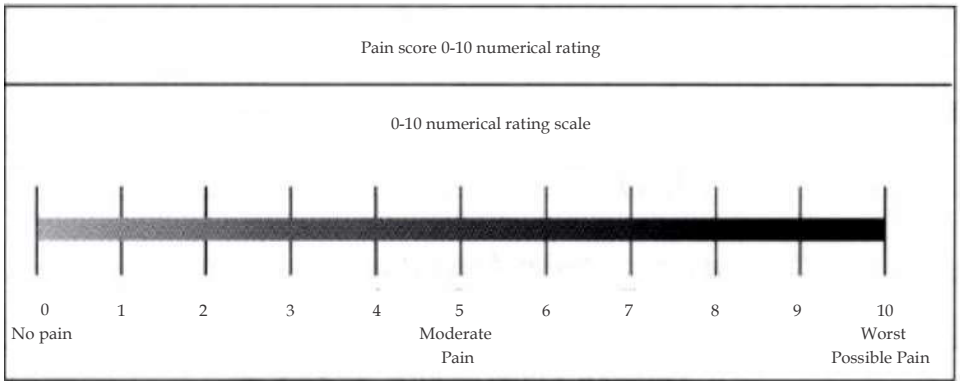

Fig. 1: Numerical rating scale

Statistical Analysis

Statistical analysis was done using statistical package for the social sciences (SPSS) 1.5 software. Data were expressed as mean standard deviation or numbers and percentages. P value less than 0.05 was considered significant. The categorical variables were compared using chi square test. The physiological parameters were compared using independent samples test. The pain scores and sedation scores were compared using Mann whitney test and chi square test respectively. The duration of analgesia was analysed with independent samples test. The total number of rescue analgesics used was analysed using chi square test.

Results

All the sixty patients included in the study were randomly divided into 30 patients in each group.

Table 1: Demographic data in study

Varibles	Group-1 (n=30) Mean (SD)	Group-2 (n=30) Mean (SD)	p-value
Age (years)	42.4 (8.1)	41.8 (8.2)	0.93
Weight (kgs) (kg/sqmetre)	59.27 (11.16)	60.73 (13.54)	0.64
Male	3 (10.0%)	8 (26.7%)	0.09
Female	27 (90%)	22 (73.3%)	

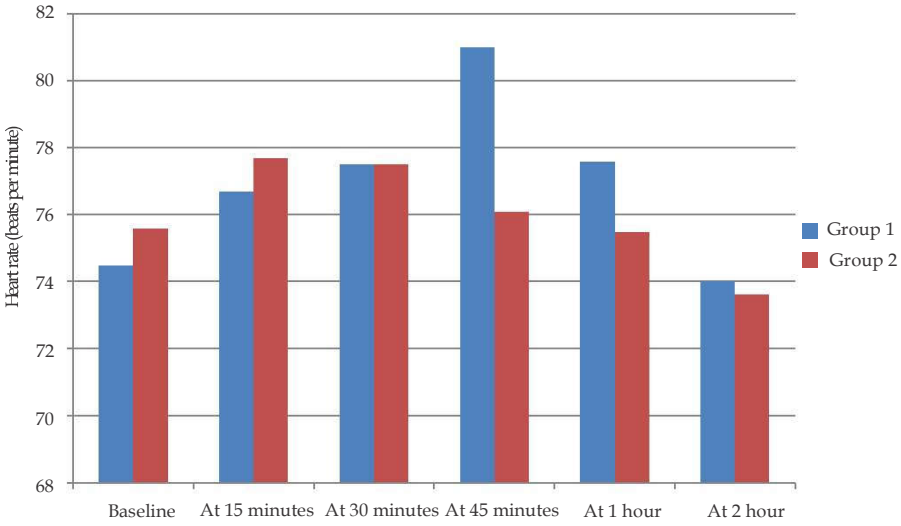

Fig. 2: Comparison of mean heart rate among both the groups at various intervals

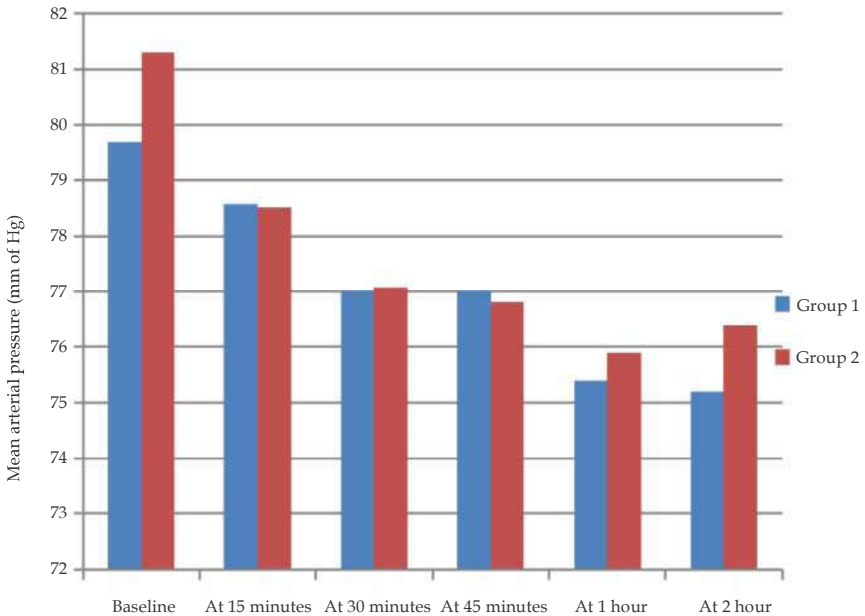

Fig. 3: Comparison of Mean arterial pressure among both the groups at various intervals

There were no significant differences between the two groups with respect to age, weight and gender (Table 1).

There was no significant differences in observed physiological variables of heart rate, mean blood pressure and percentage oxygen saturation in between the groups at various time intervals (Fig. 2).

There was no significance observed in pain scores or sedation scores monitored at different time intervals in between the groups (Fig. 5).

There was no significance observed in total duration of analgesia time for pain score >4 (Fig. 7).

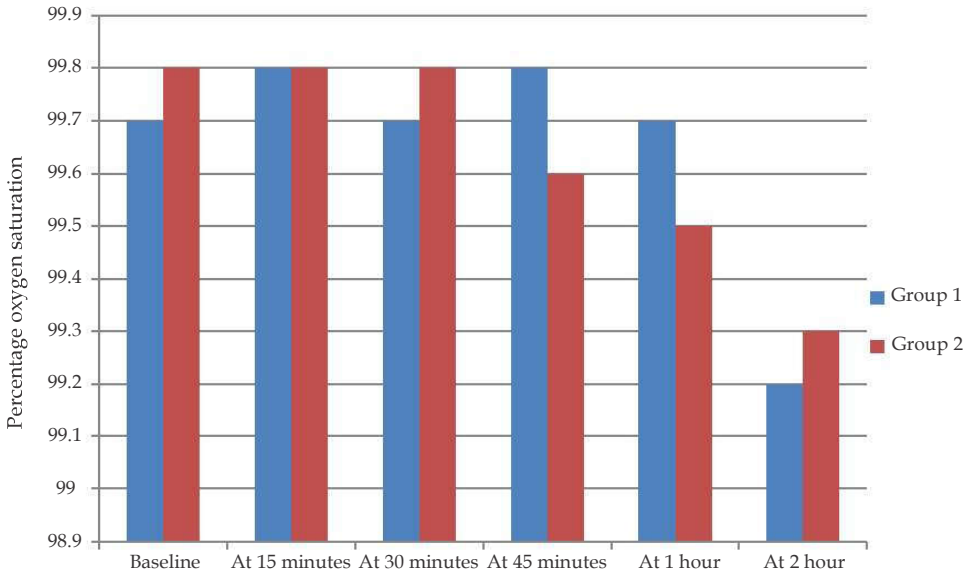

Fig. 4: Comparison of Mean Percentage oxygen saturation among both the groups at various intervals

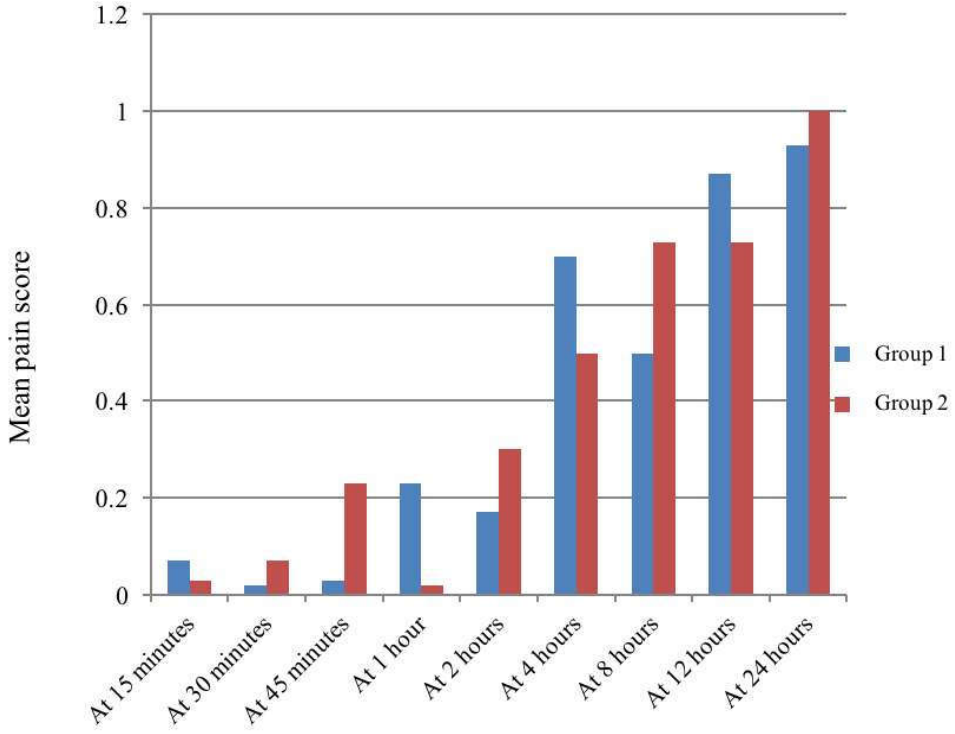

Fig. 5: Pain score and sedation score

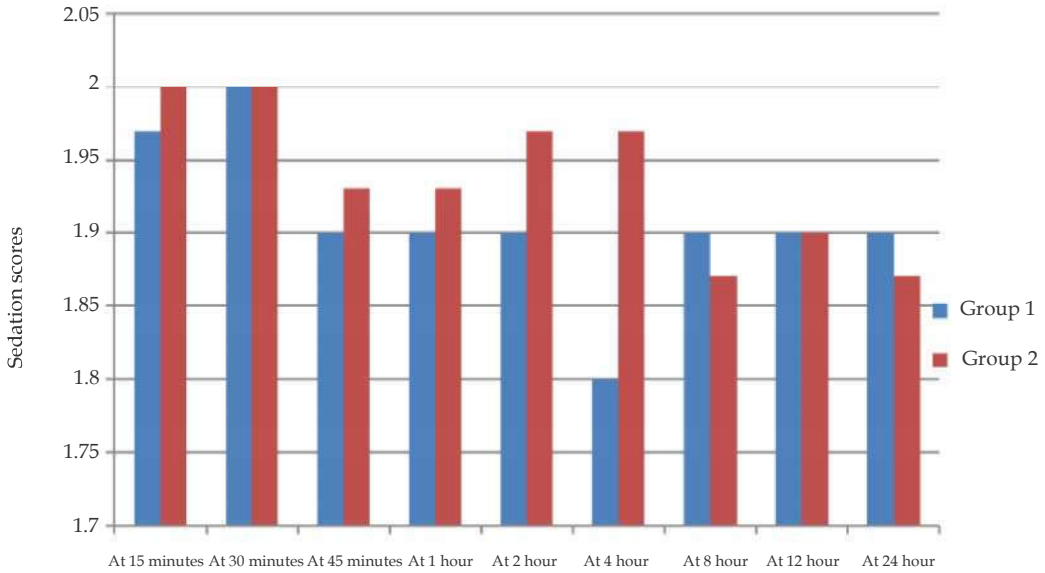

Fig. 6: Comparison of Mean Sedation scores among both the groups at various intervals

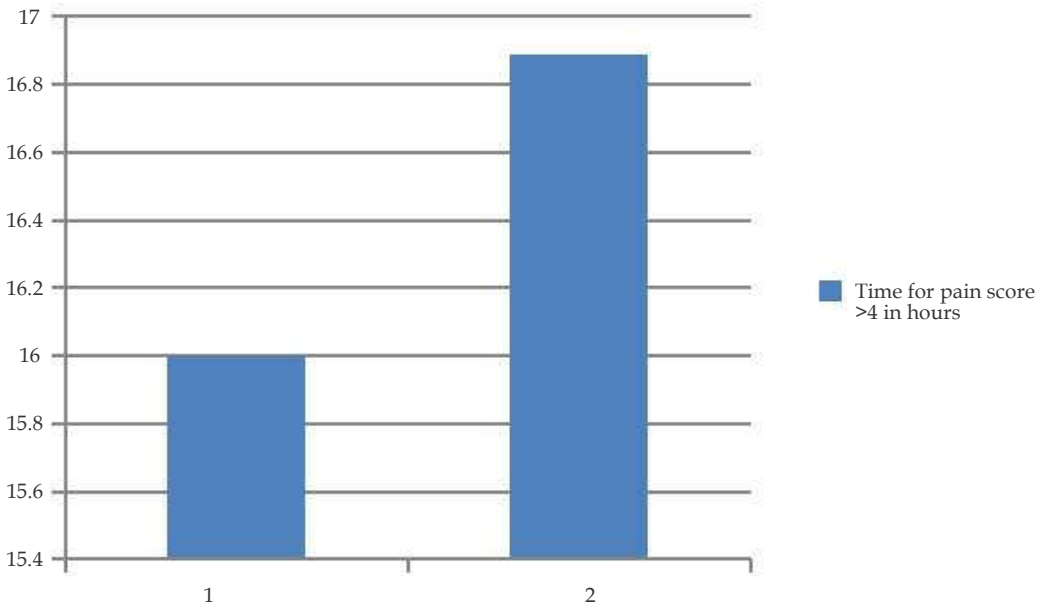

Fig. 7: Comparison of Mean Time for pain score >4 (in hours) among both the groups

Table 2: Comparison of total number of rescue analgesics in number of patients in both the groups

	Group 1	Group 2	p value
Number of rescue analgesics used in number of patients (%)	23(76.7)	21(70.0)	0.25
Rescue analgesics used once in number of patients (%)	7(23.3)	9(30.0)	0.68

There was no significance observed in number of rescue analgesics required in between the groups (Table 2).

Discussion

A substantial component of pain is experienced by patients after abdominal surgery which is derived from abdominal wall incision. The abdominal wall consists of three muscle layers the external oblique, the internal oblique and the transverses abdominis and their associated fascial sheaths. The central abdominal wall also includes the rectus abdominis and its associated facial sheath. This muscular wall

is innervated by nerve afferents that coarse through the transverses abdominis neuro fascial plane.

Table 3: shows various studies in correlation

Study	Local anaesthetic Solution	Duration of analgesia by TAPB
McDonnell (2007)[4]	Levobupivacaine 3.75 mg/ml (20 ml) bilaterally	24 hrs
McDonnell (2008)[5]	Ropivacaine 7.5 mg/ml (15-20 ml) bilaterally	6-12 hrs
Carney (2008)[6]	Ropivacaine 7.5 mg/ml (15-20 ml) bilaterally	48 hrs
El-Dawlatly (2009)[7]	Bupivacaine 5 mg/ml (15 ml) bilaterally	24 hrs
Niraj (2009)[8]	Bupivacaine 5 mg/ml (20 ml)	24 hrs
Belavy (2009)[9]	Ropivacaine 5 mg/ml (20 ml) bilaterally	24 hrs

Compared to regional analgesia, the advantages of the TAP block are absence of sympathetic and motor block and avoidance of possibility of damage to spinal cord structures. The transversus abdominis plane is the fascial plane between the internal oblique and the transversus abdominis muscles. The deposition of local anaesthetic in this plane has shown to reliably produce block that extends from T 10 dermatome to L 1 dermatome and therefore is suitable for lower abdominal surgery. When we directly visualise all anatomical structures, the needle, and the spread of local anaesthetic by ultrasound guidance, it may be associated with an increased margin of safety and optimal block qualities. Also, obese patients, post lower abdominal surgeries are often put on deep vein thrombosis (DVT) prophylaxis, and epidural catheter if present, needs removal after timing with the DVT prophylactic dose. The provision of TAP block avoids all these problems and also leads to improved patient comfort. Adequate pain relief after abdominal surgery encourages the patient to have optimum respiratory function (by doing manoeuvres like incentive spirometry), avoiding complications like basal lung atelectasis.[10]

In many studies which were conducted in recent times, TAP blocks have been described as an effective component of multimodal postoperative analgesia for a wide variety of abdominal procedures including large bowel resection, open/ laparoscopic appendectomy, cesarean section, total abdominal hysterectomy, abdominal wall hernia, open gastrectomy, laparoscopic cholecystectomy, open prostatectomy, renal transplant surgery, abdominoplasty with/without flank liposuction, and iliac crest bone graft.[11] Most reports demonstrate the efficacy of TAP blocks by highlighting some combination of reduced postoperative opioid requirement, lower pain scores, and/or reduction in opioid-related side effects.

Petersen *et al.*[12] reviewed 7 randomized, double-blinded, clinical trials of both landmark-based (n = 3) and ultrasound-guided (n = 4) TAP blocks for managing postoperative pain after abdominal surgery with incisions below the level of the umbilicus. All 7 studies compared pain-related outcomes with TAP blocks as part of a multi-modal postoperative analgesic regimen. Morphine PCA ± acetaminophen ± nonsteroidal anti-inflammatory drugs was most commonly used to complement TAP blocks. In one study, intrathecal morphine was also part of the analgesic regimen. A meta-analysis of these 7 studies (180 cases and 184 controls) demonstrated an average reduction in 24 hour morphine consumption of 22 mg (95% confidence interval: −31 mg to −13 mg) in favor of TAP block patients compared with standard management. Furthermore, TAP blocks were associated with reduced early postoperative visual analog scores (VAS) both at rest and during mobilization in 4 of the 7 studies (1 study did not record VAS scores). Postoperative sedation, as well as postoperative nausea and vomiting (PONV), was marginally reduced in patients with TAP blocks.

In a separate meta-analysis using 4 of the 7 studies reviewed by Petersen et al[12]., Siddiqui *et al.*[13] also demonstrated a morphine-sparing effect of TAP blocks in the first 24 hours after surgery. Similarly, another meta-analysis by Charlton *et al.*, which reviewed 236 participants from 5 studies (including landmark- and ultrasound-guided TAP blocks), demonstrated a significant reduction in 24 hour morphine requirements (average –22 mg, 95% confidence interval –38 mg to –6 mg) in TAP block patients compared to controls.

It has also been found that the analgesic effect of TAP block persists for atleast 24 h postoperatively and the block could be considered an integral part of multimodal analgesic strategy to control residual pain.

The TAP block will also reduce the use of morphine and its complications like nausea, vomiting, sedation, and especially respiratory depression, in obese. Hence, it also ensures that the patient can be shifted to the ward from the postoperative intensive care unit much earlier, since the complications due to opioid consumption is avoided.

Different techniques have been described in the

performance of transverses abdominis plane (TAP) block. In current study we used the ultrasound guided approach, the needle was inserted in the lumbar triangle of Petit to reach the transverses abdominis plane. Although we did not encounter any complications during TAP blocks procedure, the true incidence of complications such as systemic toxicity, vascular or visceral injury were still unknown. It is conceivable that the needle visualization might reduce the incidence or potential for complications, but studies confirming this statement is lacking.

In current study we compared the analgesic efficacy of Bupivacaine 0.25% (total dose 100 mg) with Ropivacaine 0.375% (total dose of 150 mg) in TAP block for patients undergoing laparoscopic surgeries. In our study both. Bupivacaine and ropivacaine provided equally effective analgesia with TAP block till 24 hours after the block. There is also no significant difference in hemodynamics and sedation scores in between the groups. In both the groups the mean, duration of time taken for the pain score to be >4 (moderate pain) by numerical rating scale was around 15 hours after the block. Only seven patients (23.3%) in bupivacaine group and nine patients (30.0%) in ropivacaine group received the rescue analgesic once. Regarding the duration of analgesia both the drugs provided equally effective analgesia till the end of observation period i.e 24 hours post operatively.

In a study by McDonnell Gerald *et al.* compared ropivacaine 0. 75% with saline in TAP block for caesarean delivery they found that patients who have undergone TAP block with ropivacaine had reduced 8 hour morphine requirement and a longer time to first patient controlled analgesia-morphine request. This study supports the current study since analgesia from TAP block is superior to saline group.[4]

Rafi described the use of 20 mL of "a local anaesthetic agent" for each side requiring analgesia.[14] Subsequently, McDonnell *et al.* reported the use of 20 mL of 0.5% lidocaine for each side in healthy volunteers.[4]

Over the past 3 year, a series of studies have highlighted the value of efficacy of various local anaesthetic agents in Transversus Abdominis Plane (TAP) Block, after the initial description of the technique by Rafi.[14] Transversus Abdominis Plane Block as described by Rafi involves identifying the neurovascular plane of the abdominal musculature and injecting a local anaesthetic agent therein. He performed abdominal field block via the lumbar triangle without any untoward sequelae.

With the technique of ultrasound guided nerve blockade gaining popularity, this technique was also applied to injection of bupivacaine and ropivacaine in the TAP block. However injection via Petit's triangle using double POP technique resulted in reliable deposition into the transversus abdominis plane. Moreover it may not always be possible to use ultrasound guided techniques for administering TAP Block where such facilities are not available.

The landmark-based technique for the TAP block, have been performed without difficulty in the children.[15] Alternative approaches to the TAP block using ultrasound guidance have recently been described in a case series of children undergoing inguinal hernia repair.[11] The optimal approach remains to be demonstrated. There are now a variety of techniques for the TAP block and the analgesic merit of each is being elucidated in ongoing studies. Although it is possible to ultrasonically visualize the 3 muscle layers of the abdominal wall, there is variation in these muscle layers that can restrict the use of ultrasound over the triangle of Petit.[15] As a result, the needle insertion point as described in the ultrasound studies, which is dependent on the adequate identification of the 3 muscle layers, can vary. In the current study, USG guided TAP Block is performed following the induction of general anesthesia.

This will alter the location of the injectate as will the angle of the needle insertion to skin, which contrasts to the landmark approach's description. Although there is an ever-increasing access to ultrasound, it is far from universal and there is a continuing interest in landmark techniques.[16] Moreover ultrasound machine may not be available at all places especially in peripheral health centers where the blind technique alone is the option for giving TAPB. 100% success rate with TAP block have been obtained using landmark technique for posterior approach of block.[14] To our knowledge till now no study has been performed to compare the efficacy of landmark versus ultrasound technique for posterior approach of TAP block.

TAP injection of local anaesthetic injection cephalad to the iliac crest likely involves T10–L1 nerve roots and implies that the technique may be limited to use in lower abdominal surgery.[17]

Sinha A *et al.* conducted a study to evaluate efficacy of Ropivacaine with dexmeditomidine versus ropivacaine with plain saline which concluded that addition of dexmeditomidine to local anaesthetics for performing TAP Block has provided adequate and longer duration of

analgesia and supported for early mobilization by providing continuous analgesia post operatively and also supports the current study.

Maitreyi Gajanan Mankikar, Shalini Pravin Sardesai, Poonam Sachin Ghodki *et al.* evaluated Sixty patients undergoing caesarean section under spinal anesthesia who were randomised to undergo TAP block with ropivacaine (n = 30) versus control group (n = 30) with normal saline, in addition to standard analgesia with intravenous paracetamol and tramadol. This study concluded that Mean requirement of tramadol in the first 24 h was reduced in US guided TAP block after caesarean section which supports the current study.[18]

In addition, a growing number of reports suggest that TAP blocks may also be a safe alternative to neuraxial blockade in patients who are anti-coagulated, coagulopathic, or in patients who would not tolerate the hemodynamic sequelae often associated with profound neuraxial sympathectomy.

The TAP block is an effective and safe adjunct to multimodal postoperative analgesia for abdominal surgery. Multiple studies have demonstrated its superiority over standard medical therapy for postoperative pain control. Limited data also suggest that in select patient populations, TAP blocks/catheters may provide comparable analgesia as well as patient satisfaction to epidural therapy. However, the data is less encouraging for patients who receive intrathecal morphine during C-section, where the addition of TAP blocks does not appear to improve postoperative pain control. Nonetheless, it may be a good alternative strategy for patients who are highly sensitive to opioids. Hence, current study was conducted using plain local anaesthetics for performing TAP Block for various surgeries.

D. Belavy, P.J. Cowlishaw, M. Howes *et al.* evaluated the analgesic efficacy of TAP block in patients undergoing caesarean delivery and concluded that the USG guided TAP block reduces morphine requirements after caesarean delivery when used as a component of a multimodal analgesic regimen which supports the current study.[9]

The benefit of adequate postoperative analgesia are clear and include a reduction in the postoperative stress response, reduction in postoperative morbidity, and in certain types of surgery, improved surgical outcome. Effective pain control also facilitates rehabilitation and accelerates recovery from surgery. Other benefits of effective regional analgesic techniques include reduced pain intensity, decreased incidence of side effects from analgesics and improved patient comfort.

In our experience, the TAP block has a fast learning curve and requires short performance time especially by an experienced anesthesiologist. However it is possible that different providers in different clinical circumstances may find obstacles to the routine implementation of a TAP block as part of a multimodal pain strategy to improve postoperative quality of recovery.

Conclusion

In our experience, the TAP block has a fast learning curve and requires short performance time especially by an experienced anesthesiologist. However it is possible that different s providers in different clinical circumstances may find obstacles to the routine implementation of a TAP block as part of a multimodal pain strategy to improve postoperative quality of recovery.

Our current study which is a prospective randomized double blinded study comparing the postoperative analgesic efficacy of ultrasound guided transverses abdominis plane block with bupivacaine and ropivacaine in laparoscopic surgeries showed that both (0.25%) bupivacaine and (0.375%) ropivacaine provided equally effective postoperative analgesia, better pain scores and required less doses of rescue analgesics in the first 24 hours duration after the block.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(4) (Part - II): 1275-1281
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.30

A Comparative Study of Caudal Analgesia with Bupivacaine Alone and Bupivacaine with Butorphanol in Pediatric Surgeries

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Abstract

Introduction: The assessment of pain in small children is often difficult to interpret as the most common sign of pain is crying which is also seen in a myriad of non pain full conditions. Epidural space in children favours rapid longitudinal spread of drugs and makes it effective in treating postoperative pain. *Aim:* The aim of this study was to evaluate the efficacy of caudal bupivacaine alone or in combination with butorphanol for postoperative analgesia in children undergoing infra-umbilical surgeries. *Materials and Methods:* A Simple Randamoized which includes 50 patients posted for urogenital operations such as herniotomy, orchidopexy, urethroplasty and CTEV Correction divided into two groups of 25 each. Group B received 0.25% plain bupivacaine and Group BB received 0.25% Bupivacaine with Butorphanol adjuvant. The effect of recovery from caudal blockade and duration of analgesia was compared and contrasted. *Results:* There were no significant changes in heart rate, blood pressure and oxygen saturation between two groups. Postoperative pain score was comparable in two groups in first eight hours, but it is significantly less in bupivacaine with butorphanol group which is statistically significant. There is a significant difference between the groups in the mean duration of analgesia with Group BB having a much longer duration compared to Group B. 3 patient in Group B and 5 patient in Group BB had nausea in postoperative period, which is statistically insignificant (p>0.05). No episodes of any other clinically significant postoperative complications were recorded. *Conclusion:* Butorphanol is considered to be a safe and effective adjuvant to Bupivacaine for caudal analgesia in children undergoing surgery below umbilicus.

Keywords: Bupivacaine; Butorphanol; Pediatric Surgeries

How to cite this article:

Shaik Salman, C Geetha. A Comparative Study of Caudal Analgesia with Bupivacaine Alone and Bupivacaine with Butorphanol in Pediatric Surgeries. Indian J Anesth Analg. 2019;6(4):1275-1281.

Introduction

Pain, as defined by international association for study of pain, is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. The mechanism of pain perception in pediatric[1] population is different and is complex and is not often adequately understood rather than emphasizing on the clinical evaluation alone; biopsychosocial perspective needs to be looked deeply while managing pain in this special

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Received on 23.05.2019, **Accepted on** 11.07.2019

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population. The assessment of pain in small children is often difficult to interpret as the most common sign of pain is crying which is also seen in a myriad of non painful conditions. There have been recent developments in the pediatric post operative pain management with emphasis of adequate treatment of pain early to prevent morbidity in this patient population. These developments are highly important in developing nations where the progress of anesthesia specialty has been non uniform and at a varied pace.

The various methods[2,3] of providing pain relief have some side effects which prohibit their use in children for eg. narcotics, because of their respiratory depression, the other analgesics which cannot be given for some time after general anesthesia due to the fear of vomiting and a spiration, the fear of the needles in the case of parentally administered analgesics. The regional anesthetic techniques significantly decrease post operative pain and systematic analgesic requirements. Caudal route was chosen for this study as it is one of the simplest and safest techniques in pediatric anesthesia with a high success rate. Epidural space in children favours rapid longitudinal spread of drugs and makes it effective in treating postoperative pain.

Caudal block is usually done after the introduction of general anesthesia an disused as an adjunct to intraoperative anesthesia as well as postoperative analgesia in children undergoing surgical procedures below the level of the umbilicus. Caudal analgesia can reduce the amount of inhaled and IV anesthetic administration, attenuates the stress response to surgery facilitates a rapid, smooth recovery, and provides good immediate post operative analgesia[1,3]. In order to decrease peri-operative analgesic requirements after single shot caudal epidural blockade, various additives, such as morphine, fentanyl, clonidine and ketamine with local anesthetics have been investigated.

The aim of this study was to evaluate the efficacy of caudal bupivacaine alone or in combination with butorphanol for postoperative analgesia in children undergoing infra-umbilical surgeries.

Materials and Methods

The present study is Simple Randamoized study at Osmania general hospital and Niloufer hospital, between August 2016-September 2017, who underwent lower abdominal and lower limb surgeries after obtaining institutional ethical committee and parental written informed consent.

Inclusion Criteria: Age groups 1-10 years, ASA grade I and II, Cases scheduled for operations such as urethroplasty, herniotomy, orchidopexy and CTEV correction.

Exclusion criteria: H/o of central nervous disease, sacral abnormalities, H/o of drug allergy, H/o of bleeding disorder AND skin infection at the site of block.

Patients were allocated by randomly in to two groups of 25 patients each.

Group B receive 0.25% plain Bupivacaine 1 ml/kg for caudal block.

Group BB 25 mcg/kg added to 0.25% bupivacaine 1 ml/kg.

In all children, age, body weight, and baseline vital parameters were recorded. History regarding previous anesthesia, surgery, any significant medical illness, medications and allergy was recorded. Complete physical examination, airway assessment and local examination of lower back were done.

Hemoglobin percentage, bleeding time, clotting time, blood sugar, urea, serum creatinine and urine analysis, USG. Patients were fasted for 4 hours and pre medicated with oral Midazolam 0.5 mg/kg 30 minutes before surgery. After applying standard monitors, an intravenous cannula was secured and Isolyte-p solution was infused to provide fluid during surgery. Injection Glycopyrrolate 0.01 mg/kg was administered intravenously as premedicant. General anesthesia was induced with Thiopentone sodium 5 mg/kg, 2% sevoflurane and Nitrous oxide in oxygen via mask.

Endotracheal intubation was facilitated by administering injection vecuronium bromide 0.1 mg/kg intravenously. After securing Endotracheal tube, patients were placed in left lateral position.

Procedure

After placing lateral position, skin of the back over the sacrum was scrub using povidone iodine solution, Under aseptic precautions, a short beveled 22 G needle was introduced proper position of needle confirmed by the pop sensed during penetration of sacro-coccygeal membrane of caudal epidural space, which was followed by whoosh test done using 0.5 ml of air after needle insertion negative aspiration of blood and cerebrospinal fluid, then 1 ml/kg of local anaesthetic agent 0.25% bupivacaine given to Group B and 0.25% Bupivacaine with Butorphanol adjuvant to Group BB was administered slowly.

After deposition of the drug in epidural space, patients were placed in supine position and anesthesia was maintained by 1% sevoflurane, 50% of Nitrous oxide plus 50% oxygen and top up doses of vecuronium bromide ($1/5^{th}$ of the loading dose of 0.1 mg/kg).

HR and blood pressure were recorded just before and after surgical incision and then every 5 min interval till the end of surgery, residual neuromuscular blockade was reversed and patients were transferred to the post operative ward.

Using the paediatric observations FLACC (face, legs, activity, cry, consolability) pain scale with its 0-10 score range, each patients pain intensity was assessed at the end of surgery and then every 30 min interval until the patient became fit to discharge from postoperative ward.

If the FLACC pain scale was 4 or more, rectal Paracetomol 20 mg/kg was administered.

Observations were continued for 24 hours. Complications such as postoperative nausea and vomiting (PONV), respiratory depression, urinary retention, hypotension and bradycardia were also noted. Respiratory depression was defined as a decrease in SpO_2 of less than 95% requiring supplementary oxygen. Hypotension was defined as fall of 20% mean arterial pressure from base line. Bradycardia was defined as HR below 80 beats/min for age 1 year and 60 beats/min for ages above 1 year. The parameters were compared in two groups and results subjected to appropriate statistical analysis are Hemodynamic parameters and Quality of postoperative analgesia effect.

Stastistical Analysis

All recorded data were entered using MS Excel software and analysed using spss 16 version software for determining statistical significance. Numerical variables were presented as mean and standard deviation (SD) and categorical variables were presented as frequency (%).

Student's t test was used for between-group comparisons between categorical variables.

A p value of <0.05 was taken to be significant and a p value of <0.001 was considered highly significant.

Results

This study includes 50 patients posted for urogenital operations such as herniotomy, orchidopexy, urethroplasty and CTEV Correction divided into two groups of 25 each. Group B received 0.25% plain bupivacaine and Group BB received 0.25% Bupivacaine with Butorphanol adjuvant. The effect of recovery from caudal blockade and duration of analgesia was compared and contrasted.

Table 1: Patient characteristics and clinical parameters

Patient details	Group B	Group BB
Age (in years)	3.72	3.70
Weight (in Kg)	12	12
Gender M:F Ratio	23:02	23:02
Duration of Anesthsisa (in min)	35	31
Baseline Heart Rate (Beats per min)	106.8	104
Baseline map	72.9	75

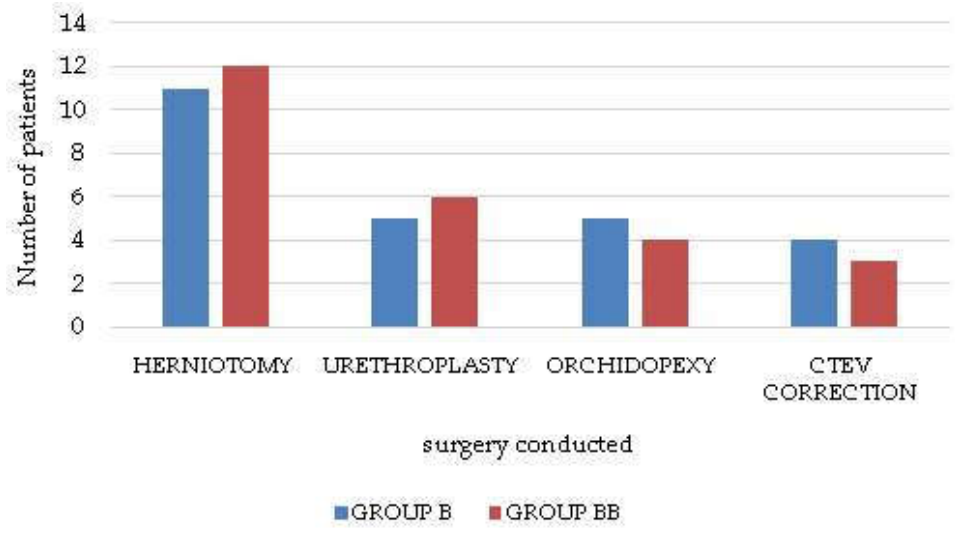

Fig. 1: Nature of Operations

Table 2: Haemodynamic changes during surgery

	Group B		Group BB		Standard deviation for B group		Standard deviation for BB group		*p* value	
	HR	MAP	HR	MAP	HR	MAP	HR	MAP	HR	MAP
Base line	104	75	106.80	72.90	8.3	4.6	8.1	5.7	>0.10	>0.10
After incision 5 min	91	70	97.7	68.9	7.7	4.3	8.3	4.6	>0.05	>0.10
10 min	91.3	70	93.5	68.1	6.9	4.9	6.8	5.1	>0.06	>0.07
20 min	89	71	91.2	68.2	6.48	5.3	6.01	5.5	>0.07	>0.10
30 min	88	71	89.5	68.2	5.5	5.8	5.45	5.7	>0.10	>0.10
60 min	85	70	86.5	70	5.3	4.4	5.25	4.7	>0.06	>0.07
90 min	82	72	85	68.1	5.1	5.9	5.1	5.2	>0.05	>0.10

Table 3: Postoperative pain scoring in two groups FLACC (face, legs, activity, cry, consolability) Score

Post Operation	Group B		Group BB		*p* Value
	Mean	SD	Mean	SD	
0 hour	0	0	0	0	
2 hour	1.4	0.49	1.12	0.33	0.0219
4 hour	2.8	0.9	2.2	0.41	0.0039
6 hour	4.38	1.35	3.72	0.79	0.0401
8 hour	7.2	0.76	5.44	1.04	< 0.0001

Table 4: Post operative complications

	PONV	Respiratory Depression	Urinary Retention	Hypotension	Bradycardia
Group B	3	Nil	Nil	Nil	Nil
Group BB	5	Nil	Nil	Nil	Nil

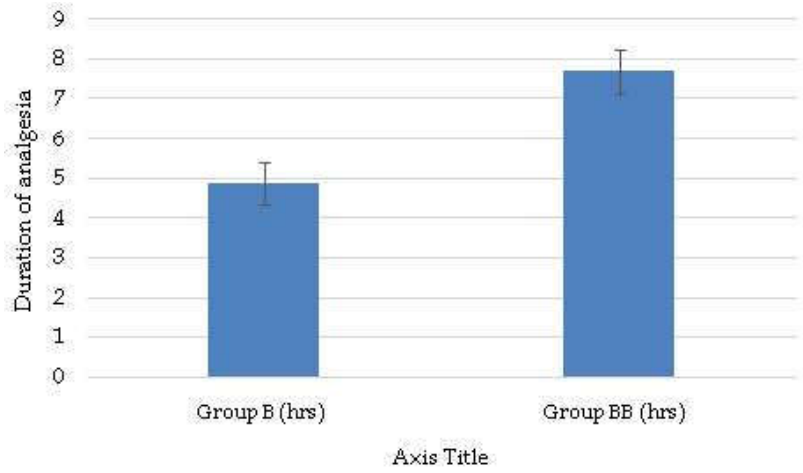

Fig. 2: Duration of analgesia

The calculated *p* value is >0.10, so this is statistically not significant. There were no differences between the two groups in age, weight, gender, duration of anesthesia, baseline blood pressure and heart rate (Table 1).

The preoperative, intraoperative and postoperative haemodynamic changes between the groups were comparable and were not statistically significant and therapeutic interventions were not required. The calculated *p* value is < 0.01 to 0.05. Hence, it is significant (Table 2).

Postoperative pain score was comparable in two groups in first eight hours, but it is significantly less in bupivacaine with butorphanol group which is statistically significant (Table 3).

There is a significant difference between the groups in the mean duration of analgesia with Group BB having a much longer duration compared to Group B [*p* value <0.0001] (Fig. 2).

The table 4 shows 3 patient in Group B and 5 patient in Group BB had nausea in postoperative period, which is statistically insignificant (*p*>0.05).

No episodes of any other clinically significant postoperative complications were recorded.

Discussion

Over the recent years, the concept of providing adequate postoperative analgesia in pediatric patients is well established, however, various methods showed side-effects limiting their use such as respiratory depression with IV opioids. With a high success rate, caudal analgesia was proved to be a simple and effective technique in children.

Caudal epidural analgesia is one of the most popular and commonly performed regional blocks in pediatric anesthesia. It is a reliable and safe technique that can be used with general anesthesia for intra and postoperative analgesia in patients undergoing abdominal and lower limbsurgeries. The main disadvantage of caudal anesthesia is the short duration of action after a single injection of local anesthetic solution. Specific character of caudal block in pediatric age group.

Increased fluidity of epidural fat Increased diffusion of local anesthetic up to 6-7 Year of age.Excellent blockade after caudal anesthesia can be achieved up to 6-7 Year of age. The volume prescription scheme of Armit age that was published many years ago still remains the most dependable, asfollows: 0.5 mL/kg: All sacral dermatomes are blocked. The upper limit of anesthesia is at least Midthoracic. When 1.25 mL/kg is injected, excessive rostral spread (above T4) canoccuritis therefore preferable not to administer more than 1 mL/kg of local anesthetic. In present study both patients receive 0.25% bupivacaine 1 ml/kg as per armitage formula. An ideal combination of local anesthetic and adjuvant should provide adequate intraoperative anesthesia, good extended postoperative analgesia without prolonging the motor blockade or producing adverse hemodynamic or respiratory consequences.

Different additives have been used in order to improve the duration of action as well as the quality of analgesia of the local anesthetic used in the single shot caudal block technique such as opioids, epinephrine, clonidine, ketamine and neostigmine. The aim of this randomized control study was to compare the duration of postoperative analgesia, sedation, as well as the incidence of any side effect of caudally administered butorphanol to bupivacaine in pediatric patients undergoing lower abdominal and lower limb surgeries.

There has been a study by Lawhorn CD, Stoner JM, Schmitz ML, Brown RE Jr, Stewart FW, Volpe P, Shirey R4 in the literature of butorphanol use for caudal anesthesia/analgesia in pediatric population undergoing genitourinary procedure. It was found that requirement of rescue analgesia in post anesthesia care unit and total numbers of morphine doses administered were significantly less in patients in whom butorphanol 30 µg/ kg was added to bupivacaine in caudal epidural analgesia. Our study's findings are consistent with their findings but the differences from the present study were: they had used 0.25% bupivacaine with 1:200,000 epinephrine and caudal epidural analgesia along with general anesthesia.

In another study, by Ohta K, Katsuno M, Kawana S, Namiki A5 butorphanol has also been used in patients of cerebral palsy undergoing elective orthopedic operations and it was found to be safe and useful for postoperative pain control in children.

One of the interesting findings of the present study is the paucity of side effects associated with caudal butorphanol as mentioned in the literature. Its high lipid solubility and high affinity for opioid receptors are additional factors that contribute to the paucity of side effects with its use.

High lipid solubility increases diffusion in the spinal cord and limits the amount of drugs remaining in the CSF, capable of reaching the brainstem where side effects are detected. In a recent trial it has been demonstrated that there were less chances of complication or side effects with caudal analgesia as compared to parenteral use of analgesics or penile block in patients for circumcision.

For the pediatric caudal epidural analgesia, other opioids like morphine, buprenorphine, fentanyl and tramadol have been used. In a study by Gaitini LA, Somri M, Vaida SJ, Yanovski B, Mogilner G *et al*. added fentanyl to bupivacaine in caudal epidural block to observe changes in plasma catecholamine levels in postoperative period. Addition of fentanyl citrate to bupivacaine in caudal epidural block in children did not influence the stress response to surgery, nor did it improve the analgesic intensity of the caudal block as described in literature.[6]

Drug like clonidine has also been used in a study by Lee JJ, Rubin AP but its use in caudal analgesia resulted in significant prolongation of duration of postoperative analgesia, with the side effects like bradycardia and urinary retention.[7] Veena Chatrath, Sarabjit Kaur. compared efficacy of caudally

administered clonidine with that of butorphanol, the mean duration of analgesia was statistically longer (p value < 0.01) in the group Butorphanol (822.0 ± 217.41 min) than Clonidine group (745.4 ± 216.69 min). The total number of 'rescue' analgesic doses required in the first 24 hrs was lesser in group B (0.80 ± 0.41) and C (0.96 ± 0.45).[8]

Caudal epidural use of morphine, buprenorphine or butorphanol in a study by Ohta K, Katsuno M, Kawana S, Namiki A. did not increase the frequency of side effects such as nausea, vomiting etc., and need for rescue analgesia was also less in these patients within 24 hours after operation.[5]

The use of tramadol in combination with 0.25% bupivacaine resulted in a significant increase in the analgesia time in study by Senel AC, Akyol A, Dohman D, Solak M. In a study by R. Pauranik, P. Gupta., added ketamine 5 mg/kg caudally and compared it with butorphanol 20 µg/kg. The study concluded the butorphanol provided superior analgesia for a longer duration than with ketamine.[10]

In our study, a total of 50 patients in the age group of 2-8 years were divided randomly in two groups (n=25). There were no differences between two groups with regard to demographic profile. Mean age in group B (receiving bupivacaine alone) was 3.72 and in group BB (receiving bupivacaine plus butorphanol) was 3.70. Sex ratio was also comparable, in both group B and group BB M:F=23:02.

During the study in both groups heart rate, blood pressure (SBP, DBP, MAP) were measured. The preoperative, intraoperative and postoperative haemodynamic changes between the groups were comparable and were not statistically significant (*p* value >0.05) and therapeutic interventions were not required.

The post operative pain score was comparable in two groups at 0,2,4,6,8 hrs, rescue analgesia was given with FLACC score more than 4. The score in butorphanol group was significantly lower with mean (5.44 ± 1.04) at 8 hrs while group B has mean (7.2 ± 0.76) with *p* value<0.0001.

In the present study the duration of analgesia is significantly longer in group BB. The mean duration of analgesia of group B was (4.875 ± 0.54 hrs) and that of group BB was (7.7 ± 0.55 hrs) with *p* value <0.0001 which is highly significant. In a study by Vinita Singh, Ashish Kanaujia and G. P. Singh. Compared efficacy of bupivacaine plus butorphanol with plain bupivacaine and plain butorphanol, in this study Sixty ASA physical status I and II patients of either sex aged 1–10 year were randomized to one of three groups. Group L received 1 ml/kg of 0.25% bupivacaine; Group B received 1 ml/kg of 25 µg/kg butorphanol diluted in normal saline; and Group LB received 1 ml/kg of 25 µg/kg butorphanol in combination with 0.25% bupivacaine, in caudal epidural anesthesia. Hemodynamic variables (HR and MAP) and respiratory rate were monitored in all patients. Sedation score, pain score and requirement of rescue analgesia were recorded at preset time intervals along with postoperative complications.[4] There was no difference among the groups regarding sedation scores, requirement of rescue analgesia and postoperative complications. Mean duration of analgesia was maximum in group BL (14.5 ± 3.5 hr, *p*<0.001), than in group L (8.8 ± 4.8 hr) and group B (6.8 ± 2.9 hr). Conclusion of this study is comparable with our study, addition of 25 µg/kg butorphanol to bupivacaine resulted in superior analgesia with a longer period compared with caudal bupivacaine and butorphanol alone, without an increase of side effects.

Kundan Gosavi, Nilam Virkar *et al.* Compared caudal Butarphanol and Clonidine as an Adjuvant to Bupivacaine.[5] This study compared duration of analgesia and side effects of butorphanol and clonidine in caudal block along with general anesthesia in this double blind, randomised, controlled prospective study. 60 ASA grade I children of 20 to 10 years posted for infraumbilical abdominal or genitor urinary surgeries were randomly divided in three groups to receive bupivacaine 0.25% 1 ml/kg with either normal saline 1 ml (group B, control) or with butorphanol 25 mcg/kg (group BB) or clonidine 1 mcg/kg (group BC) in 1 ml by caudal route. Intraoperative and postoperative haemodynamic and respiratory parameters were recorded. Quality of analgesia was assessed using modified objective pain score. Results were analysed using Student's t test and chi- square test. Both BB and BC group showed better haemodynamic profile than group B. bradycardia and hypotension were at minimum at this dose of clonidine. Clonidine group had duration of analgesia (460.6 ± 45.86 mins) significantly longer than BB (378.8 ± 13.31 mins) and B group but also had higher sedation score in immediate postoperative period and can be a good option in paediatric neuraxial blockade. Though we did not compare with clonidine our results are similar to group B, group BB where duration of analgesia is significantly longer in group with butorphanol.

Complications such as postoperative nausea and

vomiting (PONV), respiratory depression, urinary retention, hypotension and bradycardia were also noted. Respiratory depression was defined as a decrease in SpO_2 of less than 95% requiring supplementary oxygen. Hypotension was defined as fall of 20% mean arterial pressure from base line. Bradycardia was defined as HR below 80 beats/min for age 1 year and 60 beats/min for ages above 1 year. In present study 3 patient in Group B and 5 patients in Group BB had nausea in postoperative period, which was statistically in significant ($p > 0.05$). There has been no other side effects like respiratory depression, hypotension, bradycardia or urinary retention. Although the children in butorphanol group has higher sedation than with plain bupivacaine group.

Conclusion

Caudal Butorphanol 25 µg/kg, combined with 0.25% Bupivacaine 1 ml/kg, provides longer duration of postoperative analgesia, less requirement of rescue analgesia, stable intraoperative vitals, in significant changes in hemodynamics intraoperatively and fewer postoperative side effects. Hence Children remained calm, quiet and minimally sedated but easily arousal. Thus, Butorphanol is considered to be a safe and effective adjuvant to Bupivacaine for caudal analgesia in children undergoing surgery below umbilicus.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(4) (Part - II): 1283-1292
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.31

Proseal Laryngeal Mask Airway v/s Endotracheal Intubation for Gynaecological Laparoscopic Surgeries

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Abstract

Background: Proseal LMA (PLMA), is the latest entrant in the family of LMA designed for positive pressure ventilation and protection against aspiration. These features of PLMA is especially useful in laparoscopy surgeries, which is widely preferred these days and can act as an alternative to Endotracheal tube (ETT). Rigid laryngoscopy during endotracheal intubation (gold standard for safe glottic seal) causes haemodynamic responses which adds to the stress of pneumoperitoneum in laparoscopic surgeries, unlike Proseal LMA which is a supraglottic device and less invasive. *Aim:* To compare the efficacy and safety of Proseal Laryngeal Mask Airway with Portex endotracheal intubation in gynaecological laparoscopic surgeries under general anesthesia. *Setting and Design:* A prospective, randomised study was conducted in 60 females, ASA-I & ASA-II patients undergoing laparoscopic gynaecological surgery under general anesthesia. Ethical clearance and written consent was obtained before the study. Patients were randomly divided into two groups-PLMA (P) and Endotracheal tube (E) depending on the device used to secure airway. Ease, attempt of of insertion, haemodynamic parameters and postoperative complications were studied. *Results:* Insertion rate was 100% in both the groups. Vital parameters like heart rate, systolic bp, diastolic bp and mean arterial pressure were relatively lower with Proseal LMA at 1 min, 3 min and 5 min and after removal as compared to ETT. The difference was statistically significant. There was no significant difference in End tidal CO_2, SpO_2, during baseline, insertion and removal of device, before and after pneumoperitoneum, also in airway pressure during insertion, before and after pneumoperitoneum. Perioperative complication was higher with endotracheal tube. *Conclusion:* The Proseal LMA offers a safe and effective alternative for airway management in patients undergoing gynaecological laparoscopic procedures under general anesthesia.

Keywords: Proseal Laryngeal Mask Airway; Endotracheal Intubation; Laparoscopic Surgeries,

How to cite this article:

Amruta Changdeo Patil, Sonal S Khatavkar, Rosly R Jacob *et al*. Proseal Laryngeal Mask Airway v/s Endotracheal Intubation for Gynaecological Laparoscopic Surgeries. Indian J Anesth Analg. 2019;6(4):1283-1292.

Introduction

Conventional open surgeries are now progressing to keyhole laparoscopic surgeries. The wide use of laparoscopy has revolutionised open surgical procedure. laparoscopy has increased success rates with decreased morbidity in surgical patients. Few disadvantages due to pneumoperitoneum mainly concerns anesthesia techniques. Thus, different anaesthetic techniques are being practised by modifying use of LMA. LMA has challenged the standard ETT used during general anesthesia.[1]

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Received on 18.04.2019, **Accepted on** 27.06.2019

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Till date, the cuffed tracheal tube was considered as the gold standard for providing a safe glottic seal, especially for laparoscopic procedures under general anesthesia. The disadvantages of tracheal intubation, which involves rigid laryngoscopy, are in terms of concomitant haemodynamic responses and damage to the oropharyngeal structures at insertion. Postoperative sore throat is also a serious concern. This precludes the global utility of the tracheal tube and requires a better alternative.[2]

The Proseal LMA was introduced by Dr. Archie Brain in 2000.[3] The Proseal Laryngeal Mask Airway (PLMA), the latest entrant in the family of LMA, is a useful tool in airway management.[4]

Proseal LMA which is a supraglottic device and less invasive is considered to cause lesser haemodynamic response.[5] The Proseal laryngeal mask airway (PLMA) has a dorsal cuff which pushes the mask anterior to provide a better seal around the glottic aperture and permits high airway pressures without leak. The drain tube parallel to the ventilation tube permits drainage of passively regurgitated gastric fluid.[2] The built in bite block reduces the chances of damage to the device by inadvertent biting by the patient.[1]

In laparoscopic surgeries, increased abdominal pressure from pneumoperitoneum requires higher airway pressures for adequate pulmonary ventilation, for which the PLMA has proved to be adequate in previous studies.[6] PLMAs have been the subject of study by various authors over many years.

From 1981, Dr. Archie Brain's first prototype LMA to the year 2000, a variety of special LMA were released with PLMA being the latest. Since then many studies, like in 2002, J. Roger Maltby, Michael T. Beriault, Neil C. Watson *et al.* conducted, 'The LMA-ProSeal is an effective alternative to tracheal intubation for laparoscopic cholecystectomy', however further studies were required. In 2005, Cook, Lee and Nolan analyzed and summarized the published literature relating to the PLMA. They found that compared to the classic LMA, PLMA insertion takes a few seconds longer, but overall success is equivalent. In 2010, Lalwani J, Dubey KP, Sahu BS, Shah PJ conducted a study Proseal Laryngeal Mask Airway: An alternative to endotracheal intubation in paediatric patients for short surgical procedures and proved that PLMA is a safe and effective alternative to endotracheal intubation.

Hence, we made an earnest attempt to compare this device with the standard endotracheal tube in gynaecological laparoscopic surgeries for the ease of insertion, haemodynamic changes occurring during insertion, before pneumoperitoneum, after pneumoperitoneum and after removal of the device. We also compared the airway pressure on insertion, on pneumoperitoneum, 10 minutes after pneumoperitoneum, after release of pneumoperitoneum and perioperative complications in both the groups.

Materials and Methods

After obtaining Institutional Ethics Committee clearance, the study was carried out in 60 female patients belonging to ASA (American Society of Anaesthesiologists) grade I and II, aged between 18 to 45 years, scheduled for elective gynaecological laparoscopic surgeries. The design of study was a Prospective, randomized control, comparative study extended over a period of one year in our institute.

We conducted the study on 60 patients, after dividing 30 patients in each group for better validity of results. Keeping the significance level of 5%, power of study at 80% and based on the study by Lim Y *et al.*,[9] the sample size was calculated using Winpepi Statistical package. Randomization was done using a computer generated random number table. After obtaining informed written consent in their own understandable language, patients were randomly assigned to one of the two groups:

Group 'P' (Proseal laryngeal mask airway was used) - 30

Group 'E' (Endotracheal tube was used) - 30

Patients belonging to ASA I or II, between the age of 18-45, mouth opening> 2.5 cms with availability of informed consent were taken and patients with ASA III or more, other comorbidities, URTI, increased risk of aspiration (pregnancy, hiatus hernia, reflux disorders), BMI >30 kg/m^2, posted for emergency surgeries were excluded.

Pre-operative Evaluation

Patients were assessed for routine investigations. The procedure was explained to the patient and written informed consent was taken.

All patients were kept fasting for 8 hours. In the preoperative room, the patient's baseline pulse, blood pressure and heart rate were taken. In the operating room, all monitors were attached - pulse oximeter, ECG and non-invasive blood pressure cuff and a wide bore 20 G intravenous line established. The patients were pre-medicated with

intravenous inj. Glycopyrrolate 0.004 mg/kg, inj. Ondansetron 0.1 mg/kg, inj. Midazolam 0.02 mg/kg, inj. Pentazocine 0.3 mg/kg, then preoxygenated with 100% O_2 for 3 minutes. General anesthesia was induced with inj. Propofol 2 mg/kg and inj. Vecuronium 0.1 mg/kg. After induction, in group P, appropriate size of PLMA (size 3) was used and appropriate size portex cuffed ETT (size 7/7.5 mm internal diameter) was used in group E patients. Same person inserted the PLMA or ETT in all the 60 cases, while the haemodynamic and other parameter monitoring was performed by another person not able to visualise the device. Correct placement of device was confirmed by manual ventilation, auscultation, capnography. Once confirmed, positive pressure ventilation started on closed circuit (tidal volume-8 ml/kg). Maximum 3 attempts were allowed, if more attempts were required case was excluded from the study. Anesthesia was maintained with isoflurane (0.6 - 1 MAC) in 60% N_2O / 40% O_2 mixture. Controlled mechanical ventilation was applied to maintain the end tidal CO_2 between 30-40 mm of Hg. Gastric tube of number 12 or 14 Fr was inserted through the drain tube. Two attempts were allowed before gastric tube insertion was considered a failure and repositioning of PLMA was done.

Haemodynamic responses as pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, oxygen saturation and end tidal carbon dioxide were recorded prior to induction, 1 min, 3 min, 5 min after endotracheal intubation or PLMA insertion, before and after pneumoperitoneum and after removal of the respective device. The airway pressure was noted on insertion, on pneumoperitoneum, 10 minutes after pneumoperitoneum and after release of pneumoperitoneum in both the groups. After the procedure, reversal was done by using Inj. Neostigmine 0.05 mg/kg and Inj. Glycopyrrolate 0.008 mg/kg. Also perioperative complications like cough, laryngospasm, bronchospasm, aspiration, blood on device and sore throat in both the groups were noted. Time and ease for insertion were also noted for ETT, PLMA and ryles tube.

For the analysis of quantitative data student t test (for parametric data) or Mann Whitney's U test (for non parametric data) was used. For the analysis of categorical data chi square test of significance was used. The *p* value for statistical significance was set at 0.05.

Results

In this prospective randomised study, sixty female patient aged 18-45 years with ASA I/II fitness undergoing gynaecological laparoscopic surgeries were studied to evaluate haemodynamic changes and post operative complications, after securing airway with proseal or ETT. Surgeries like Diagnostic laparoscopy with dilatation and curettage, Diagnostic laparoscopy with hysteroscopy, Laparoscopic tubal ligation were included. Demographic profile data of patient (age, weight, height) in both groups were comparable and the difference was statistically insignificant (> 0.05). In group P, PLMA was inserted in the first attempt in 27 patients and in second attempt in 3 patients. All patients in the group E were intubated in the first attempt itself. Insertion of PLMA was achieved in group P in 14.30 ± 2.45 seconds and patients in the group E were intubated in 14.57 ± 2.04 seconds. There was no significant difference between the two groups associated with time taken for insertion. (*p* value = 0.07) (Table 1).

Table 1: Insertion of Device

	Group P	Group E	*p* value
No. of attempts of insertion	I = 27 patients II = 3 patients	I = 30 patients II = 0 patients	0.07
Time taken for insertion of device (seconds)	14.30 ± 2.45	14.57 ± 2.04	0.07
Time taken for RT insertion (seconds)	11.0 ± 3.05	12.40 ± 1.47	0.02

Table 2: Comparison of heart rate between two groups

Heart Rate	Group P Mean ± SD	Group E Mean ± SD	*p* Value	Significance
Baseline	81.23 ± 2.97	80.67 ± 4.0	0.53	Not Significant
1 Min After Insertion	83.0 ± 2.72	87.07 ± 1.68	<0.001	Significant
3 Min After Insertion	81.90 ± 2.74	86.0 ± 1.64	<0.001	Significant
5 Min After Insertion	81.17 ± 2.45	85.0 ± 1.64	<0.001	Significant
Before Pneumoperitoneum	80.73 ± 1.92	81.0 ± 2.71	0.66	Not Significant
After Pneumoperitoneum	84.20 ± 2.05	85.0 ± 1.70	0.10	Not Significant
After Removal of Device	82.0 ± 1.68	87.0 ± 1.46	<0.001	Significant

Comparison of Vital Parameters

Relatively lower values were observed in group P than group E at 1 min (p <0.001), 3 mins (p <0.001), 5 mins (p <0.001) and after removal of device (p <0.001), which were found to be statistically significant (Table 2).

Relatively lower values were observed in group P than group E at 1 min (p value <0.001), 3 mins (p value <0.001), 5 mins (p value <0.001) and after removal of device (p value <0.001) and were found to be statistically significant. The difference between the groups at baseline (p = 0.42), before pneumoperitoneum (p value = 0.38) and after pneumoperitoneum (p value =0.07) were not found to be statistically significant (Table 3).

Relatively lower values were observed in group P than group E at 1 min (p <0.001), 3 mins (p <0.001), 5 mins (p <0.001) and after removal of device (p <0.001) which were statistically significant. The differences between the groups at baseline (p = 0.81), before pneumoperitoneum (p = 0.25) and after pneumoperitoneum (p = 0.20) were found to be statistically not significant (Table 4).

Relatively lower values were observed in group P than group E at 1 min (p <0.001), 3 mins (p <0.001), 5 mins (p <0.001) and after removal of device (p <0.001). The differences between two groups were found to be statistically significant. The difference between the groups at baseline (p = 0.33), before pneumoperitoneum (p = 0.17) and after pneumoperitoneum (p = 0.56) were not found to be statistically significant (Table 5 and Graph 1).

Comparison of $EtCO_2$ between two groups

There was no significant difference in $EtCO_2$ in both the groups at baseline (p = 0.66) 1 min (p = 0.63), 3 mins (p = 0.10), 5 mins (p = 0.77) after insertion of device, before pneumoperitoneum (p = 0.07)

Table 3: Comparison of systolic blood pressure between two groups

Systolic Blood Pressure	Group P Mean ± SD	Group E Mean ± SD	p Value	Significance
Baseline	123.97 ± 1.65	123.60 ± 1.86	0.42	Not Significant
1 Min After Insertion	128.07 ± 1.72	133.03 ± 1.29	<0.001	Significant
3 Min After Insertion	127.0 ± 1.25	132.0 ± 1.53	<0.001	Significant
5 Min After Insertion	125.03 ± 1.79	129.93 ± 1.43	<0.001	Significant
Before Pneumoperitoneum	123.87 ± 1.59	124.37 ± 2.65	0.38	Not Significant
After Pneumoperitoneum	128.73 ± 1.61	129.4 ± 3.75	0.07	Not Significant
After Removal of Device	125.0 ± 1.64	130.0 ± 1.64	<0.001	Significant

Table 4: Comparison of diastolic blood pressure between two groups

Diastolic Blood Pressure	Group P Mean ± SD	Group E Mean ± SD	p Value	Significance
Baseline	84.0 ± 1.64	83.87 ± 2.54	0.81	Not Significant
1 Min After Insertion	86.13 ± 1.57	90.97 ± 1.52	<0.001	Significant
3 Min After Insertion	85.0 ± 1.25	90.0 ± 1.64	<0.001	Significant*
5 Min After Insertion	84.0 ± 1.33	88.0 ± 1.64	<0.001	Significant*
Before Pneumoperitoneum	83.90 ± 1.24	84.8 ± 3.42	0.25	Not Significant
After Pneumoperitoneum	87.0 ± 1.53	87.87 ± 4.56	0.20	Not Significant
After Removal of Device	85.0 ± 1.53	90.07 ± 1.48	<0.001	Significant

Table 5: Comparison of Airway Pressure between two groups

Airway Pressure	Group P Mean ± SD	Group E Mean ± SD	p Value	Significance
On Insertion	21.60 ± 1.99	22.27 ± 1.63	0.16	Not Significant
On Pneumoperitoneum	25.27 ± 1.99	24.60 ± 1.49	0.14	Not Significant
10 Min After Pneumoperitoneum	26.73 ± 2.13	25.80 ± 1.51	0.06	Not Significant
On Release of Pneumoperitoneum	21.67 ± 1.49	22.80 ± 1.51	0.07	Not Significant

and after pneumoperitoneum (p = 0.40) and after removal of the airway device (p = 0.06) (Graph 2).

Comparison of SpO_2 between two groups

There was no significant difference in SpO_2 in both the groups at baseline (p = 0.99) 1 min (p = 0.73), 3 mins (p = 0.17), 5 mins (p = 0.18) after insertion of device, before pneumoperitoneum (p = 0.09) and after pneumoperitoneum. (p = 0.40) and after removal of the airway device (p = 0.58) (Graph 3).

There was no significant difference in the mean airway pressure observed between both the groups at insertion (p = 0.16), on pneumoperitoneum (p = 0.14), 10 min after pneumoperitoneum (p = 0.06) and on release of pneumoperitoneum (p = 0.07) (Table 6 and Graph 4).

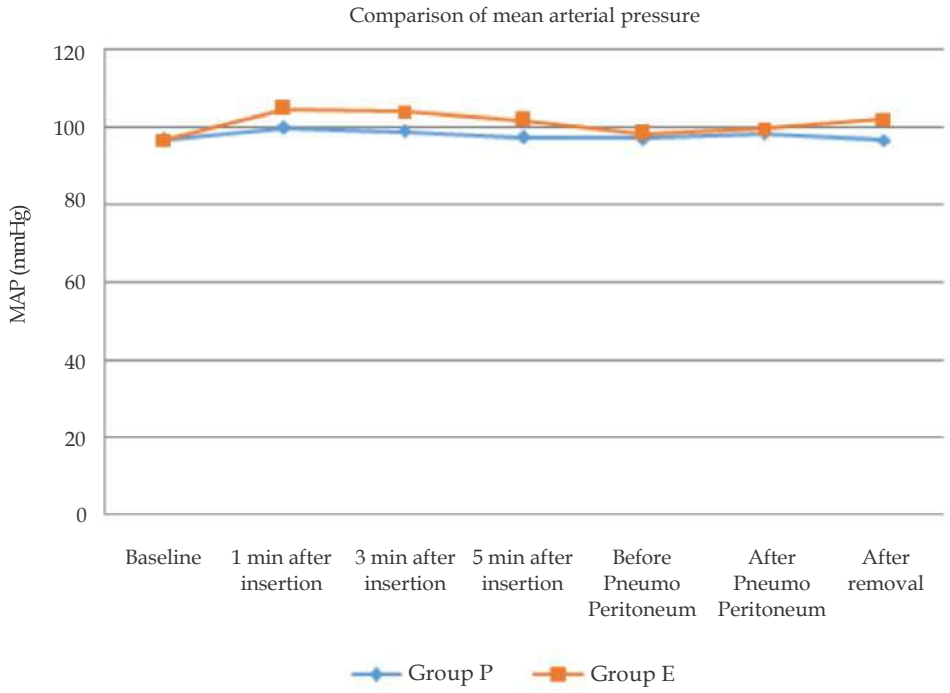
Incidence of perioperative complications in both groups

The difference in the perioperative complications observed between both the groups was statistically significant, with cough (p = 0.04). blood on device (p = 0.03) and sore throat (p = 0.04) lesser in P group.

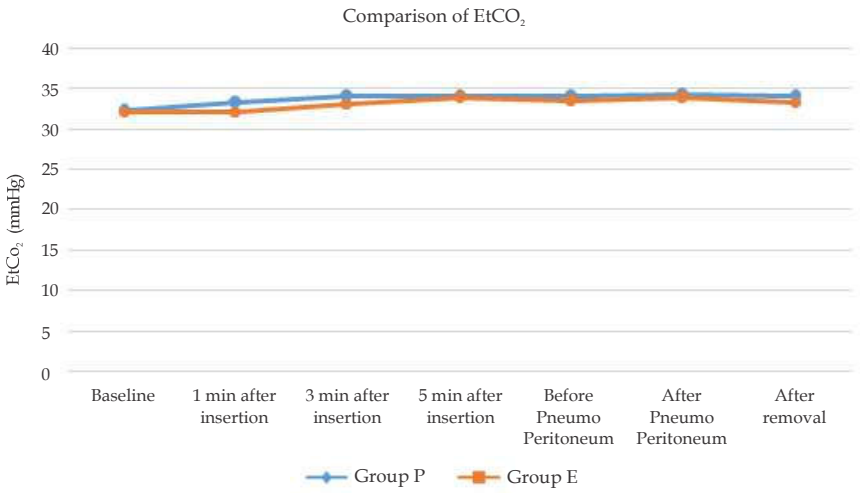
Pie-Charts Showing Incidence of Perioperative Complications (Chart 1)

Table 6: Incidence of perioperative complications in both groups

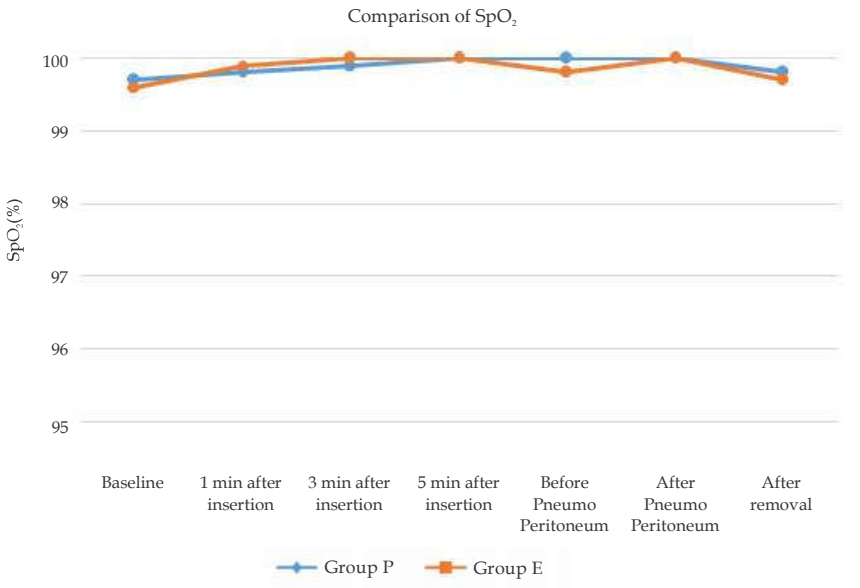
Complications	Group P		Group E		p Value
	Number	%	Number	%	
Cough	2	6.6	5	16.6	0.04
Laryngospasm	0	0	0	0	
Bronchospasm	0	0	0	0	
Blood on device	1	3.3	3	10	0.03
Aspiration	0	0	0	0	
Sore Throat	2	6.6	6	20	0.04



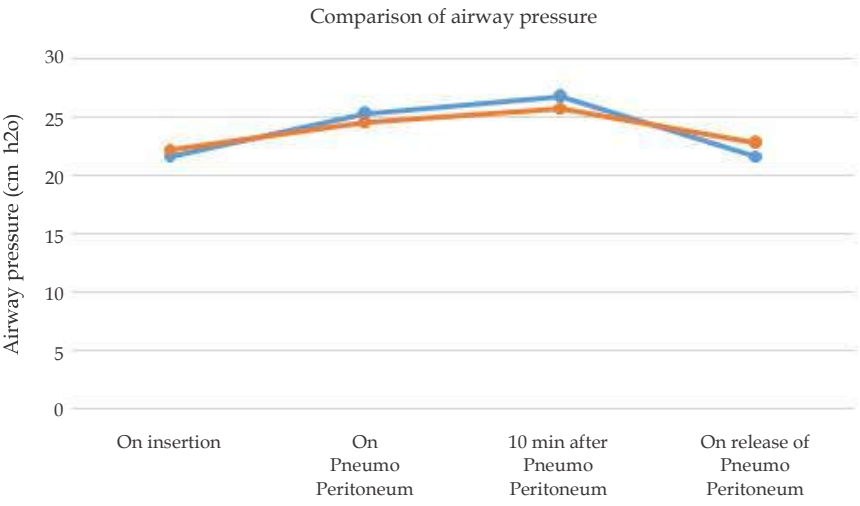
Graph 1: Showing comparison of mean arterial pressure in both the groups



Graph 2: Showing comparison of $EtCO_2$ in both the groups



Graph 3: Showing comparison of SpO_2 in both the groups



Graph 4: Showing comparison of airway pressure in both the groups

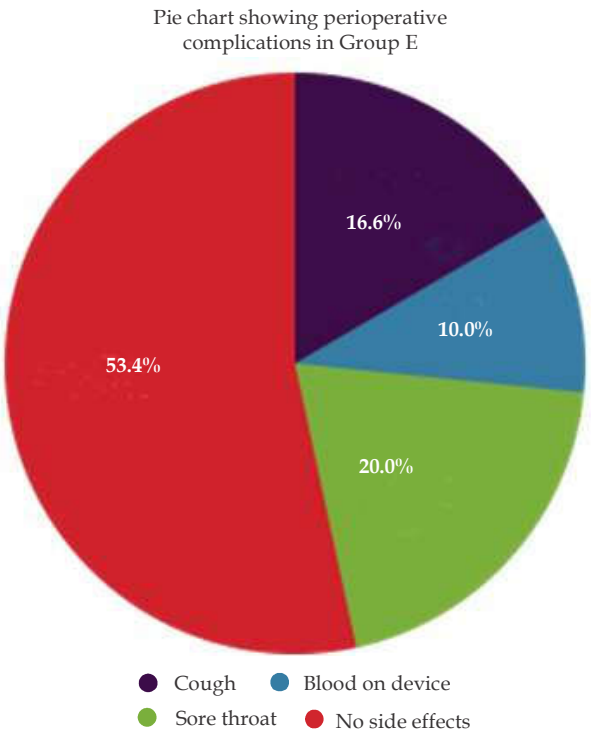


Chart 1: Showing Incidence of Perioperative Complications

Discussion

Laparoscopic surgeries are associated with pneumoperitoneum leading to increase in intra-abdominal pressure and intra-thoracic pressure, thus ETT is considered as the gold standard.[11] Endotracheal tube insertion is associated with haemodynamic changes due to laryngoscopy[12] and postoperative disadvantages like sore throat, cough and hoarseness.[13]

Reid and Brace were the first to describe the haemodynamic changes in response to laryngoscopy and intubation.[14] On direct laryngoscopy, in less than 5 seconds these changes begin, peak at 1-2 minutes and return towards the baseline in 5 minutes.[15]

The Proseal LMA is a new entrant in the family of LMA with added features over the classic LMA. Reduced risk of gastric insufflations, regurgitation and aspiration are associated with usage of PLMA. Maltby *et al.* postulated that laparoscopic surgery was an important test for evaluating the effectiveness of SADs use in positive pressure ventilation.[8]

After approval from the Hospital research and ethics committee, a prospective, randomized, comparative study was conducted on 60 adult female patients undergoing gynaecological laparoscopic surgeries under general anesthesia.

After applying the inclusion and exclusion criteria, the patients were randomly divided into two groups of 30 each using a computer generated random number table.

Our aim was to compare the efficacy and safety of Proseal laryngeal mask airway with portex endotracheal intubation in sixty adult female patients undergoing gynaecological laparoscopic surgeries under general anesthesia.

Ease of Insertion of Device

The first attempt success rate in group P was 90% and 100% at the second attempt, while all patients in the group E were intubated in the first attempt itself. The difference between the two groups was statistically not significant. (p value = 0.07).

In a study conducted by M Misra *et al.*, The Pro-seal LMA and tracheal tube: A comparison of events at insertion of the airway device, showed 100% success at insertion in both the groups with success rate at first attempt 88% for PLMA and 100% for ETT. For PLMA, first/ second/ third attempt observed in 44/ 4/ 1 patients respectively.[7]

Time Taken for Insertion of Device

The mean time taken for insertion of device was 14.30 ± 2.45 seconds in group P and 14.57 ± 2.04 seconds in group E. The difference between the two groups was not statistically significant (p value = 0.07).

The findings observed in our study were concurrent with the study done by Avhad V, Comparison of safety and efficacy of Proseal laryngeal mask airway v/s endotracheal intubation for gynaecological diagnostic laparoscopy, in 2017. The mean time taken for insertion was 18.2 ± 5 seconds for PLMA and 25.6 ± 8.1 seconds in ETT, which was statistically significant. Successful PLMA insertion at first attempt in 35 patients and second attempt in 5 patients, while for ETT, 33 patients in first and 7 patients in second attempt and the difference was observed to be insignificant.[16]

Comparison of Vital Parameters

Comparison of heart rate between the two groups

Values observed in group P were relatively lower than group E at 1 min (p <0.001), 3 mins (p <0.001), 5 mins (p <0.001) and after removal of device (p <0.001), which were found to be statistically

significant.

The differences observed between two groups at baseline (p = 0.53) before peritoneum (p = 0.66) and after pneumoperitoneum (p = 0.10) were not found to be statistically significant.

In 2005, P Shroff, S Kamath in their randomized comparative study between the proseal laryngeal mask airway and the endotracheal tube for laparoscopic surgery observed mean heart rate values with PLMA as 98 ± 22 per min, 104 ± 16 per min, 98 ± 17 per min, 98 ± 17 per min, and 92 ± 13 per min and with ETT as 99 ± 10 per min, 102 ± 11 per min, 99 ± 13 per min, 109 ± 13 per min and 103 ± 7 per min at pre induction, after induction, before and after pneumoperitoneum and postoperatively respectively. The difference observed between the two groups as regards to the mean heart rate was statistically significant.[1]

Comparison of Systolic Blood Pressure:

Values observed in group P were relatively lower than group E at 1 min (p value = 0.42), 3 mins (p value <0.001), 5 mins (p value <0.001) and after removal of device (p value <0.001) were found to be statistically significant.

The differences observed between the groups at baseline (p = 0.42), before pneumoperitoneum (p value = 0.38) and after pneumoperitoneum (p value =0.07) were not found to be statistically significant.

Kalpana Shah, in 2017, studied the 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. In this study, it was seen that all the hemodynamic parameters in PLMA group were better than in the ETT group and this finding was statistically significant (p < 0.05).[10]

Comparison of Diastolic Blood Pressure

Values observed in group P were relatively lower than group E at 1 min (p <0.001), 3 mins (p <0.001), 5 mins (p <0.001) and after removal of device (p <0.001) which were statistically significant.

The difference between the groups at baseline (p = 0.81), before pneumoperitoneum (p = 0.25) and after pneumoperitoneum (p = 0.20) were not found to be statistically significant.

Sharma B, Sahai C *et al.*, conducted a study of 100 consecutive cases of laparoscopic surgery. Their results were pre-induction DBP 77.82 ± 12.27 mm of Hg reached to 79.21 ± 16.35 mm of Hg at 1 min and 82.01 ± 16.45 mm of Hg at 5 mins after insertion of PLMA (p-value 0.053), which was statistically significant. They concluded that there were minimum haemodynamic responses to insertion of Proseal Laryngeal Mask Airway.[6]

Comparison of Mean Arterial Pressure

Values observed in group P were relatively lower than group E at 1 min (p <0.001), 3 mins (p <0.001), 5 mins (p <0.001) and after removal of device (p <0.001). The difference between two groups was found to be statistically significant.

The difference between the groups at baseline (p = 0.33), before pneumoperitoneum (p = 0.17) and after pneumoperitoneum (p = 0.56) were not found to be statistically significant.

Saraswat N, Kumar A *et al.* compared Proseal LMA and Endotracheal tube in patients undergoing laparoscopic surgeries under general anesthesia. They concluded statistically significant increase in heart rate and mean blood pressure was observed 10 seconds after intubation and persisted till 3 mins after intubation and also during extubation in the ETT group. However statistically significant increase in PLMA group was seen only 10 seconds after insertion.[2]

Comparison of End Tidal Carbon Dioxide

There was no significant difference in $EtCO_2$ in both the groups at baseline (p = 0.66), 1 min (p = 0.63), 3 mins (p = 0.10), 5 mins (p = 0.77) after insertion of device, before (p = 0.07) and after pneumoperitoneum (p = 0.40) and after removal of the airway device (p = 0.06).

Comparison of SpO_2

There was no significant difference in SpO_2 in both the groups at baseline (p = 0.99) 1 min (p = 0.73), 3 mins (p = 0.17), 5 mins (p = 0.18) after insertion of device, before (p = 0.09) and after pneumoperitoneum (p = 0.40) and after removal of the airway device (p = 0.58).

In 2003, Maltby JR *et al.* conducted a study, LMA – Classic and LMA – Proseal are effective alternatives to endotracheal intubation for gynaecologic laparoscopy. They observed the differences between LMA-C/PLMA and ETT groups for SpO_2, SpO_2 and $PETCO_2$ were not statistically significant before or during peritoneal insufflations.[8]

Airway pressure

There was no significant difference in the mean airway pressure observed between both the groups at insertion (p = 0.16), on pneumoperitoneum (p = 0.14), 10 min after pneumoperitoneum (p = 0.06) and on release of pneumoperitoneum (p = 0.07).

In 2012, Handan G *et al.* studied comparison of haemodynamic and metabolic stress response caused by endotracheal tube and Proseal LMA in laparoscopic cholecystectomy. They concluded that although the peak airway pressures increased after carboperitoneum in both the groups, it did not disrupt ventilation and the difference was not statistically significant.[5]

Perioperative complications

The difference in the perioperative complications observed between both the groups was statistically significant, cough (p = 0.04), blood on device (p = 0.03) and sore throat (p = 0.04) with values higher in E group.

In 2003, Maltby JR *et al.* observed a ten-fold difference in frequency of coughing at removal of the ETT 87% vs LMAC/PLMA 8%, which was statistically significant (P < 0.001). Sore throat 24 hr postoperatively was more common with ETT than LMA-C/PLMA (28% vs 17%; p < 0.05). No patient reported numbness of the tongue or other morbidity attributable to the airway devices.[8]

Conclusion

Proseal LMA was found to be better than ETT in the following ways:

1. Lesser haemodynamic response on insertion and removal.
2. Reduced postoperative complications like cough, blood on device and sore thoat.

The ease and time taken for insertion of Proseal Laryngeal Mask Airway is comparable to endotracheal tube. It provides similar efficiency like ETT for controlled positive pressure ventilation.

Thus the Proseal LMA offers a safe and effective airway management alternative in patients undergoing gynaecological laparoscopic procedures under general anesthesia with controlled ventilation with the added advantage of minimal haemodynamic response and postoperative complications.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(4) (Part - II): 1293-1298
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.32

Effects of Clonidine on Spinal Anesthesia with Hyperbaric Bupivacaine

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Abstract

Background: Clonidine is one of the drugs that have been extensively studied by administering through oral, intravenous and intrathecal routes to prolong the spinal anesthesia. A lot of studies have shown oral clonidine premedication to prolong duration of sensory block and motor block. This study is undertaken to evaluate the effect of oral clonidine as premedicant on spinal anesthesia with 0.5% hyperbaric bupivacaine. *Methods:* A double blind randomized controlled study was carried out on 100 participants who underwent elective surgeries under spinal anesthesia. The participants were allocated into experimental (oral Clonidine) and control group (50 each) equally. Heart rate, level and duration of sensory and motor blockades were observed. *Results:* The mean time to highest sensory blockade was lower in experimental group (5.28 min) when compared to control group (7.76 min). The observed difference was statistically significant (p<0.001). Similarly, there was a statistically significant difference in the mean duration of motor blockade between the groups, wherein the experimental group had a longer duration (264 min) compared to the control group (208.50 min) (Table 4). *Conclusion:* Premedication with oral clonidine 150µg, 1 hour prior to spinal anesthesia is adequate to provide clinically useful prolongation of sensory blockade without significant adverse effects.

Keywords: Clonidine; Pre-medication; Sensory blockade; Spinal anesthesia.

How to cite this article:

Ananda Bhat, Parimala B, Balajibabu PR. Effects of Clonidine on Spinal Anesthesia with Hyperbaric Bupivacaine. Indian J Anesth Analg. 2019;6(4):1293-1298.

Introduction

Spinal anesthesia during initial days was mainly performed using local anaesthetics. Later interest developed with regard to adding additives to local anaesthetics, to prolong spinal anesthesia. In the context of "Augmentation strategies" for epidural and intrathecal analgesia, discovery of opioid receptors and the subsequent development of epidural and intrathecal opioid administration is undoubtedly one of the most significant advances in pain management in the last three decades.[1]

The alpha 2 agonist clonidine has shown properties that are potentially beneficial for oral premedication to reduce sympathetic activity, shivering, and oxygen consumption during recovery from anesthesia. In addition, Clonidine does not result in drying of secretions; minimizes fluctuations in the haemodynamic profile during anaesthetic induction and decreases the anaesthetic

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Received on 08.05.2019, **Accepted on** 08.06.2019

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requirements of both opioid and volatile anaesthetics. Clonidine provides significant benefits for preoperative anxiety and analgesia.[2]

Clonidine is one of the drugs that have been extensively studied by administering through oral, intravenous and intrathecal routes to prolong the duration of action of spinal anesthesia. However, it is of interest to find the effectiveness of oral clonidine given as a premedicant on the duration of bupivacaine spinal anesthesia. A lot of studies have shown oral clonidine premedication to prolong duration of sensory block and motor block.[3-5] This study was undertaken to evaluate the effect of oral clonidine as a premedicant, on spinal anesthesia with 0.5% hyperbaric bupivacaine.

Objectives

This study was carried out to assess following effects of oral clonidine (150 µg), as a premedicant on hyperbaric bupivacaine (0.5%) spinal anesthesia.

1. Onset and duration of sensory and motor blockade.
2. Haemodynamic effects.

Materials and Methods

Study design and participants

A double blind randomized controlled study was carried out in the Department of Anaesthesiology of a tertiary teaching institution for a period of one year. All the patients who underwent elective surgeries under spinal anesthesia during the study period were selected for the study. A total of 100 patients participated in the study.

Inclusion criteria

1. Age between 20-60 years
2. ASA I & II patients
3. Elective lower abdominal and lower limb surgeries performed in supine position
4. Weight: 40 – 60 kg
5. Height: Around 150 cm

Exclusion criteria

1. ASA III & IV patients
2. Hypertensive patients on beta blockers, calcium channel blockers
3. Patients on digoxin
4. Patients who require opioids, intravenous or inhalational anaesthetics as supplementation for regional anesthesia
5. Patients who had inadequate block requiring general anesthesia.

Randomization and sampling

The participants were allocated into experimental and control group equally. Randomization was carried out based on computer generated random numbers. Each group consisted of 50 participants.

Group A (Control): Placebo and 3 ml (15 mg) hyperbaric bupivacaine (0.5%) spinal anesthesia.

Group B (Experiment): Oral clonidine (150 µg) as premedicant and 3 ml (15 mg) hyperbaric bupivacaine (0.5%) spinal anesthesia.

Ethical approval and informed consent

Approval was obtained from the Institutional Ethics Committee prior to the commencement of the study. Each participant was explained in detail about the study and informed consent was obtained prior to the data collection.

Procedure

The participants were pre-medicated the previous night with T. Alprazolam 0.5 mg HS and Inj. Ranitidine 50 mg intravenous and Inj. Ondansetron 4 mg was administered intravenously 30 minutes before shifting to operation theatre. Baseline parameters, namely heart rate, non invasive blood pressure (NIBP) and SpO_2 were recorded before pre-medication. Oral Clonidine (150 µg) with sips of water was administered to the participants in the experimental group, 60 minutes before anesthesia. Preloading was done with 10 – 15 ml/kg of Ringer's Lactate solution over thirty minutes followed by infusion of 8 – 10 ml/kg/hour intravenously as maintenance fluid. HR and BP recorded just before spinal anesthesia was taken as "0" min reading. Under aseptic precautions, lumbar puncture was done in the lateral position at L2-L3 space, using 26 G Quincke's spinal needle. 3 ml of 0.5% hyperbaric bupivacaine was injected at the rate of 1ml in 3 sec with table flat and patient was immediately turned supine and supplemental oxygen started.

Data collection

Haemodynamic monitoring: Continuous monitoring of ECG, HR, SpO_2, NIBP was carried out. *Hypotension* was defined as decrease in SBP of > 30% from the baseline value and was treated with bolus intravenous fluid and intravenous bolus dose of

Inj. Ephedrine 6 mg. *Bradycardia* was defined as HR <60/min; recorded and treated with intravenous Inj. Atropine 0.6 mg.

Sensory blockade (*elicited by pin prick*): Dermatome levels of sensory anesthesia were checked every five minutes for the first thirty minutes, every 10 minutes during the intraoperative period and every fifteen minutes thereafter till the level regresses to L1 dermatome. Highest level of sensory block was noted. Onset of sensory blockade was considered as the time in minutes from injection of the intrathecal drug to the time for the block to attain its highest level. Duration of sensory blockade was time interval between the onset of sensory blockade to regression to L1.

Motor blockade (*assessed by Bromage score*): Motor blockade was assessed every five minutes for the first thirty minutes, and every 10 minutes during the intra operative period and every fifteen minutes thereafter till complete recovery from motor blockade.[4] Onset of motor blockade was noted as the time taken from the deposition of intrathecal drug to time taken to reach grade 3 motor blockade. Duration of motor blockade was noted as the time interval between onset of grade 3 motor blockade to complete recovery from motor blockade. The Bromage scoring is given in table 1.

Table 1: Bromage score for the study participants:

S. No	Score	Interpretation
1	0	No change in movement of legs and feet
2	1	Barely able to flex knees. No foot movement change
3	2	Unable to flex knees and barely move feet
4	3	Unable to move feet and knees

Data analysis

Data was entered and analyzed using SPSS version 20 software. Results on continuous data were presented as mean values. Independent sample t test and chi square test were used to evaluate the statistical significance between the groups. A p value < 0.05 was considered statistically significant.

Results

Majority of the participants in both the groups were males and belonged to ASA I. (Table 2). Both the groups were comparable with respect to their background characteristics. The mean age of the participants in group A was 37.2 years while the same in group B was 38.3 years. The mean body weight and mean height were also similar between the groups (Table 3).

Majority of the participants underwent herniorraphy (56% and 52% in Groups A & B respectively). In majority of participants the sensory level of blockade was achieved at the level of T6 (72% and 68% in Groups A & B respectively) (Table 4).

The mean time to highest sensory blockade was lower in experimental group (5.28 min) compared to control group (7.76 min). The observed difference was statistically significant (p<0.001). There was a statistically significant difference in the mean duration of sensory blockade between the groups, wherein the experimental group had a longer duration (223 min) compared to the control group (141.30 min). Similarly, there was a statistically significant difference in the mean duration of motor blockade, wherein the experimental group had a longer duration (264 min) compared to the control group (208.50 min) (Table 5).

Our study showed a significant difference in the mean heart rates between the groups throughout the duration of anesthesia. It was observed that the mean heart rates were lower in the experimental group compared to the control group throughout the anesthetic period (p < 0.05) (Table 6).

Table 2: Background characteristics of the study participants

S. No	Characteristics	Group A N (50)	Group B N (50)	p value
1	*Gender*			
	Male	32(64.0)	34(68.0)	0.673
	Female	18(36.0)	16(32.0)	
2	*ASA distribution*			
	ASA I	38(76.0)	36(72.0)	0.648
	ASA II	12(24.0)	14(28.0)	

Table 3: Mean value of Background characteristics of the study participants

S. No	Characteristics	Group A N (50)	Group B N (50)	*p* value
1	Mean age (years)	37.20 ± 10.65	38.33 ± 9.67	0.583
2	Mean weigh (kg)	68.42 ± 10.25	68.14 ± 10.80	0.894
3	Mean height (cm)	159.48 ± 7.49	158.62 ± 5.99	0.528

Table 4: Distribution of surgical procedures and anaesthetic characteristics of two groups

S. No	Characteristics	No of patients in Group A N(50)	No of patients in Group B N(50)
1	*Type of surgery*		
	Appendicectomy	11(22.0)	12(24.0)
	Herniorraphy	28(56.0)	26(52.0)
	Varicose veins (ligation & stripping)	6(12.0)	5(10.0)
	Fracture tibia(ORIF)	5(10.0)	7(14.0)
2	*Highest sensory level*		
	T4	3(6.0)	5(10.0)
	T5	6(12.0)	5(10.0)
	T6	36(72.0)	34(68.0)
	T7	3(6.0)	2(4.0)
	T8	2(4.0)	4(8.0)
3	*Complications*		
	Bradycardia (HR < 60/min)	6(12.0)	6(12.0)
	Hypotension (Fall in SBP > 30% of baseline)	2(4.0)	3(6)
	Nausea	4(8.0)	5(10.0)
	Vomiting	0	0
	Shivering	4(8.0)	3(6.0)
	No complications	34(68.0)	33(66.0)
4	*Drugs*		
	Atropine (0.6 mg)	6(12.0)	6(12.0)
	Ephedrine (6 mg)	2(4.0)	3(6.0)
	No drugs	42(84.0)	41(82.0)

Table 5: Comparison of duration of motor and sensory blockade between the groups:

S. No	Parameters	Group A	Group B	*p* value	T test
1	Time to highest sensory level (min)	7.76 ± 1.31	5.28 ± 1.89	0.001	8.258
2	Time to regression to L1 (min)	141.00 ± 10.93	223.30 ± 15.24	0.001	31.033
3	Time to grade 3 motor block (min)	5.60 ± 1.21	5.40 ± 1.29	0.727	0.797
4	Duration of motor blockade (min)	208.50 ± 8.16	264.00 ± 11.34	0.001	28.092

Table 6: Mean heart rate (HR) in the two groups at various time intervals

S. No	Time intervals	Group A N(50)		Group B N(50)		*p* value
		Mean HR	SD	Mean HR	SD	
1	0 minute	90.82	9.14	87.34	7.82	0.044
2	60 minute	89.36	8.63	83.70	7.4	0.001
3	90 minute	89.90	8.72	84.00	8.46	0.001
4	120 minute	90.12	8.78	82.82	8.48	0.001
5	180 minute	90.01	8.71	84.20	8.47	0.001

Discussion

The α-2 agonist Clonidine has shown properties that have potential applications as an oral premedication. A lot of studies have shown that premedication with Oral Clonidine prolongs the duration of sensory and motor blockade. In our study, oral clonidine dose of 150 µg was administered to the experimental group patients. The mean time taken to achieve the highest level of sensory blockade was lower in the Clonidine group when compared to the controls ($p<0.001$). However, for the existing dosage, our study could not demonstrate significant changes in the hemodynamic parameters between the Clonidine and control groups.

Manish[3] in his study found the time to highest sensory level in the placebo group was 7.3 ± 0.9 min and in patients pre medicated with clonidine it was 4.2 ± 0.5 min. This study showed that the clonidine group of patients had significantly faster onset of sensory blockade[4]. Harbhej[4] found that time to highest sensory level was lower in the Clonidine group, similar to our study. Similar results were obtained in studies done by Koichi Ota[5] and Singh H[6].

Our study demonstrated a very strong statistically significant difference between the two groups as suggested by the ***p***-value of <0.001 indicating that duration of sensory blockade was significantly prolonged in the clonidie group of patients[3,4,7,8].

Our study compared the total duration of motor blockade between the two groups of patients. Patients in control group had motor block for duration of 208 ± 8.16 min as compared to patients in clonidine group who had motor block for a longer duration of 264 ± 11.34 min. On statistical analysis there was a very strong statistically significant difference between the two groups as suggested by the *p*-value of < 0.001[3,4,6,8].

In our study, the heart rate of patients in the two groups at various time intervals was compared. The mean heart rate in the clonidine group of patients was significantly less at time interval of 0, 60, 90, 120 and 180 minutes compared to the control group patients. The significant decrease in heart rate in the patients premedicated with clonidine could be due to the centrally mediated effect of clonidine and inhibition of noradrenaline release from peripheral pre-junctional nerve endings[3,4,9].

Conclusion

The results of our study correlate with most of the earlier studies. Premedication with oral clonidine 150 µg, 1 hour prior to spinal anesthesia is adequate to provide clinically useful prolongation of sensory blockade without significant adverse effects. However prolonged motor blockade can be uncomfortable for patients. The mechanism whereby oral clonidine may affect spinal anesthesia is unclear. Oral clonidine may exert its effects within the CNS, at peripheral nerve roots, or by potentiation of effects of local anesthetics. Because we did not explore mechanisms of action, our study did not determine whether effects of oral clonidine on spinal anesthesia occurred within the CNS or within peripheral nerves. Thus, further studies are recommended to determine exact sites of action of oral clonidine on spinal anesthesia. Further studies with reference to postoperative analgesic requirements and sedation score are recommended.

Conflict of interest: Nil

Funding: Nil

Ethical approval: Obtained

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(4) (Part - II): 1299-1304
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.33

A Comparative Study of Oral Gabapentin and Oral Clonidine as Preemptive Analgesia under Spinal Anesthesia for Abdomino-Pelvic Surgeries

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Abstract

Aim: To assess the effect of oral Gabapentin and oral Clonidine used as Preemptive analgesia to attenuate postoperative pain in patients undergoing elective Abdomino-Pelvic surgeries under Spinal Anesthesia. *Objective:* To assess postoperative analgesic benefit, their postoperative efficacy with respect to duration of analgesia and total postoperative requirement and side effects if any of both the groups. *Material and Method:* 60 patients of either sex of age between 18-65 years, ASA grade I & II, patient admitted to Khaja banda nawaz teaching and general hospital for elective abdominal surgeries under spinal anesthesia were included in the study. The patients were randomly allocated into two groups of 30 each, group G received Gabapentin 300 mg tablet orally 90 min before surgery, group C received clonidine 100 µg tablet orally 90 min before surgery. Duration of postoperative analgesia, Degree of postoperative pain (VAS score) and added rescue analgesia required in 24 hrs were recorded postoperatively. *Result:* Analysis revealed the postoperative analgesic efficacy of oral Gabapentin showed better pain tolerance compared to that of oral Clonidine. The Ramsay sedation score showed a significant sedative effect by Gabapentin than in Clonidine at 90 mins, haemodynamic parameters changes suggested Gabapentin to be haemodynamically stable than clonidine, Morphine consumption in 24 hrs was significantly high in Clonidine group with increased incidence of nausea and vomiting. *Conclusion:* Oral Gabapentin 300 mg given before 90 minutes as preemptive analgesia was more effective in reducing postoperative pain and morphine consumption, also providing better anxiolysis in patients undergoing abdomino-pelvic Surgeries under spinal anesthesia compared to Oral Clonidine 100 µg.

Keywords: Analgesia; Clonidine; Gabapentin.

How to cite this article:

Ankita Hajare, Irfan A Waris. A Comparative Study of Oral Gabapentin and oral Clonidine as Preemptive Analgesia under Spinal Anesthesia for Abdomino-Pelvic Surgeries. Indian J Anesth Analg. 2019;6(4):1299-1304.

Introduction

Anesthesia as a subject by itself originated in an endeavor to offer pain relief to the patient during surgical procedures. But acute pain following surgery has been managed inadequately because of wide variety of myths and fears. The incidence of post operative pain has been found to be between 25%-76%.[1]

Preemptive analgesia is an antinociceptive treatment that prevents establishment of altered processing of afferent input, which amplifies postoperative pain. The concept of preemptive analgesia was formulated by Crile at the beginning

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Received on 15.04.2019, **Accepted on** 19.06.2019

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of the previous century on the basis of clinical observations.

Three different definitions have been used as the basis for the recent clinical trials. Preemptive analgesia has been defined as treatment that:

1. Starts before surgery;
2. Prevents the establishment of central sensitization caused by incisional injury (covers only the period of surgery);
3. Prevents the establishment of central sensitization caused by incisional and inflammatory injuries (covers the period of surgery and the initial postoperative period).[2]

Owing to this 'protective' effect on the nociceptive system, pre-emptive analgesia has the potential to be more effective than a similar analgesic treatment initiated after surgery. Gabapentin, a structural analog of gamma aminobutyric acid, is used as an anticonvulsant drug since 1993. Their main site of action is α_2-δ ligand that has analgesic, anxiolytic and sleep-modulating activities Pre-treatment with gabapentin can block the development of hyperalgesia. Studies have demonstrated that mechanical hyperalgesia surrounding the wound in postoperative patients and experimentally, heat-induced, secondary hyperalgesia share a common mechanism and that central neuronal sensitization contributes to post-operative pain. Gabapentin has a selective effect on the nociceptive process involving central sensitization.[3,4]

Clonidine, a centrally acting α_2 agoinst is a potent antihypertensive drug has shown properties that are potentially beneficial for premedication to reduce sympathetic activity, to minimize fluctuations in the hemodynamic profile during anesthetic induction and to decrease anesthetic requirement for both opioid and volatile anesthetics. Clonidine provides significant benefits for preoperative anxiety and analgesia. Clonidine has non-opiate antinociceptive properties, which might be used as an alternative to postoperative analgesia without opioid-induced side effects.[5,6]

Hence the present study will be done to study & compare effects of Oral Gabapentine & Oral Clonidine on Post-operative analgesia in abdomino-pelvic surgeries when used along with central neuraxial blockade as a Preemptive analgesia.

Materials and Methods

A prospective randomized double blind study was conducted in Khaja Banda Nawaz Teaching and general hospital Kalaburagi for the collection of data. 60 patients of ASA grade I and II between age group 18-65 years scheduled for elective abdomino-pelvic Surgeries, with estimated duration of surgery 90-120 minutes, to be performed under SAB were enrolled in the study after obtaining clearance from the institutional ethical committee. After taking a detailed history, thorough general physical examination, and all pertinent investigation were carried out to exclude any systemic disease. Exclusion criteria included: 1) Patient refusal, 2) history of Uncontrolled Hypertension, Diabetes, and Liver disease & Peripheral vascular disease 3) Pregnant & Lactating patients, 4) Patients on Antihypertensive drugs, Sedatives, Hypnotics, Antidepressants, Corticosteroids, 5) Patients with Chronic pain syndrome & patients who have taken NSAID in last 48 hrs, 6) Patients having absolute contraindication for spinal anesthesia 7) Patients already taking oral Gabapentin, oral Clonidine.

Consent was taken, the procedure was explained to each patient. Absolute fasting of at least 8 hours was advised, without (prior) administering any premedication. ***Visual Analog Score and Ramsay Sedation score***, was explained to the patients. Patient's basal pulse rate and basal blood pressure was recorded. A peripheral intravenous line with 20 gauge cannula was secured in one of the upper limbs. Patients were preloaded with 10 ml/kg of Ringer lactate 30 minutes prior to the scheduled time of surgery and all Haemodynamic parameters were recorded. Patients were randomly divided in two groups by a staff nurse who was not involved in the study.

Group G: recieved Tablet gabapentin 300 mg orally 90 mins preoperatively.

Group C: recieved Tablet Clonidine 100 µg orally 90 mins preoperatively.

Hemodynamic parameters were noted. Upon the arrival in Operation room, Baseline Non-Invasive Blood Pressure (NIBP), Electrocardiogram (ECG), Pulse Rate (PR) and Oxygen Saturation (SpO_2%) was noted & monitored, thereafter Under aseptic precautions Lumbar puncture was performed with 25 gauge Quincke's spinal needle using a midline approach with the patients in the left or right lateral decubitus position at lumbar 3-4 inter space and when a free flow of clear cerebrospinal fluid is obtained, the local anaesthetic agent that is 3.5 ml of 0.5% hyperbaric Bupivacaine administered. Immediately after the injection the needle withdrawn, the patient turned supine, onset of sensory block upto T6 dermatome assessed bilaterally by loss of pinprick sensation with a short

hypodermic needle and we will allow the surgery to begin.

Parameters measured

- Ramsay sedation score, Heart rate, Systolic & Diastolic BP just before giving the drug orally in the ward on the day of surgery till taking the patient to OT.
- Heart rate, Systolic & Diastolic BP just before the start & the end of the spinal subarachnoid block on OT table.
- Onset of sensory blockade, Maximum sensory blockade, Duration of two segment sensory regression.
- Post-operatively, patients pain by VAS at 1, 4, 8, 12, 24 hours after surgery.
- Duration of analgesia.
- Morphine received in this 24 hr was noted.
- Nausea & Vomiting, if any, & other side effects of both drugs were recorded.

Statistical Analysis

Student's Unpaired, t' test, chi-square test, Kolmogorov-Smirnov test.

Significant figures: Two tailed $p<0.05$ taken as significant.

Statistical software: The Statistical software namely SAS 9.2, SPSS 18 for Windows (SPSS Inc., Chicago, Illinois)., Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables.

Results

Table 1: Age, gender and weight wise distribution of patients

Parameters	Clonidine	Gapapentine
Gender		
Male	17	16
Female	13	14
Age in years Mean ± SD	46.40 ± 21.02	46.93 ± 19.69
Weight in Kgs. Mean ± SD kgs.	60.43 ± 8.02	61.4 ± 7.77

Table 2: Comparison of haemodynamic parameters in oral Clonidine and oral Gabapentine group from Preoperative baseline, after morning dose of drug, and Intra-operative duration

Haemo-dynamic parameters	Preoperative Baseline		After Morning Dose of Drug				Intraoperative at 140 min	
			10 mins		90 mins			
	C (n=30) Mean ± SD	G (n=30) Mean ± SD	C (n=30) Mean ± SD	G (n=30) Mean ± SD	C (n=30) Mean ± SD	G (n=30) Mean ± SD	C (n=30) Mean ± SD	G (n=30) Mean ± SD
Systolic blood pressure (SBP)	117.60 ± 22.06	125.07 ± 14.31	122.27 ± 11. 15	126.20 ± 12.73	115.26 ± 11.62	121.60 ± 11.24	108.73 ± 10.65	119.46 ± 9.03
Diastolic blood pressure (DBP)	77.00 ± 12.05	76.86 ± 10.85	76.60 ± 10.03	78.46 ± 8.70	71.53 ± 9.83	75.26 ± 9.18	67.8 ± 9.99	74.33 ± 7.83
Heart rate	77.27 ± 7.49	80.33 ± 9.56	79.13 ± 7.09	81.60 ± 7.76	74.40 ± 6.22	80.73 ± 8.46	74.20 ± 7.32	79.40 ± 5.61

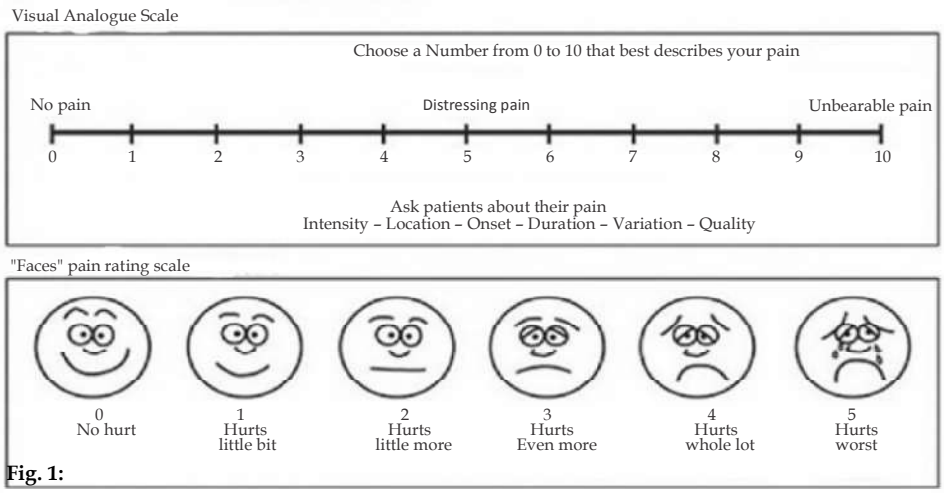

Fig. 1:

Mean age in Clonidine group was 46.40 ± 21.02, and in oral Gabapentin group was 46.93 ± 19.69 (p 0.397). Mean weight in Clonidine group was 60.43 ± 8.02, and in oral Gabapentin group was 61.4 ± 7.77 (p 0.328). There was no significant difference in the age distribution of patients between the groups (p >0.05) (Table 1).

By applying Student's Unpaired 't' test, there is a significant difference between mean values of SBP, DBP and Heart rate after morning dose of drug at 10 minutes, at 90 minutes and Intra-operative at 140 minutes in Clonidine and Gabapentine groups (p < 0.05) (Table 2).

By applying Student's Unpaired, t' test there is a no significant difference between time of sensory, maximum sensory block, duration of 2 segment regression when Clonidine group is compared with Gabapentine group (p > 0.05) (Table 3).

Sedation score in group Clonidine was 1 in 10 patients (33.33%) and 2 in 8 patients (26.66%) which suggests more number of patients were Anxious or restless or both. In Gabapentin group sedation score was 2 in 7 patients (23.33%) and 3 in 13 patients (43.33%) suggesting that more number of patients were awake and responding to commands. Also, 5 patients (16.66%) had a score of 4 and 2(6.66%) patients had score of 5 in the Gabapentin group suggesting they were deeply sedated (Table 4).

Gabapentin group in comparison with Clonidine had significantly lower VAS at 8 h after surgery (p < 0.05). The VAS pain scores at measured times 1st, 4th, 12th & 24th hr were lower in the Gabapentin group than the Clonidine group. The difference was not considered significant (p > 0.05). Patients who were premedicated with Gabapentin showed better pain tolerance compared to those who had been given Clonidine (Table 5).

Duration of analgesia: p value between Clonidine group vs Gabapentin group was 0.001 which was statistically significant suggesting that total duration of analgesia was more in Gabapentin group than in Clonidine.

Duration of Surgery: There was no significant difference for the duration of surgery when both the groups were compared (p > 0.05).

Morphine Consumption: The total postoperative IV morphine in Gabapentin group was significantly less than in the Clonidine group; (p < 0.001).

1 of 30 the Patients in Gabapentin group did not require Morphine IV ; whereas 100% (all 30) patients who received Clonidine required Morphine IV.

Gabapentin group showed lesser incidence of requiring Morphine, but in those who did require, they showed longer duration and intensity of pain compared to Clonidine group. Patients in the Clonidine group showed higher incidences of requiring relief (Table 6).

Table 3: Comparison of Sensory Block parameters in oral Clonidine and oral Gabapentin

Sensory block	Clonidine (n=30) Mean ± SD	Gabapentine (n=30) Mean ± SD	Student's unpaired 't' test value	'p' value and result
Time of sensory onset to T10	172.66 ± 19.81	173.00 ± 24.91	0.057	p>0.05, not significant
Maximum sensory block T6	292.33 ± 22.33	295.00 ± 18.89	0.57	p>0.05, not significant
Duration of 2 segment regression	104.33 ± 11.50	100.67 ± 12.78	0.46	p>0.05, not significant

Table 4: Comparison of Ramsay Sedation Score in oral Clonidine and oral Gabapentin group from preoperative baseline and 90 min. after drug preoperatively

Ramsay Sedation Score	Gabapentine (n=30)		Clonidine (n=30)	
	Baseline No. (%)	90 min after drug No. (%)	Baseline No. (%)	90 min after drug No. (%)
1	30(100%)	3(10%)	30(100%)	10(33.33%)
2	0	7(23.33%)	0	8(26.66%)
3	0	13(43.33%)	0	8(26.66%)
4	0	5(16.66%)	0	4(13.33%)
5	0	2(6.66%)	0	0
6	0	0	0	0

Table 5: Comparison of Postoperative Visual Analog Score (VAS) in oral Clonidine & Gabapentin at 1st, 4th, 8th, 12th and 24th hours

Post Operative visual analog score	Gabapentine (n=30) Mean ± SD	Clonidine (n=30) Mean ± SD	'p' value
1st hour	4.23 ± 1.75	4.33 ± 1.71	0.823
4th hour	3.33 ± 1.66	3.77 ± 1.99	0.356
8th hour	2.43 ± 1.95	3.70 ± 1.93	0.014
12th hour	2.26 ± 1.89	3.00 ± 2.08	0.154
24th hour	1.43 ± 1.38	1.61 ± 1.12	0.581

Table 6: Comparison of duration of analgesia and surgery and I.V morphine consumption in oral Clonidine and oral Gabapentine

	Gabapentine (n=30) Mean ±SD	Clonidine (n=30) Mean ±SD	'p' value and result
Duration of Analgesia (mins)	238.33 ± 50.45	217.00 ± 11.45	p<0.001, significant
Duration of Surgery (mins)	115.33 ± 13.06	117.00 ± 12.07	p>0.05, not significant
Total Morphine consumption in 24 hrs (I.V.)	9.84 ± 5.28 mg	13.92 ± 6.65 mg	p<0.001, significant

Discussion

Preoperative anxiety has been found to be one of the major predictor of post operative pain. The postoperative period was defined as the period between arrival of the patient in recovery room to 7 days after surgery, with day 1 being 24 hours after surgery.

The world needs to have cheaper, safer economical ways of postoperative pain management in contrast to highly technologically dependent majors prevalent in western world. Opioids have been the mainstay of post operative pain management but these have adverse effects of respiratory depression, pruiritis, constipation, and development of tolerance.

Results of our study shows that at 8th postoperative hour, mean VAS scores of Gabapentin group was significantly lesser than Clonidine group (p=0.014). The Postoperative morphine consumption in Gabapentin group was significantly less than Clonidine (p<0.01). Also, patients who were premedicated with Gabapentin showed better pain tolerance compared to those who had been given Clonidine, the results are in accordance with studies conducted by Mohd Hossein Ghafari *et al.*[7], Sussan Soltani Mohammadi *et al.*[8] which states that VAS pain scores were significantly lower in the two groups compared to the placebo group, Total morphine consumption in gabapentin group was significantly less than clonidine and gabapentin administration significantly decreased morphine consumption by 25% in comparison to clonidine.

Our study shows significant association between Ramsay sedation score & when both drugs are compared, Gabapentin showed a better sedative. study conducted by Jay Brijesh *et al.*[9], Vikas Saini *et al.*[10] and Singhal *et al.*[11] states that clonidine is effective in attenuating preoperative anxiety & stress response to endotracheal intubation when compared to gabapentin (p<0.05). Majumdar et al.[12] conducted a similar study and observed that both drugs are equally effective in producing preoperative sedation. In our study the time for 2 segment sensory regression was prolonged in Clonidine group but it was not considered statistically significant when compared to Gabapentin group.

The effect of clonidine on hemodynamic parameters is similar to the study done by H.Talebi *et al.*[14]. They observed decrease in HR and SBP with clonidine 200 mcg compared to placebo group which is highly significant. Fassoulaki A *et al.*[15] observed that gabapentin 1600 mg given at various time intervals decreases blood pressure but HR did not differ at all time intervals which was similar to our study in which Clonidine, showed significant fall in Systolic & Diastolic Blood pressure in comparison to Gabapentin group.

In a trial of 60 cases in which our research was applied,

1. The postoperative analgesic efficacy of oral Gabapentin showed better pain tolerance compared to those who had been given oral Clonidine.
2. The Ramsay sedation suggested good anxiolysis with Gabapentin.

3. As haemodynamic parameters changes in Gabapentin group were statistically insignificant, Gabapentin is considered haemodynamically stable.
4. Morphine consumption in 24 hrs was significantly high in Clonidine group compared to Gabapentin.
5. There were no significant change in time of sensory onset, maximum sensory block and duration of 2 segment regression when Clonidine was compared with drug Gabapentin.
6. In comparison of side effects, there was increased incidence of nausea and vomiting in Clonidine group.

Conclusion

We conclude that, Oral Gabapentin 300 mg given before 90 minutes as preemptive analgesia was more effective in reducing postoperative pain and morphine consumption, also providing better anxiolysis in patients undergoing abdomino-pelvic Surgeries under spinal anesthesia compared to Oral Clonidine 100 µg.

Conflict of Interest: None

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1305-1309
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.34

Ultrasound Guided Combined Superficial Cervical Plexus Block-Interscalene Block for Anesthesia in Clavicular Fractures: A Retrospective Observational Cohort Study

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Abstract

Background: Even though various peripheral nerve blocks are used for analgesia in clavicular fractures. The use of ultrasound guided combined superficial cervical plexus block and interscalene blocks as a sole anaesthetic technique for surgical fixation of clavicular fractures are not well, established. *Materials and Methods:* A retrospective chart review of patient undergoing clavicular fracture surgeries was performed. Patients received combined superficial cervical plexus block and interscalene block were included in the study. Block success and complication rate were evaluated. *Results:* Of the 20 patients underwent clavicular fracture surgery, 12 of them received ultrasound guided combined superficial cervical plexus block and interscalene block. Block success rate was found to be 100%. Time for rescue analgesia found to be 6.66 ± 0.84 hours. And there were no occurence of any Complications. *Conclusion:* We concluded that ultrasound guided combined superficial cervical plexus block and interscalene block can be used as a sole anaesthetic technique in clavicular fracture repair.

Keywords: Interscalene Block; Clavicular Fractures; Brachial plexus

How to cite this article:

S Arun, Deepan C, Jomy Thomas. Ultrasound Guided Combined Superficial Cervical Plexus Block-Interscalene Block for Anesthesia in Clavicular Fractures: A Retrospective Observational Cohort Study. Indian J Anesth Analg. 2019;6(4):1305-.

Introduction

Clavicle fractures comprised up to 4% of all fractures among all age groups[1]. Isolated clavicle fractures comprising 44.1% of all fractures in shoulder gridle[2].

Surgical treatment of clavicular fractures had show significant advantages like increased postoperative strength[3], quicker time to return to normal activities and low re-fracture rates[4,5,6]. Traditionally the clavicular fracture surgeries were performed under general anesthesia. Analgesia for clavicular fractures can be challenging for anaesthesiologist secondary to complex and varied innervation. Literatures describing hetrogenous innervation of clavicle and overlying skin. The sensory innervation of clavicle have contribution from both cervical and brachial plexus[7].

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Received on 27.05.2019, **Accepted on** 11.07.2019

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The contemporary literature surrounding the optimal regional anaesthetic technique for clavicular surgery which can provide superior postoperative analgesia and minimizing symptoms intra-operatively is lacking. The various nerve blocks that are used to anaesthetize the clavicle superficial cervical plexus block, interscalene brachial plexus block, supraclavicular block, and a combination of both interscalene and superficial cervical plexus block[8].

Many factors play arole in selecting the optimal regional anaesthetic methods like fracture location and complexity, incision over mixed innervation and surgical positioning and manipulations.

Eventhough interscalene blocks were used for shoulder surgeries, the dual innervation of the clavicular area suggest that a single interscalene block maynot be sufficient for the surgical pain[9].

With the advent of point of care ultrasonography reports of successful usage of combined peripheral nerve blocks are emerging. Ultrasound guided techniques increased the success rates and reduce the complications associated with the procedures as well as drugs. The reduction of local anaesthetics with ultrasound guided techniques had helped us to perform multiple blocks without the risk for toxicity.

Herring AA *et al*.[10] and vandepitte *et al*.[11] reported a successful use of superficial cervical plexus block and interscalene block for clavicular surgery. Gray *et al*.[12] stated that clavicular surgery also a indication for superficial cervical plexus block.

The objective of our retrospective cohort study is to demonstrate the effectiveness of combined superficial cervical plexus block and interscalene block as a sole anaesthetic that can be used for patients undergoing clavicular fractures repair.

Materials and Methods

After obtaining approval from the hospital institutional review board, a retrospective chart review of patients undergoing shoulder surgery over a period of 3 years starting from July 2015 was performed. The anaesthetic records including preoperative evaluation, intraoperative records and post anesthesia records were obtained from the medical records department. The postoperative records including hospital course, physician notes also obtained, patient demographics, surgical procedure, intraoperative anaesthetics and PACU course were recorded.

Patients with clavicular fractures repair under interscalene and superficial cervical plexus block were recorded. Among those the local anaesthetic used, concentration of the drug, volume used were noted. Block success and acute complications if any also noted from the charts.

Standard contraindications to placement of nerve blocks included patient refusal, coagulopathy and drug allergy and infection of intended site.

In accordance with the hospital protocol appropriate informed consent were obtained from the patients.

Block success is defined as one which did not necessitate conversion to general anesthesia. Rescue analgesia time noted from the records. Hemodynamic parameters were also noted.

Patients who were converted to general anesthesia (block failure) and those patients were block duration are not recorded are excluded from the study.

Anaesthetic Methods

Ultrasound guided combined interscalene and superficial cervical plexus block were performed under ultrasound guidance (LOGIQ GE Health Care), 12MHz linear transducer was used.

The transducer positioned in transverse plane and the carotid artery was identified at the level of cricoid. Then the transducer was moved laterally to identify the anterior and middle scalene muscles and we can able to found the brachial plexus in between. A Lateral to medial, in-plane needle insertion was done. Once inside the interscalene groove and after careful aspiration and needle tip confirmation 15 ml of 0.25% ropivacaine was injected.

After the performance of the interscalene block the needle was withdrawn and redirected to the cervical plexus. The hyperechoic fascia of the sternocleidomastoid muscle on its posterolateral border was identified and the cervical plexus will be identified as small hypoechoic nodules superficial to pre vertebral facia overlies the interscalene groove. The needle tip was adjusted to inject 10 ml of 0.25% ropivacaine adjacent to the plexus.

Statistical analysis

Descriptive statistics of the study are calculated and data emerged were analysed using SPSS statistics software. Continious quantitative data were expressed as numbers, mean and standard deviation and qualitative data were expressed as numbers and percentage.

Results

The retrospective chart review conducted on all clavicular fracture surgeries over the 3 year period yielded a total of 12 patients for analysis. Patient inclusion detailed in consort diagram (Fig. 1).

Among the 20 patients who had clavicular fracture at the review period only 12 of them underwent a combined interscalene and superficial cervical plexus block asa sole anaesthetic technique for clavicular fracture repair. The patient charecteristics are summarized in Table 1.

Of the 12 patients, 10 patients underwent open reduction and internal fixation while 2 of them had implant removal. All the 12 patient didn't necessitate any systemic analgesic supplementation or conversion to general anesthesia intraoperatively. None of these patient had developed any complication in the intra and postoperative period (horner syndrome, respiratory compromise). Mean duration for rescue analgesia was found to be 6.6 ± 0.849 hrs. Inj Tramadol 50 mg had been used as rescue analgesia in these patients. The outcomes of surgery and anesthesia are summarized in Table 2.

Table 1: Patient Charecteristics

	Mean ± Standard deviation
Age	49.91 ± 13.93
Height (m)	1.62 ± 0.08
Weight (kg)	65.16 ± 6.45
BMI (kg/m2)	25.24 ± 4.56

Table 2: Outcomes of Anesthesia and Surgery

Surgery Duration (Minutes)	94.16 ± 10.57
Time For Rescue Analgesia(Hrs)	6.66 ± 0.84
Acute complications	none
Block success rate	100%

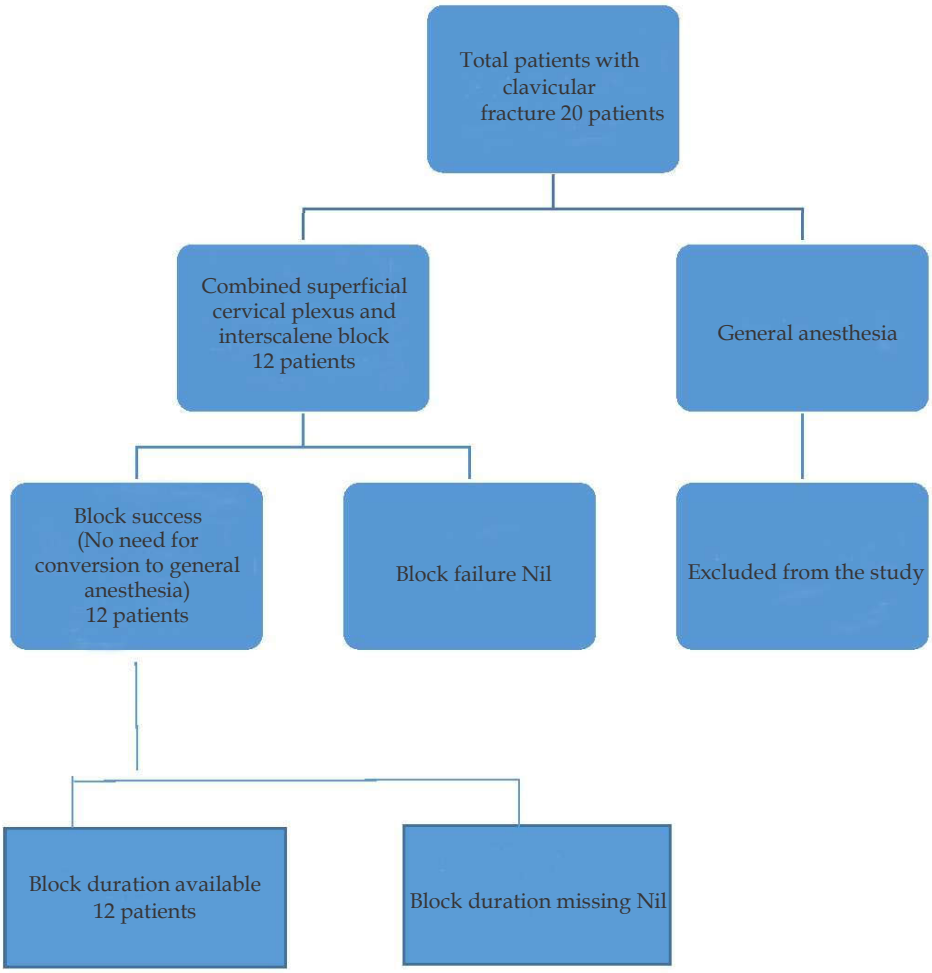

Fig. 1:

Discussion

The combined interscalene and superficial cervical plexus block has been shown to be promising anaesthetic technique for clavicular fracture surgeries.

Since clavicle received innervation both from cervical plexus as well as from brachial plexus the combined interscalene and superficial cervical plexus block may be the best option for the surgical fixation of clavicle fractures.

Herring *et al.*[10] reported the the ultrasound guided superficial cervical plexus block for analgesia and anesthesia in emergency settings.

Ushema *et al.*[13] reported the successful use of supraclavicular along with C5, C6 nerve blocks for clavicular surgery. This supports the innervation of clavicular surface by supraclavicular nerve a branch of superficial cervical plexus.

Vandepitte *et al.*[11] also reported successful combined interscalene and superficial cervical plexus block usage in surgical repair of clavicular fracture in a pregnant women.

Balban O *et al.*[14] in their retrospective study found that ultrasound guided combined superficial cervical plexus and interscalene blocks had been successfully used as a sole anesthesia for clavicular fracture patients without any complications. This was further confirmed by seni pot sangbam *et al.*[15] in their prospective observational study.

Contractor *et al.*[16] reported horner syndrome and hoarsness of voice in some patients and also the usage dexmedtomidine 1 mcg/kg.

But in our study we didn't found any side effects. And in our study we didn't use any additional sedatives and analgesics other than the nerve block. The duration of rescue analgesia was found to be 6 hrs, which is comparable to other studies.

Reverdy *et al.*[17] reported a high patient satisfaction rate in patient who underwent surgery for clavicular fracture under combined superficial cervical plexus block interscalene block.

The use of ultrasonography in the study had further reduced the complication associated with these nerve blocks.

Limitations

This study is limited by the small number of cases as hospital admissions for clavicular surgeries are usually low. A randomized controlled trial of larger sample size comparing the two groups will have a stronger implication on the outcome of the study.

Conclusion

Based on our experience we suggest that the combined superficial cervical plexus block and interscalene block can be used as a sole anaesthetic method for patients with clavicular fracture repair. A further randomized control studies are required to determine which constitute the better method for clavicular fracture repairs.

Acknowledgement

I would like to thank my wife Dr. Aparna for her assistance with the study. We didn't have any financial support or sponsorship and there is no conflict of interest.

Conflict of interest: NIL

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Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1311-1118
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.35

Prospective Study to Evaluate the Role of Vasopressin in Hypernatremia Treatment in Brain Dead Patients

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Abstract

Brain dead patients are potential organ donors but the pathological changes associated with braindeath can affect graft survival. Among various effects of braindeath endocrine and autonomic changes are noteworthy. Central diabetes insipidus characterized by reduced level of anti-diuretic hormone in brain dead patients can result in hypernatremia which inturn may affect the survival of the transplanted liver graft. Managing hypernatremia with exogenous vasopressin replacement improves the liver graft function.Vasopressin also maintains haemodynamic stability and reduce excessive free water loss as urine. It is given as intravenous infusion at 0.01-0.04 U/min or maximum 2.4U/hour.

Keywords: Braindeath; Endocrine dysfunction; Anti-diuretic hormone (vasopressin); Central diabetes insipidus; Hypernatremia; Liver transplantation; Liver graft survival; Vasopressin infusion.

How to cite this article:

G Balaji, B Jeyarani. Prospective Study to Evaluate the Role of Vasopressin in Hypernatremia Treatment in Brain Dead Patients. Indian J Anesth Analg. 2019;6(4):1311-1118.

Introduction

Traumatic brain injury or other physiological change to the brain (e.g. cerebral hemorrhage, CVA) may result in irreversible loss of brain stem function, leading to brain death. These patients can donate viable organs to those who in need of them.

Brainstem dysfunction causes many changes in normal physiology. These alterations in the cell homeostasis may adversely affect the viability of donated organs which can affect the graft function. Understanding the brain death pathophysiology helps us managing the adverse sequele reasonably, which inturn improves the viability of the transplanted organs.

Of the major changes autonomic and endocrine malfunctions are significant. Central Diabetes insipidus as a result of failure of posterior pituitary to secrete adequate anti-diuretic hormone (vasopressin) is a common endocrine dysfunction seen in the brain-dead patients.

Diabetes insipidus is characterized by high serum osmolarity and hypematremia. Hypernatremia is serum sodium level > l45 mEq/L[3].

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Received on 07.05.2019, **Accepted on** 08.06.2019

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Organs usually donated are cornea, liver, kidneys, heart/heart valves. Organs sensitive to hypematremia are kidney, liver, heart. Donor liver grafts with hypernatremia are prone to rejection on transplantation. Adverse ouycome is more likely when the sodium level is more than 155 mEq/L, in particular when the hypernatremia duration is longer before organ harvesting.[3]

Various studies have highlighted the effect of high serum sodium level on liver graft survival. So administering exogenous vasopressin as intravenous infusion to replace its deficiency to treat hypernatremia can improve the of the transplanted organs especially the liver. Which is the aim of our study.

In this study we have attempted to treat hypematremia using vasopressin in clinically brain-dead patients who were waiting for apnoea test and brain death certification, by assessing the serum sodium levels before and after starting the vasopressin therapy. Vasopressin also improves the blood pressure, as hypotension is a known and frequent complication of brain stem injury and brain death.

Aim of the Study

To evaluate the role of vasopressin in the treatment of hyperatremia in clinically brain-dead patients using intravenous vasopressin infusion at a dose of 0.01-0.04 U/min or maximum 2.4 U/hr in 40 clinically brain-dead patients.

Materials and Methods

It is a prospective study of vasopressin in the management of hypermatrmia in clinically brain-dead patients, conducted in Government General Hospital, Chennai, during the period 2010–2011.

Study Design

Prospective, interventional. After obtaining institutional ethical committee clearance, 40 clinically brain-dead patients with hypermatremia were selected using following criteria:

Inclusion Criteria

- Clinically brain-dead patients (ASA PS 6), diagnosed by neurosurgeon or neurophysian using brainstem reflex tests, waiting for apnoea test and brain death certification.
- Traumatic injury
- Serum Na^+ level > 145 meq/L
- Urine output > 4 ml/kg/hr

Exclusion Criteria

- Brain-dead patients with serum Na+ < 1 46 meq/L
- Urine output < 1 .5-2m 1/kg/hr
- Patients with known renal pathology
- Allergy to vasopressin group of drugs

Outcome Measures

- Serum Na^+ level (by venous or arterial sample)
- Urine output
- Blood pressure
- Pulse rate
- Serum potassium
- Serum creatinine

Monitoring Interval

Blood pressure- 1st hour — every 15 mins, 2nd & 3rd hour — every 30 mins, subsequent hours — hourly monitoring (if stable with supports) for 6 hours.

All other parameters were monitored second hourly.

Materials

1. l8G venflon
2. Heparin
3. ABG analysis source
4. Intra venous fluids (5%D, RL, 1/2NS)
5. Monitors-Monitors: ECG, Pulse oximetry, Capnography, NIBP
6. Vasopressin injection

Study Method

After receiving information about a clinically braindead patient information from any ward or ICU, patients were examined and clinical brain death certification was confirmed twice at 4-6 hours interval. Investigations were evaluated to rule out other possibilities of unconciousness like intoxication.

After verifying the inclusion criteria and confirming the diagnosis of hypermatremia, written

consent was obtained from patient's attenders and intravenous vasopressin infusion was started at a dose range of 0.01-0.04 U/min. 20 units (1 ampoule) vasopressin is diluted in 500m1 NS to get 0.04U/ ml.

The parameters mentioned above were monitored at specified time intervals for 6-hours.

Single blinded study where the patient was blind.

Results

1. Serum Na+ reaches the target value (<145 mEq/L)
2. Decreased but not to the target level
3. No change in serum Na^+ level
4. Persistently increasing levels noted

Interpretation of results

Response to vasopressin

1. ***Present:*** If there was decrease in serum Na+ level (to target level <145 mEq/L or decrease >10 to 15% from baseline).
2. ***Not Present:*** If there was no change or increasing levels.

Statistics

Statistical analysis was done to determine the significance (friedman test and paired t test were used).

Observation and Results

Male, Female distribution in this study was 75%, 25% respectively. In this study 85% cases were road traffic accident, 15% cases were fall from height. Mean age was – 33.3. There was a consistent decrease in serum sodium level in every hour. There was significant decrease in serum sodium at the end. There was a consistent decrease in urine output. There was a definite increase in mean arterial pressure at the end of 6 hrs. There was no significant difference, in serum sodium control, among the male and female population. Mode of injury didn't produce any significant difference in sodium control and blood pressure variation in this study.

Table 1: Frequency Table: Demographic profile: Sex

Sex	Frequency	Percent
Male	30	75.0
Female	10	25.0
Total	40	100.00

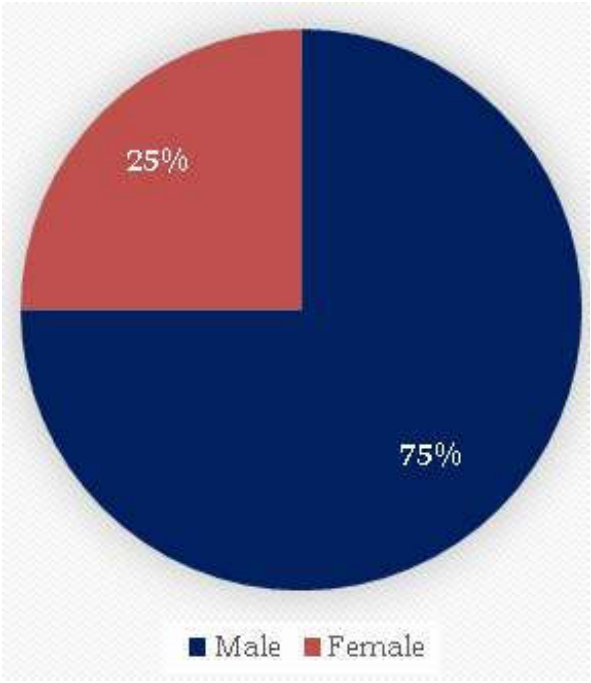

Fig. 1: Sex distribution

Table 2: Frequency Table: Mode of Injury

Mode of Injury	Frequency	Percent
RTA	34	85.0
Fall from Height	6	15.0
Total	40	100.00

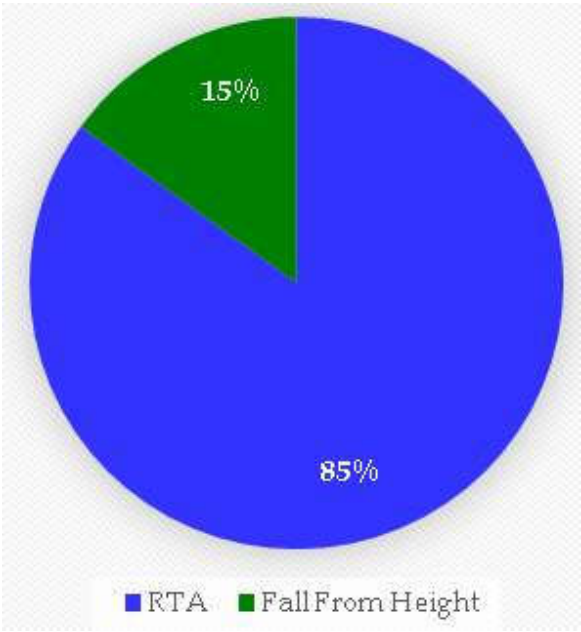

Fig. 2: Mode of injury

Table 3: Descriptive statistics: Age

	N	Minimum	Maximum	Mean	Std.Deviation
Age in years	40	15	60	33.30	12.041

Table 4: Descriptive Statistics, Freidman Test – to compare the hourly serum sodium values.

Serum Sodium

Serum sodium	N	Mean	Std. Deviation	Minimum	Maximum	P-value
Initial	40	160.10	8.041	146	179	
1 hr	40	158.28	7.582	146	175	
2 hrs	40	154.77	7.026	142	170	
3 hrs	40	151.15	7.145	138	166	
4 hrs	40	147.98	7.767	135	166	<0.001**
5 hrs	40	145.12	9.030	132	171	
6 hrs	40	142.48	10.195	130	174	

Table 5: Paired Samples Statistics

Paried T-Test to compare the initial and final serum sodium values.

Serum sodium	Mean	N	Std. Deviation	Std Error Mean	P –value
Initial	160.10	40	8.041	1.271	<0.001**
6 hrs	142.48	40	10.195	1.612	

Fig. 3: Hourly serum sodium level

Table 6: Friedman Test – to compare the hourly urine output values

Descriptive statistics

Urine output	N	Mean	Std. Deviation	Minimum	Maximum	P-value
Initial	40	240.50	31.861	180	320	
1 hr	40	222.38	31.297	165	300	
2 hrs	40	205.50	32.715	160	290	
3 hrs	40	188.25	33.846	140	290	
4 hrs	40	174.50	35.225	130	280	<0.001**
5 hrs	40	162.50	38.213	125	290	
6 hrs	40	149.88	42.115	110	280	

Fig. 4: Hourly urine output

Table 7: Mean arterial pressure Descriptive Statistics

Friedman Test – to compare the MAP values

Mean arterial pressure	N	Mean	Std Deviation	Minimum	Maximum	p-value
Initial	40	74.97	4.633	66	88	
15 mins	40	77.10	6.515	67	105	

30 mins	40	77.70	4.603	68	88	
45 mins	40	78.70	4.575	70	90	
1 hrs	40	79.63	4.436	70	91	
1.30 hrs	40	81.68	4.305	74	89	<0.001**
2 hrs	40	83.33	4.486	75	94	
2.30 hrs	40	85.60	4.301	78	97	
3 hrs	40	87.43	4.069	80	99	
4 hrs	40	91.48	4.309	84	101	
5 hrs	40	95.60	4.361	87	104	
6 hrs	40	98.50	4.546	92	108	

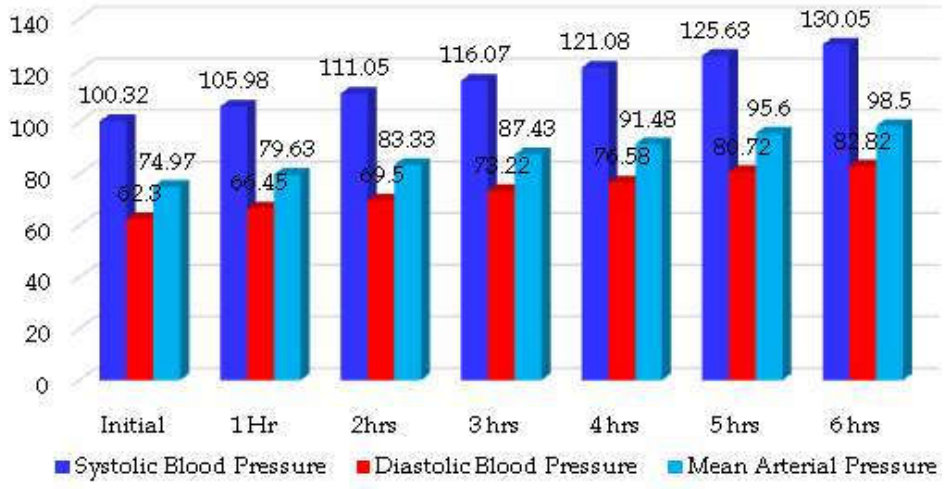

Fig. 5: Hourly MAP

Table 8: Paried Samples Statistics

Paried T- Test – to compare the initial and final MAP values

Mean arterial pressure	Mean	N	Std. Deviation	Std. Error Mean	P- Value
Initial	74.97	40	4.633	.732	<0.001**
6 hrs	98.50	40	4.546	.719	

Discussion

Vasopressin is a nano peptide with a half life 10-15 minutes and undergoes renal and hepatic metabolism. It is administered intravenously or intramuscularly. Desmopressin is a long acting (half life 1.5-2.5 hours) analog with less vasopressor property. It can be given intravenously, sub cutaneously, intranasally or orally.

Vasopressin has two major effects in braindead patients,

1. V2 receptor mediated free water retention- which helps in the management of hypermatremia in brain-dead patients due to the endocrine failure that follows posterior pituitary infarction, which is otherwise harmful to the potentially transplan table organs, especially when serum sodium concentration >l55 mEq/L. (if the diagnosis is confirmed and the patients relatives give consent for organ donation).
2. V1 receptor mediated vasoconstriction – which helps to maintain/improve hemodynamic status in brain-dead patients, who are usually prone to hemodynamic instability due to the frequently accompanying autonomic failure.

From observation and statistical analysis there was almost a steady decline in serum sodium in every hour sample with a significant decrease in sodium level at the end of 6th hour noticed in 31 patients.

Mean initial sodium was 160.10 mmol/L and final sodium concentration was 142.48 mmol/L.

There were consistent reduction in urine output in every hour and significant decrease in urine output at the end of 6th hour also noticed in those 31 patients.

Mean initial urine output was 240.50 L/hr and final urine output was 149.88 L/hr.

The pathology in these 31 patients could be the central diabetes insipid us due to posterior pituitary infarction.

In 9 patients there was no significant fall in serum sodium level and urine output, so the pathology in these patients may be different-could be nephrogenic diabetes insipidus.

Considerable improvement in blood pressure (in terms of Systolic Blood pressure, Diastolic Blood pressure, Mean Arterial Pressure) is also seen in almost all patients.

Mean initial Blood pressure:

Systolic Blood pressure	: 100.32 mmHg
Diastolic Blood pressure	: 62.30 mmHg
Mean arterial pressure	: 74.97 mmHg

Mean final Blood pressure:

Systolic Blood pressure	: 130.05 mmHg
Diastolic Blood pressure	: 82.82 mmHg
Mean arterial pressure	: 98. 50 mmHg

Sex distribution: Male-75% Female-25%.

There was no significant difference in terms of drug dosage or response in serum sodium level or blood pressure or urine output due to sex distribution.

So vasopressin infusion in clinically brain dead hypernatremic patients produced,

1. Significant & definite decrease in serum sodium level over 4-6 hours.
2. Definite decrease in urine output.
3. Considerable improvement or stability in haemodynamic status (Blood pressure), as denoted by decrease in catecholamine requirement with time.

As explained in review of literature these findings are supported by various studies.

Effect of Vasopressin on serum sodium control is supported by Charles Ralston, Warwick - Butt *et al.*[9] and Lee YJ, Shen EY, Huang -FY, Kao HA, Shyur SD *et al.*[10]

Catecholamine sparing effect of vasopressin is supported by Pennefather *et al.* (Pennefather SH, Bullock- RE, Mantle D, Dark JH)'[11], Kenneth Katz, Jack Lawler, Jennifer Wax, Robert 0' Connor, Vinay Nadkarn *et al.*[12,] Kinoshita- Y, Yahata K, Yoshioka T, Onishi S. Sugimoto T *et al.*[15] Yoshioka -T, Sugimoto H, Uenishi M, Sakamoto -T, Sadamitsu D, Sakano T, Sugimoto T[18] Luciana Mascia, Ilaria Mastromauro and Silvia Grottoli *et al.*[19]

Diabetes insipidus

Central diabetes insipidus: Head injury, either surgical or traumatic, in the region of the pituitary and or hypothalamus may cause central DI. Other causes include hypothalamic or pituitary tumors, cerebral aneurysms, CNS ischemia, and brain infiltrations and infections. Finally, central DI may be idiopathic or familial. Vasopressin is preferred for short term uses especially when there is hypotension. Desmopressin is preferred for long term uses Desmopressin (DDAVP) is an analog of AVP with a relatively potent antidiuretic effect and negligible vasopressor activity.

Nephrogenic diabetes insipidus: Nephrogenic DI may be congenital or acquired. Hypercalcemia, hypokalemia, post-obstructive renal failure, lithium, foscarnet, clozapine, demeclocycline, and other drugs can induce nephrogenic DI. The preferred treatment of nephrogenic DI is adequate intake of water. Thiazide diuretics paradoxically reduce the polyuria associated with DI and they are used to treat non-lithiuminduced nephrogenic DI.

Conclusion

Hypernatremia a frequent electrolyte disturbance from cental origin in braindead patients can be effectively treated with injection vasopressin infusion. It also mitigates the hypotension that frequently occurs in these group of patients. Other options include inj.desmopressin (lacks vasopressor effect) and IV fluids with high free water and IV fluids with less sodium content.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1319-1324
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.36

Prevention of Hypotension Following Subarachnoid Block; Efficacy of Preloading with Hydroxyethyl Starch Versus Ringer's Lactate Solution

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Abstract

Background: Arterial hypotension is a potential hazard associated with spinal anesthesia. Routinely, crystalloids and colloids are used for managing hypotension. While crystalloids easily move out of the intravascular space, colloids are confined to the intravascular space, thereby minimizing the risk of hypotension. This study was carried out to compare the efficacy of 10% Hydroxyethyl starch with Ringer's lactate solution. *Methods:* This double blind randomized controlled trial was carried out on 100 patients who underwent spinal anesthesia during the study period. The study participants were randomized into experimental group (6% Hydroxyethyl starch, 10 ml/Kg) and control group (Ringer's lactate, 20 ml/Kg). Blood pressure and heart rate were recorded periodically up to 60 minutes. Sensory level of blockade was checked after 5 minutes. *Results:* It was observed that as the surgery prolonged, the incidence of hypotension increased among the controls compared to the experimental group. While the initial incidence was higher among the experimental group (24%), the incidence was greater for the controls beyond 25 minutes (42%). The difference in the incidence was statistically significant (p<0.05). *Conclusion:* Hydroxyethyl starch is superior to Ringer's lactate solution in prevention of Hypotension following spinal anesthesia. Incidence of hypotension is reduced but not completely eliminated. Hydroxyethyl starch also has several other advantages such as prophylaxis against venous thrombosis and decreased allergic potential.

Keywords: Hydroxy ethyl starch; Hypotension; Ringer lactate; Spinal anesthesia.

How to cite this article:

Balajibabu PR, Ananda Bhat. Prevention of Hypotension Following Subarachnoid Block; Efficacy of Preloading with Hydroxyethyl Starch Versus Ringer's Lactate Solution. Indian J Anesth Analg. 2019;6(4):1319-1324.

Introduction

Spinal anesthesia is one of the widely practiced anaesthetic techniques over years for lower abdominal and lower limb surgeries. If spinal anesthesia is applied with proper skills and care, it is a safe procedure which provides satisfactory outcomes. It is a preferred method of choice among the patients and surgeons considering the benefits and comforts achieved on-table. Spinal anesthesia for routine surgical procedures assumes special importance in developing countries because of economic reasons, lack

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Received on 08.05.2019, **Accepted on** 08.06.2019

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of availability of sophisticated anaesthetic apparatus and compressed gases in the remote areas.

The potential hazard associated with spinal anesthesia is arterial hypotension. This can cause significant morbidity and mortality. Methods used to reduce the incidence and severity of spinal hypotension includes head down position, prophylactic vasopressors, leg elevation and strapping, use of inflatable boots and preloading the patients with intravenous fluids. Crystalloids solutions being of lower molecular weight will enter the interstitial space due to lack of intrinsic colloid osmotic pressure resulting in pulmonary edema which interferes with tissue oxygen exchange. Colloids are higher molecular substances than crystalloids and are similar to plasma in oncotic pressure and remain confined to intravascular space with little expansion of interstitial space.

It is indeed a challenge to manage arterial hypotension on table. Although several studies have been carried out to evaluate the effectiveness of spinal anesthesia, very few studies have been carried out to address the adverse effect, mainly hypotension. An analysis into the therapeutics involved in the management of arterial hypotension will go a long way in minimizing the morbidity and mortality associated with spinal anesthesia.

Objectives

1. To compare the preloading efficacy of Ringer's lactate, 20 ml/kg and Hydroxyethyl starch 6%, 10 ml/kg body weight, for prevention of Hypotension following subarachnoid Block.
2. To evaluate the adverse outcomes of Hydroxyethyl starch among the study participants.

Methodology

Study setting and participants

This double blind randomized controlled trial was carried out in the Department of Anesthesiology of a tertiary teaching institution for a period of 10 months. All the patients who were scheduled for surgeries involving spinal anesthesia during the study period were selected for the study. Based on the selection criteria, a total of 100 participants were included in the study.

Inclusion criteria

- Patient belonging to ASA Grade I & II.
- Body Weight 40 to 80 kilograms.
- Age 20 to 60 years of both the sexes.
- Patients undergoing various elective and emergency operations under spinal anesthesia in whom minimal blood loss is anticipated.

Exclusion criteria

- Any patients in whom spinal anesthesia is contraindicated.
- Patients with cardio vascular, respiratory & central nervous system disorders.

Randomization and grouping

The study participants were grouped into experimental and control groups. The experimental group consisted of 50 participants who received 6% Hydroxyethyl starch, 10 ml/Kg. The control group consisted of 50 participants who received Ringer lactate, 20 ml/Kg. All the participants were randomly allocated into the groups using computer generated random numbers.

Ethical approval and informed consent

Approval was obtained from the Institutional Ethics Committee prior to the commencement of the study. Each participant was explained in detail about the study and informed consent was obtained prior to the commencement of data collection.

Procedure

Following routine investigations and pre-anaesthetic evaluation, all participants were pre-medicated with injection Midazolam 0.02 mg/kg and injection Atropine 0.6 mg, through intra venous route, 30 minutes before surgery.

Basal parameters like heart rate, Oxygen saturation and blood pressure were monitored. A peripheral intravenous line with 18 or 20 gauge canula was secured in one of the upper limbs. Volume infusion was determined in accordance to the body weight. In both the groups, the solutions were infused over a period of 20 minutes. After pre-loading all patients received ringer lactate infusion for fluid maintenance.

Under aseptic precautions lumbar puncture was performed with 23 gauge spinal needle (Quinke's

Needle) through midline approach with patient in the right lateral or left lateral decubitus position, 10^0 head down tilt. After free flow of CSF, 2 ml of Lignocaine with 200 mcg of adrenaline was injected. Immediately after the injection the needle was withdrawn the patient turned to supine position.

Data collection

Blood pressure and heart rate were recorded at an interval of every minute up to 5 minutes, every 5 minutes up to 30 minutes, every 10 minutes up to 60 minutes. Sensory level of blockade was checked after 5 minutes. Hypotension was defined as decrease in the systolic blood pressure more than 25% from the basal parameter. Hypotension was managed with Trendelenberg's position, increase in fluid infusion rate, and 100% oxygen by mask. If hypotension continued despite the above measures, injection Mephenteramine sulphate was administered intravenously 3 mg bolus at 1 minute interval until the blood pressure increased to acceptable levels. Bradycardia was treated with intravenous injection of Atropine 0.6 ml.

Data analysis

Data was entered and analyzed using SPSS version 20 software. Difference between the mean for values of systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate was tested for statistical significance using student 't' test for independent group at 5% level of significance.

Results

Majority of the participants in both the groups belonged to 21-30 years (48% and 52% respectively). Most of the participants weighed between 51-60 kilograms in both the groups (54% and 48% respectively). The level of sensory blockade was at T4 for the controls (52%) and T6 for experimental group (48%) (Table 1).

The incidence of hypotension between the groups is given in table 2. It was observed that as the surgery progressed, the incidence of severe hypotension increased among the controls compared to the experimental group. While the initial incidence was higher among the experimental group (24%), the incidence was greater for the controls beyond 25 minutes (42%). The difference in the incidence was statistically significant (p<0.05).

The difference in the mean systolic blood pressure over the duration of anesthesia is given in table 3. It was observed that although the initial fall in the systolic blood pressure occured in both the groups, there was a significantly higher reduction in the systolic blood pressure in the controls compared to the experimental group, as evidenced by increase in the difference of mean systolic blood pressure. The observed difference was statistically significant. (Table 3) Similar observations were seen with mean diastolic pressure (Table 4).

Our study observed a significant reduction in the mean arterial pressure among the controls within 5 minutes of start of surgery while the mean arterial pressures among the experimental group remained fairly stable throughout the surgery. The observed difference was statistically significant (p<0.05). (Table 5) However, the overall differences in the mean heart rate compared between the two groups at different time intervals did not show significant variation between the groups and also within the groups. (Table 6) Overall, the number of participants requiring Inj. Mepheteramine was higher among the controls (14%) compared to the experimental group (4%) (Table 7).

Table 1: Background characteristics of the study participants

S. No	Characteristics	Control (Group A) N=50 (%)	Experimental (Group B) N=50 (%)
1	*Age (in years)*		
	21–30	24 (48.0)	26 (52.0)
	31–40	13 (26.0)	12 (24.0)
	41–50	7 (14.0)	11 (22.0)
	51–60	6 (12.0)	1 (2.0)
2	*Sex*		
	Male	34 (68.0)	29 (58.0)
	Female	16 (32.0)	21 (42.0)
3	*Weight distribution (in kilograms)*		
	41–50	3 (6.0)	5 (10.0)
	51–60	27 (54.0)	24 (48.0)
	61–70	15 (30.0)	17 (34.0)
	71–80	5 (10.0)	4 (8.0)
4	*Type of surgery*		
	Herniorraphy	15 (30.0)	13 (26.0)
	Appendicetomy	13 (26.0)	13 (26.0)
	Total abdominal Hystrectomy	7 (14.0)	12 (24.0)
	Skin grafting	5 (10.0)	3 (6.0)
	Eversion of Sac of Hydrocele	5 (10.0)	3 (6.0)
	Subfasical ligation of varicose vein	2 (4.0)	3 (6.0)
	Varicocele ligation	1 (2.0)	1 (2.0)
	Ovarian cyst removal	1 (2.0)	1 (2.0)
	Orchidopexy	1 (2.0)	1 (2.0)
5	*Level of sensory blockade*		
	T4	26 (52.0)	23 (46.0)
	T6	22 (44.0)	24 (48.0)
	T8	2 (4.0)	2 (4.0)
	T10	0(0.0)	1 (2.0)

Table 2: Showing incidence of severe hypotension in Group A and B following spinal anesthesia

S. No	Time	Control (Group A) N = 50 (%)	Experimental (Group B) N = 50 (%)	*p*-Value
1	0–5	0	16 (24)	*p*<0.05
2	6–10	0	12 (24)	*p*<0.05
3	11–15	5 (10)	7 (14)	*p*<0.05
4	16–20	6 (12)	3 (6)	*p*<0.05
5	21–25	10 (20)	3 (6)	*p*<0.05
6	26–30	21 (42)	7 (14)	*p*<0.05
7	31–35	7 (14)	2 (4)	*p*<0.05
8	36–40	1 (2)	0	*p*<0.05
9	>40	2 (4)	0	*p*<0.05

Table 3: Mean systolic blood pressure at different intervals of time after spinal anesthesia

Time (in minutes)	Group A	Group B	*p* – Value
0	120 mm Hg	120 mm Hg	*p*>0.05
1	119 mm Hg	121 mm Hg	*p*>0.05
2	113 mm Hg	118 mm Hg	*p*<0.05*
3	107 mm Hg	118 mm Hg	*p*<0.05*
4	103 mm Hg	116 mm Hg	*p*<0.05*
5	100 mm Hg	115 mm Hg	*p*<0.05*
10	98 mm Hg	115 mm Hg	*p*<0.05*
15	96 mm Hg	115 mm Hg	*p*<0.05*
20	98 mm Hg	114 mm Hg	*p*<0.05*
25	99 mm Hg	117 mm Hg	*p*<0.05*
30	101 mm Hg	117 mm Hg	*p*<0.05*
40	100 mm Hg	118 mm Hg	*p*<0.05*
50	104 mm Hg	119 mm Hg	*p*<0.05*
60	104 mm Hg	118 mm Hg	*p*<0.05*
75	98 mm Hg	120 mm Hg	*p*<0.05*

**p* value significant at 95% level

Table 4: Mean diastolic pressure at different time intervals after spinal anesthesia

Time (in minutes)	Group A	Group B	*p* – Value
0	75 mm Hg	78 mm Hg	*p*>0.05
1	76 mm Hg	78 mm Hg	*p*>0.05
2	73 mm Hg	77 mm Hg	*p*>0.05
3	70 mm Hg	75 mm Hg	*p*>0.05
4	68 mm Hg	74 mm Hg	*p*<0.05*
5	69 mm Hg	74 mm Hg	*p*<0.05*
10	65 mm Hg	72 mm Hg	*p*<0.05*
15	63 mm Hg	73 mm Hg	*p*<0.05*
20	64 mm Hg	76 mm Hg	*p*<0.05*
25	65 mm Hg	75 mm Hg	*p*<0.05*
30	66 mm Hg	74 mm Hg	*p*<0.05*
40	66 mm Hg	76 mm Hg	*p*<0.05*
50	67 mm Hg	75 mm Hg	*p*<0.05*
60	64 mm Hg	75 mm Hg	*p*<0.05*
75	68 mm Hg	76 mm Hg	*p*<0.05*

*p value significant at 95% level

Table 5: Average mean arterial pressure at different time intervals after spinal anesthesia

Time (in minutes)	Group A	Group B	*p* – Value
0	90 mm Hg	92 mm Hg	*p*>0.05
1	90 mm Hg	92 mm Hg	*p*>0.05
2	84 mm Hg	90 mm Hg	*p*>0.05
3	81 mm Hg	89 mm Hg	*p*<0.05*
4	78 mm Hg	87 mm Hg	*p*<0.05*
5	77 mm Hg	87 mm Hg	*p*<0.05*
10	76 mm Hg	87 mm Hg	*p*<0.05*
15	74 mm Hg	87 mm Hg	*p*<0.05*
20	76 mm Hg	89 mm Hg	*p*<0.05*
25	77 mm Hg	87 mm Hg	*p*<0.05*
30	77 mm Hg	88 mm Hg	*p*<0.05*
40	77 mm Hg	89 mm Hg	*p*<0.05*
50	80 mm Hg	89 mm Hg	*p*<0.05*
60	81 mm Hg	88 mm Hg	*p*<0.05*
75	78 mm Hg	93 mm Hg	*p*<0.05*

**p* value significant at 95% level

Table 6: Mean Heart Rate at different time intervals after spinal anesthesia

Time (in minutes)	Group A	Group B
0	89 per minute	85 per minute
1	88 per minute	85 per minute
2	88 per minute	85 per minute
3	87 per minute	85 per minute
4	84 per minute	84 per minute
5	86 per minute	83 per minute
10	86 per minute	83 per minute
15	89 per minute	83 per minute
20	87 per minute	82 per minute
25	89 per minute	83 per minute
30	88 per minute	83 per minute
40	86 per minute	82 per minute
50	85 per minute	83 per minute
60	84 per minute	84 per minute
75	81 per minute	84 per minute

Table 7: Mephenteramine requirements among the study participants

	Group A	Group B
No. of patients requiring Inj Mephenteramine	7 (14%)	2 (4%)

Discussion

Arterial Hypotension is a major and most common complication following spinal anesthesia. The resultant decrease in the cardiac output may cause inadequate cerebral and/or coronary blood flow, culminating in death. Hypotension has been defined differently in many studies. Some define hypotension as fall in blood pressure by 20% and others by 30% from the basal blood pressure, while some studies have defined hypotension as blood pressure less than 80 mmHg. In our study we have considered fall by more than 25% as hypotension. Incidence of Hypotension varies depending upon number of factors such as level of sympathetic blockage, site of operation, nature of operation, patient's age, health condition and blood volume. Since blood pressure can be described as the product of cardiac output and total peripheral vascular resistance, the usual management has been directed towards one of these two factors, namely, use of peripheral vasoconstrictors to increase the total peripheral resistance or the use of drugs with chronotropic or inotropic cardiac action to augment the output of the heart. Another method of increasing cardiac output is to augment the venous return by the expansion of blood volume.

Prophylactic administration of crystalloid before spinal anesthesia has been considered a safe and effective method of reducing the incidence of Hypotension. About 75% of any crystalloid diffuses into interstitial space; its efficacy in expanding plasma volume is only transient. Although crystalloid administration is safe in most patients it may be disadvantageous in certain groups, such as those with renal impairment or congestive cardiac failure if infused in large volumes. Excessive crystalloid administration may rarely produce pulmonary edema and peripheral edema and have little effect on plasma volume, especially in geriatric patients especially after the sympathetic block wears off. Recently attention has been focused on the Prophylactic administration of colloid solutions for the prevention of hypotension during spinal anesthesia. The more logical choice in preventing hypotension during spinal anesthesia is administration of colloids, since it remains in the intravascular compartment for longer period depending on its physical properties.

In our study the incidence of hypotension has been found to be 62% in control group and 18% in experimental group. After subarachnoid block there was a progressive fall of blood pressure up to 20 minutes and maximum hypotension occurred within 10–15 minutes. There was a statistically significant difference in the incidence of hypotension in control group compared to experimental group (p<0.05). We found that Hydroxyethyl starch is superior to Ringer lactate in preventing hypotension following spinal anesthesia.

Our observation was close to the study conducted by[1] who observed higher incidence of hypotension (52%) in lactated Ringers solution group compared to (15%) the hetastarch group.[2] in his study found no hypotension in the albumin group compared with an incidence of 29% in the crystalloid group.[3] Also found lower incidence of hypotension (45%) in the Hetastarch group compared to (85%) in Ringer lactate group. Siddik SM *et al.* also had similar findings showing increased incidence of hypotension (80%) in Ringer lactate group when compared to (40%) in 10% hydroxy ethyl starch group.[4] Similar results were observed in studies done by Hiroshi Ueyama *et al.*[5]

Hydroxy ethyl starch is a colloid which replaces lost albumin, which is mainly responsible for the oncotic pressure in the blood. It is essential that substances like hydroxyethyl starch should have sufficient molecular weight so as to prevent its excretion rapidly out of the body. Hydroxy ethyl starch exerts a colloid oncotic pressure of 58.5 cm H_2O and one litre of hydroxyethyl starch increases the plasma oncotic pressure of patients in hypovolemic shock by 36%.

In order to achieve a long intravascular stay necessary for an effective plasma volume improvement, Hydroxyethyl starch molecules should be above the renal threshold. Hydroxy ethyl starch is primarily eliminated via the kidneys. Hydroxyethyl starch fraction that is subjected to slower renal elimination is cleaved first by intracellular gamma amylases and their intravascular alpha glomerular filtration. The rate of degradation to renally excretable fraction of Hydroxyethyl starch depends on the degree of molar substitutions and the substitution pattern. Hydroxyethyl starch following acute or chronic administration is subject to transient storage in liver, spleen and other organ until broken down and eliminated by tissue glucosidases. Patients with normal renal function rapidly eliminate hydroxyethyl starch. The residual Hydroxyethyl starch dose is metabolized in tissues by tissue glucosidases and excreted in the kidneys. Patients with total chronic renal failure tend to be subject to extensive tissue storage of Hydroxyethyl starch as a consequence of the non dialyzability. Hydroxyethyl starch is therefore contraindicated in these patients. About 46% of the participants who

were administered Hydroxyethyl starch excreted it in the urine within two days and 64% within eight days.

The more stable hemodynamic status observed after colloid administration probably relates to its remaining in the intravascular compartment longer than crystalloids. Extra vascular redistribution of crystalloids may be so rapid that it may be impossible to infuse them fast enough to maintain intravascular volume.[6] reported that colloid osmotic pressure decrease by only 1.7 mm Hg after preloading with 3% dextran 70 before epidural anesthesia for caesarean section, compared with a 5.6 mm Hg decrease after preloading with Ringer lactate.

In our study we did not come across any allergic reactions to the Hydroxyethyl starch. In our study we found that hydroxyethyl starch is superior to Ringer's lactate in prevention of Hypotension following spinal anesthesia. Incidence of hypotension is reduced but not completely eliminated. Hydroxyethyl starch also has several other advantages such as prophylaxis against venous thrombosis and decreased allergic potential in comparison to gelatin.

Conclusion

In our study we have found that Hydroxyethyl starch is more effective, than lactated Ringer's solution in preventing hypotension in patients undergoing surgeries under spinal anesthesia. However, the incidence of hypotension was only reduced but not completely eliminated in this study. The dose response relationship in eliminating the incidence of hypotension needs to be further explored.

Conflict of interest: Nil

Funding: Nil

Ethical approval: Obtained

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1325-1332
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.37

A Comparative Study of Analgesia with Ropivacaine and Dexmedetomidine vs Ropivacaine and Fentanyl in Epidural Anesthesia in Lower Limb Surgeries

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Abstract

Background: The popular techniques of regional anesthesia used for surgeries of lower limbs are Subarachnoid block is better term anesthesia and epidural anesthesia. Limitations of intrathecal anesthesia are short duration of analgesia, onset of sympathetic blockade rapidly and brief postoperative analgesia duration. *Aim:* To evaluate the synergistic effect of addition of dexmedetomidine to ropivacaine 0.75% and fentanyl to ropivacaine .75% in epidural anesthesia for surgeries of lower limbs. *Materials and Methods:* The study conducted in Gandhi hospital during period between December 2016 to November 2017. Institutional ethical committee clearance as well as informed consent from all patients was obtained from all patients. One hundred patients, who had various elective lower limb surgical procedures belonging to ASA class I and II were included in the study. Group RD (n = 50)–15 ml of 0.75% ropivacaine + 1.0 µg/kg of dexmedetomidine, Group RF (n=50) 15 ml of 0.75% ropivacaine and Fentanyl 1 µg/kg. *Results:* The mean time of onset of sensory blockade in group RD is 5.26 ± 1.49 mins and in RF 10.04 ± 2.5 mins. There is highly statistical significant difference between the groups (p = 0.000). The mean time taken for the onset of motor blockade is 11.22 ± 2.61 mins in group RD and 15.36 ± 3.28 mins in group RF There is statistical significant difference between the groups (p = 0.000). There is no statistically significant difference in the mean heart rate, mean systolic blood pressure, diastolic blood pressure and mean arterial pressure between groups at various intervals. Bradycardia and dry mouth seen only in the RD group none was in RF group. Hypotension, nausea and vomiting, tremors observed in both groups on comparision were stastically insignificant. *Conclusion:* Dexmedetomidine can be used as a more potent and safer alternative to Fentanyl in epidural anesthesia as a adjuvant to ropivacaine.

Keywords: Dexmedetomidine; Ropivacaine; Fentanyl; Epidural Anaesthesia

How to cite this article:

Burra Ramesh Kumar, Appa Rao Mekala. A Comparative Study of Analgesia with Ropivacaine and Dexmedetomidine vs Ropivacaine and Fentanyl in Epidural Anesthesia in Lower Limb Surgeries. Indian J Anesth Analg. 2019;6(4):1325-.

Introduction

The most popular regional anesthesia techniques used for lower limb surgeries are intrathecal anesthesia and epidural anesthesia. Intrathecal anesthesia also called as sub arachnoid block has a fewer constraints like duration of anesthesia being shorter, extension of anesthesia cannot be made for prolonged surgeries, onset of sympathetic blockade being rapid, shorter post operative analgesia duration and troublesome complication of postdural puncture headache (PDPH). Hence the most preferred anaesthetic technique for lower

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Received on 22.03.2019, **Accepted on** 14.05.2019

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limb surgeries these days is epidural anesthesia.[1] As it provides surgical anesthesia effectively and can meet the duration of surgical needs extensively, provides prolonged post operative analgesia, the incidence of hemodynamic changes is reduced as a result of sympathetic blockade as it produces segmental anesthesia unlike subarachnoid block anesthesia and there is no PDPH incidence as the dura is not pierced are the advantages of epidural anesthesia. For epidural anesthesia, different local anesthesia are used[1]. The disadvantage of lidocaine is its duration of action being intermediate and the disadvantage of bupivacaine though long acting, is increased fatal cardiac toxicity incidence after accidental intravascular injection, because of low dosage for cardiovascular collapse and central nervous system toxicity (cc/cns)[2]. Because of this reason, an increase in search for alternative drugs with desirable blocking properties of bupivacaine but with a greater margin of safety. The newer long acting amide local anaesthetics were Ropivacaine and levobupivacaine which have a wide margin of safety compared to bupivacaine, with all advantages.[2] Since, Ropivacaine has all the advantages of bupivacaine with lower cardiac toxicity,[3] it may be an ideal local anaesthetic for epidural anesthesia. Ropivacaine was found to be an effective local anaesthetic for epidural anesthesia in many studies.[4,5,6,7] Hence in our study ropivacaine was selected as the study drug. Fentanyl is a highly selective μ receptor agonist, which is mainly responsible for its analgesic properties. It acts by increasing intra-cellular calcium concentration which in turn increases K^+ conductance and hyperpolarization of cell membranes. This decreased membrane conductance decreases both pre and postsynaptic responses. Analgesia is produced principally through interaction with μ receptors at supra spinal sites. Fentanyl also binds to κ receptors causing spinal analgesia, sedation and anesthesia. Hence in this study, 0.75% ropivacaine with dexmedetomidine and 0.75% ropivacaine with fentanyl were compared as epidural anesthesia in lower limb surgeries.

Materials and Methods

A prospective, randomized, double blind, case control, observational, interventional comparative study is designed during period between December 2016 to November 2017 in 50 patients. The study was undertaken after obtaining institutional ethical committee clearance as well as informed consent from all patients. Patients who met all inclusion criteria were randomly selected. No distinction is made between males and females. Informed written consent was obtained from all the patients. Using a computer generated random number table, randomization was done. One hundred patients, scheduled for various elective lower limb surgical procedures belonging to ASA class I and II were included in the study. Group RD (n = 50)- 15 ml of 0.75% ropivacaine + 1.0 μg/kg of dexmedetomidine (inj. Dextomid-1 ml = 100 mcg, 1 ml) Group RF (n = 50) 15 ml of 0.75% ropivacaine (Ropivacaine 0.75% preservative free – ROPIN 0.75% 20 ml ampoules, Neon laboratories, India) fentanyl 1 μg/kg inj Fentanyl -1 ml = 50 mcg, 2 ml.

Inclusion criteria: patients who were adult patients who were aged between 18 to 66 years of both sex, patients belonging to ASA class I and II, weight which is greater than 50 kgs and height should be between 150 to 180 cms.

Exclusion criteria: patients who refused regional anesthesia, who were pregnant, lactating, posted for emergency surgeries, obese patients with BMI greater than 30, patients having intracranial pressure raised, severe hypoyolemia, bleeding coagulopathy, local infection, uncontrolled hypertension, diabetes mellitus, neurological disorder, deformities of spine, cardiac and hepatic disease, allergy to local anaesthetics and dexmedetomidine.

A routine pre-anaesthetic examination was conducted on the evening before surgery assessing history and general condition of the patient, airway assessment by Mallampatti grading, nutritional status, height and weight of the patient, a detailed examination of the Cardiovascular system, Respiratory system and Central nervous system and examination of the spine. At bed time on the previous night, the patients were premedicated with tablet alprazolam 0.5 mg and tablet ranitidine 150 mg orally before surgery. On the previous night, they were kept nil orally 10 pm onwards. Patient's basal pulse rate and blood pressure were recorded on the day of surgery. In one of the upper limbs, a peripheral intravenous line with 18 gauge cannula after local anesthesia was secured. Recordings of heart rate, non-invasive measurement of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), continuous electrocardiogram (ECG) monitoring and oxygen saturation (SpO_2) was done in all the patients who were preloaded with 500 ml of Ringer lactate 30 minutes prior to the epidural procedure. Multi parameter monitor was connected. Patients were in sitting position

for epidural anesthesia after that draped with the sterile clothes. Under aseptic precautions, after infiltrating skin with the 2% xylocaine waited for 2 minutes. By loss of resistance technique to air using 18G Tuohy needle via the midline approach at either L2-3 or L3-4 inter spinous space, next epidural space was identified. An epidural catheter was fixed and threaded at 3 cms inside the epidural space. After aspiration, a test dose of 3 ml of 2% lignocaine with 1:200000 adrenaline was injected through the catheter. Study drug prepared by another colleague anaesthetist who was unaware Of the study according to the randomized study numberd enerated against the patient. Drug 15 ml which was a mixture of the ropivacaine 0.75% and added study drugs. Dexmedetomidine or fentanyl. Dexmedetomidine which comes in ampoules 1 ml contains 100 µg/ml taken in the insulin syringe 0.1 ml contains 10 µg. According to the body weight dexmedetomidine solution added to the 0.75% ropivacaine solution. In our study we are taking as 1.0 µg/kg of dexmedetomidine. Fentanyl which comes in 2ml and 10 ml ampoules in which 1 ml contains 50 µg/ml. Drug was taken in 2 ml syringe in which 1ml contain 50 µg/ml. insulin syringe also used where drug requirement was more than one ml (for exact calculation of the drug according to body weight) added to the 0.75% ropivacaine according to the body weight. In our study we are taking 1 µg/kg of fentanyl. Using a short bevel 22 gauge needle, sensory blockade was assessed and on either side, it was tested in the mid clavicular line on the chest, trunk and lower limbs. Using modified Bromage scale, motor blockade in the lower limbs was assessed. Grade 0 means no motor block, grade 1 means inability to raise extended leg, able to move knees and feet, grade 2 means inability to raise extended leg and move knee, able to move feet and grade 3 means complete motor block of the lower limbs. Ramsay Sedation scale scoring was 1 if alert and wide awake (S1), 2 if arousable to verbal command (S2), 3 if arousable with gentle tactile stimulation (S3), 4 if arousable with vigorous shaking (S4) and 5 if unarousable (S5). Till the end of 1 hour, measurements of blood pressure, heart rate, and oxygen saturation was ecorded every 5 minutes and then every 15 minutes till the end of surgery. Using SPSS version 20.0, statistical analysis was done. By calculating mean, standard deviation, range, descriptive statistics was done. Using unpaired t- test two way repeated measure ANOVA and chisquare, the inferential statistics (test of significance) was done.

Results

Table 1: Demographics.

Age Distribution

Age in years	Group RD	Group RF
15–25	8	10
26–35	11	8
36–45	11	10
46–55	12	11
56–65	8	11
Total	50	50
Minimum age in years	18	20
Maximum age in years	56	60

Sex Distribution

Sex	Group RD Number (%)	Group RF Number (%)
Male	31 (62%)	36 (72%)
Female	19 (38%)	14 (28%)
Total	50 (100%)	50 (100%)
Weight (Kgs)	Group RD	Group RF
P Value-0.27	56.10 ± 6.11	58.64 ± 5.17
Height (cms)	Group RD	Group RF
Mean height in cms	169.03	170
Minimum height in cms	152	150
Maximum height in cms	180	180

Table 1 shows that the minimum age in groups RD and RF were 20 and 18 years respectively. The maximum age in both groups RD and RF was 65 years respectively. Between the Group RD and Group RF, there was no statistical significant difference in the age of patients. Both groups were similar with respect to age distribution (p>0.05). Between the groups, there is no statistical significant difference in the sex distribution of the patients. In both the groups there is a predominance of male patients. The mean body weight in group RD is 56.10 ± 6.11 kg and group RF is 58.64 ± 5.17 kg There is no statistical significant difference in the body weight of patients between the groups (p = 0.27). The mean height in group RD is 169.03 cm and RF is 170 cm. There is no statistical significant difference in the height between the groups.

Table 2: Type of surgical procedure, mean time for onset of sensory and motor block (mins), maximum level of sensory blockade attained, motor blockade grade.

Type of surgery	Group RD Number (%)	Group RF Number (%)
Both bones leg	12 (24%)	13 (26%)
Femur	23 (46%)	25 (46%)
Knee surgery	15 (30%)	12 (24%)

	Group RD	Group RF
Mean time for sensory onset (mins), SD	5.26 (1.49)	10.04 (2.55)
Mean time for motor onset (mins), SD	11.22 (2.61)	15.36 (3.28)

Maximum sensory level	Group RD	Group RF
T5	5	0
T6	38	31
T8	6	17
T10	1	2

Motor Blockade Grade	Group RD	Group RF
Bromage 1	0	15
Bromage 2	34	35
Bromage 3	16	0

Ramsay Sedation Score	Group RD	Group RF
S1	0	17
S2	15	33
S3	29	0
S4	6	0

Table 2 shows that there is no difference in type of surgical procedures in both the groups. The mean duration of surgery is 90.83 ± 23.12 mins in group RD and 96.83 ± 27.49 mins in group RF There is no statistically significant difference between the groups. The mean time of onset of sensory blockade in group RD is 5.26 ± 1.49 mins and in RF 10.04 ± 2.5 mins. There is highly statistical significant difference between the groups (p = 0.000). The mean time taken for the onset of motor blockade is 11.22 ± 2.61 mins in group RD and 15.36 ± 3.28 mins in group RF There is statistical significant difference between the groups (p = 0.000). Group RD had the highest level of T5 and highest level in RF group was T6. There is no significant difference between the two groups (p>0.05). Number of patients with Bromage 1 were 15 in group RF and 0 in group RD, whereas patients with Bromage 3 were 0 in group RF and 16 in group RD. More intense motor blockade of Bromage 3 was found in patients in group RD compared to patients in group RF, the p value being 0.001 is highly significant. Group RD had the highest score of 4 and highest score in group RF was 2. Dexmedetomidine had greater scores compared to fentanyl. There is statistically highly significant difference between the groups (p=0). The mean duration of sensory block is 359.30 ± 61.94 mins in group RD and 198.0 ± 24.05 mins in group RF There is statistically highly significant difference between the groups (p=0.001). The mean duration of motor blockade is 233.70 ± 15.26 mins in group RD 149.00 ± 14.21 mins in group RF. There is statistically highly significant difference between the group (p=0.001).

Figure 1 shows that there is no statistically significant difference in the mean heart rate between groups at various intervals. 4 patients in RD group developed bradycardia which was treated with inj.atropine 0.6 mg.

Figure 2 shows that there is no statistically significant difference in systolic blood pressure between both the groups. 7 patients in group RD and 4 patients in group RF developed hypotension which was treated with intravenous fluids and inj mephentermine.

Figure 3 shows that there is no statistically significant difference in diastolic blood pressure between both the groups.

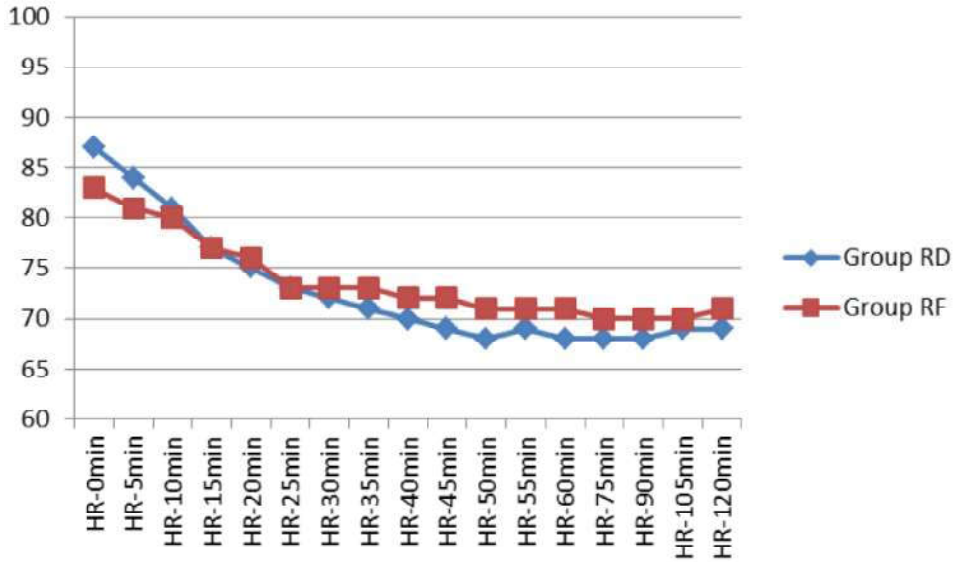

Fig. 1: Mean heart rate (bpm) at various time intervals.

Figure 4 shows that there is no statistically significant difference in mean arterial pressure between both the groups.

Table 3: Side effects

Side effect	Rd Group	Rf Group	p value
Bradycardia	4	0	0.02
Hypotension	7	4	0.16
Nausea & vomiting	4	8	0.109
Tremors	5	9	0.125
Dry mouth	4	0	0.02

Table 3 shows that bradycardia and dry mouth seen only in the RD group none was in RF group. Hypotension, nausea and vomiting, tremors observed in both groups which were stastically insignificant.

Initial four hours of the post operative period requirement of epidural top up was not required in the RD group, 50% of patients in RD group required epidural top ups in next 4–8 hrs, whereas after next 8 hrs all the patients in the two groups required epidural top ups. Another finding found that the intensity of the pain is less in the RD group compare to the RF group.

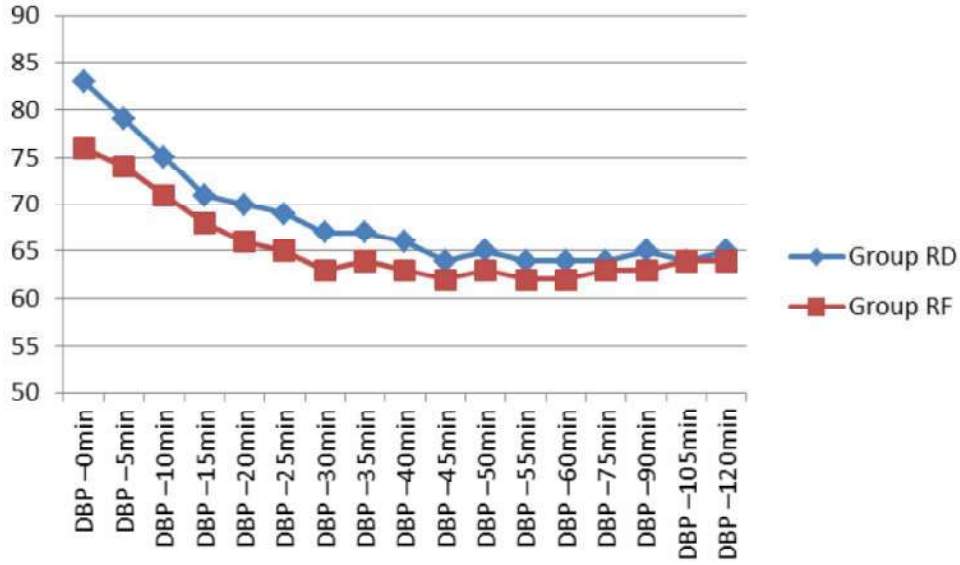

Fig. 2: Mean systolic blood pressure (mmHg) at various intervals.

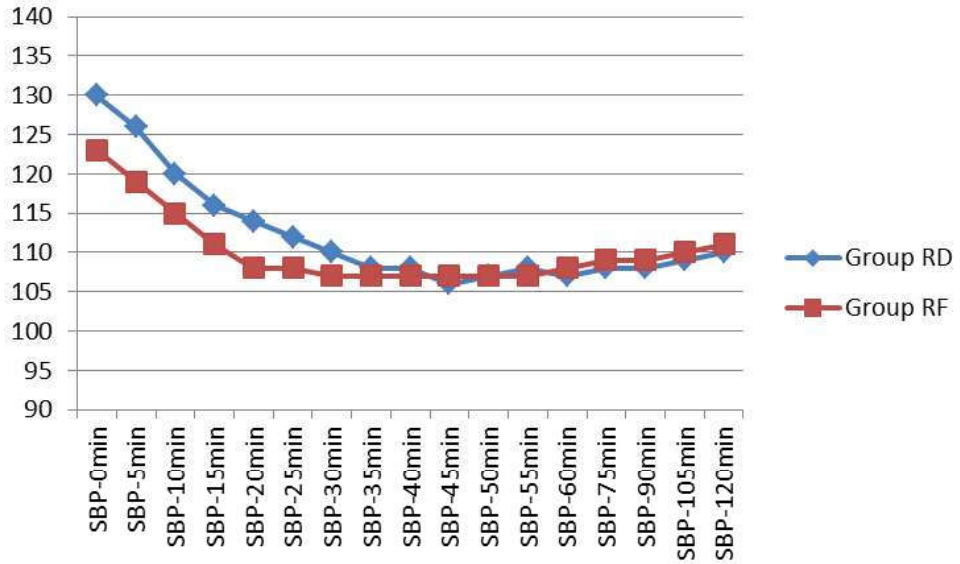

Fig. 3: Mean diastolic blood pressure (mmHg) at various time intervals.

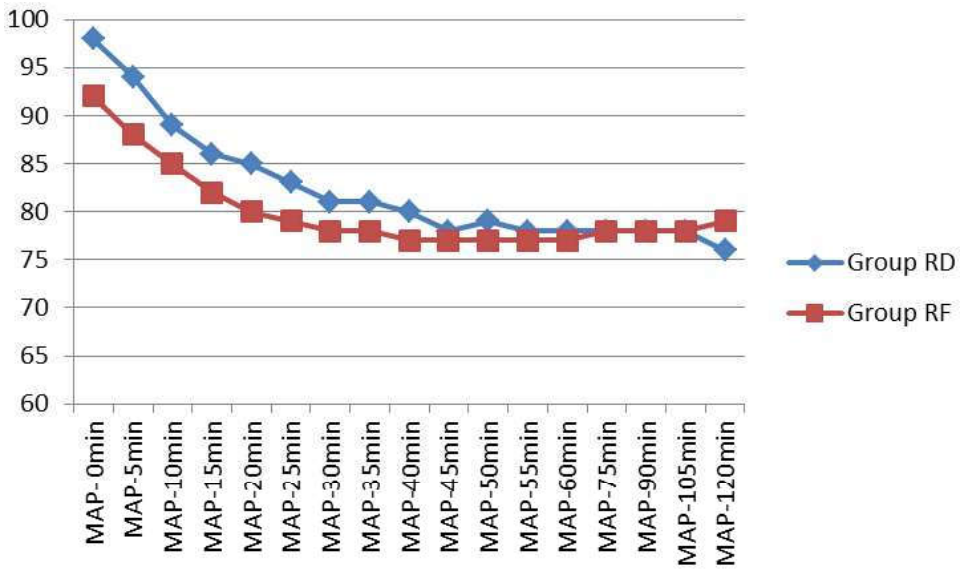

Fig. 4: Mean arterial pressure (mmHg) at various time intervals.

Discussion

Ropivacaine and dexmedetomidine and fentanyl were the drugs selected for epidural anesthesia in our study. For epidural anesthesia for lower limb orthopaedic surgeries, Ropivacaine is being regularly used. Ropivacaine, has structural similarity to bupivacaine. Dexmedetomidine has been studied by various authors as an adjuvant to epidural local anaesthetic[8,9] Fentanyl is frequently used iv opioid and intrathecal and epidural opioid for post operative pain and cancer pain also as known for its cardiac stability.[10] So in our study taken as adjuvant with ropivacaine in epidural anesthesia. For epidural anesthesia, few studies have compared ropivacaine and dexmedetomidine and with fentanyl also. In our study the mean time for onset of sensory analgesia at T10 is 5.26 ± 1.49 mins in group RD and 10.04 ± 2.55 mins in group RD. This is statistically highly significant (p<0.001), whereas Bajwa SJ *et al.*[11] showed onset of sensory analgesia at T10 in ropivacaine + dexmedetomidine group was 7.12 ± 2.44 mins VS 9.14 ± 2.94 mins in ropivacaine + fentanyl group and this is also statistically significant similar to our study. Though Saravia P.S.F *et al.*[12] found no significant change in the onset time for sensory block between ropivacaine and ropivacaine dexmedetomidine groups. The studies conducted by Bajwa SJ[13] showed onset of sensory analgesia at T10 in ropivacaine + dexmedetomidine group was 8.52 ± 2.36 min vs 9.72 ± 3.44 min in ropivacaine + clonidine group and this is statistically significant similar to our study. And supports our study. In our study the maximum level of sensory block in group RD was T4 (n = 5) and in group RF was T8. The range of block was very wide in both the groups (T12–T4). Bajwa SJ, Arora V, Kaur J *et al.*[11] showed maximum level of sensory block at T4–6 level in group RD compared to T5–T7 in group RF which was similar with our study, supports our results also. Saravia PSF *et al.*[12] found maximum level of sensory block at T6 between only ropivacaine and ropivacaine with dexmedetomidine groups. The study conducted by Bajwa SJ *et al.*[13] showed maximum level of sensory block at T5–6 level in group RD compared to T6–T7 in group RC which compares with our study, supports our study. In our study the duration of sensory block is longer with RD group than the RF group. This is statistically highly significant (p<0.001). Similar to our study conducted by Bajwa SJ *et al.*[11] who observed the mean duration of analgesia to be 366.62 ± 24.42 mins in group RD compared to 242.16 ± 23.86 mins within group RF which was highly significant. Supports our study even though in our study duration of sensory block of RF group less than the study conducted by the Bajwa SJ *et al.*[11] but duration of sensory block by RD similar to this study supports our result. Onset of motor blockade the onset of motor blockade was 11.22 ± 2.61 min in group RD and 15.36 ± 3.28 mins in group RF. This is statistically significant. The study conducted by Bajwa SJ *et al.*[11] showed that there is significantly earlier motor block onset in the (18.16 ± 4.52) patients who were administered RD as compared to RF group (22.98 ± 4.78). In our study motor blockade is

assessed using modified Bromage scale and onset was taken as soon as the patient developed grade I motor blockade. In our study it was found that group RD produced more intense motor block than group RF. 16 patients in RD group had grade 3 motor block compared with 0 patients in group R. Also 15 patients in RF group had grade 1 motor block compared with 0 patients in group RD group. This is statistically highly significant (p<0.001). In a study conducted by Bajwa SJ *et al.*[11] Motor block was assessed using modified Bromage scale and complete motor block was achieved significantly earlier in RD group than the RF group so it supports our study. Saravia PSF *et al.*[15] found maximum motor block at level 3 in 68% and 32% had grade 1 and 2 block with no patient remained in grade 0 motor block in ropivacaine and dexmedetomidine group patients. Whereas in plain ropivacaine group, 29% of patients remained with grade 0 motor block, 47% and 24% grade 1 and 2. Our study compares with this study as more number of patients had grade 3 motor blockade in both the studies. The duration of motor block with RD group is more prolonged than with group RF, which is statistically highly significant (p<0.001). A study similar to our study conducted by Bajwa SJ *et al.*[11] earlier return of motor power to Bromage 0 in the RF group (178.52 ± 23.29) as compared to RD group patients (259.62 ± 21.38) (p = 0.009) Supports our study In a study conducted by Saravia PSF *et al.*[15] found the duration of motor blockade was significantly higher in the ropivacaine with dexmedetomidine group, averaging 30% higher than that observed in the ropivacaine plain group similar to our study. The studies conducted by Bajwa SJ *et al.*[16] showed the mean duration of motor blockade was 246.72 ± 30.46 mins in ropivacaine + dexmedetomidine group and 228.44 ± 27.18 mins in ropivacaine + clonidine group. This was not statistically significant. There is no statistically significant difference in the heart rate between the two groups at various time intervals. 4 patients in RD group developed bradycardia which was treated with inj.atropine 0.6 mg. No patients in group RF developed significant bradycardia. The above result is consistent with the study conducted by Bajwa SJ *et al.*[11] wherein there was no statistically significant difference in the heart rate intra and postoperatively. There was no statistically significant difference in SBP, DBP, MAP monitored at various intervals between the two groups. In the studies conducted by Bajwa SJ *et al.*[11], no statistical significant difference was found in SBP, DBP, MAP in both the groups which compares with our study. Group RD had sedation score of 4 and in group RD was 2 which is high when compared. Dxmedetomidine had greater scores compared to Fentanyl. This is statistically highly significant (p=0.001). Similar results were observed by Bajwa SJ *et al.*[11] Dexmedetomidine has gained a lot of popularity as a sedative agent and similar findings were observed in our study as 38% and 42% of patients exhibited grade II and grade III sedation as compared to 16% and 2% of patients in the RF group, respectively. These sedation scores were highly significant on statistical comparison (p<0.001). Only 12% of the patients in the RD group had sedation scores of 1 as compared to 82% wide and awake patients in RF group which was a highly significant statistical entity (p<0.001). Similar results were also observed by Bajwa SJ *et al.*[11] Mean sedation scores were significantly higher in dexmedetomidine group compared to clonidine group (p<0.0001). In RD group, 4 patients developed bradycardia which was treated with inj.atropine 0.6 mg and hypotension seen in 7 patients in group RD and 4 patients in group RF which was treated with intravenous fluids and inj mephentermine 6 µg. Nausea and vomiting was noticed 4 patients in RD group where as 8 patients in RF group which was treated with inj iv ondansetron 4 mg. Dry mouth was noticed 4 patients in RD group and none in the RF group. Patients were reassured above it. Tremors was noticed 5 patients in RD group where as 9 patients in RF group treated with injection iv pethidine 25 mg. All above side effects also noticed in the study conducted by the Bajwa SJ *et al.*[11] and supports our study. Dry mouth incidence in RD group less compared to the study conducted by Bajwa SJ *et al.*[11] in our study we have used 0.6 µg/kg where as they used 1 µg/kg. On other side effects except the dry mouth are not stastically significant. After completion of the surgery if the patient complains of the pain epidural top up given with the 0.2% ropivacaine 8 ml only. The postoperative analgesia requirement as epidural topups was less in the RD group than the RF group. This was supported by the study conducted by the Bajwa SJ *et al.*[11] studied synergistic properties of LA and dexmedetomidine. They showed the ability to reduce the dose of local anesthetic in both the groups but also the postoperative analgesia duration was significantly prolonged in patients in whom dexmedetomidine was administered as adjuvant with LA.

Conclusion

Dexmedetomidine given epidurally with ropivacaine produces synergistic effect of profound

and motor blockade and sensory blockade duration being prolonged. There is relatively less incidence of complications and side effects when dexmedetomidine used as adjunct in the epidural anesthesia. Hence its concluded that dexmedetomidine can be used as a more potent and safer alternative to Fentanyl in epidural anesthesia as a adjuvant to ropivacaine.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1333-1342
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.38

Pain on Propofol Injection: Comparative Study of Pre-Treatment with Intravenous Lignocaine, Ondansetron and Fentanyl for the Prevention of Pain

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Abstract

Context: Propofol is a sedative-hypnotic intravenous anaesthetic agent. It causes a high incidence of pain during intravenous injection which leads to patient dissatisfaction. *Aim:* The aim of this study was to determine whether pre-treatment with intravenous lignocaine, ondensetron and fentanyl was effective in reducing propofol induced pain. *Settings and Design:* In a prospective, randomized, double blind study 150 ASA physical status I and II patients, aged 20-60 years, undergoing elective surgery under general anesthesia, were allocated randomly into three groups. *Methods and Material:* Group A received IV lignocaine 42 mg (2 ml), Group B received IV ondansetron 4mg and Group C received IV fentanyl 100 mcg. Mid-arm was occluded before drug injection then released after 1 min followed by propofol injection. Patients were assessed according to Mc Crirrick and Hunter pain scoring system at 0, 5, 10, 15 and 20 seconds. Statistical analysis: ANOVA with Dunnett's post hoc test and chi-square test were used to analyze results. *Results:* Two patients in Group A and one patient in Group B had 'no pain' during the observation period. Group B and Group C have more 'mild pain' than Group A while it is comparable in Group B and C. 'Moderate pain' is comparable between Group A and B while Group A has more 'moderate pain' than Group C and Group B has more 'moderate pain' than Group C. Only one patient in Group A had 'severe pain'. *Conclusion:* Pre-treatment with lignocaine, ondensetron and fentanyl was effective in reducing pain on propofol injection but the superiority of one drug over the other cannot be commented.

Keywords: Fentanyl; Lignocaine; Ondensetron; Pain on injection; Propofol.

How to cite this article:

Chetan Arun Patil, Neha P Kamble, Manoj Kumar N Gajbhare. Pain on Propofol Injection: Comparative Study of Pre-Treatment with Intravenous Lignocaine, Ondansetron and Fentanyl for the Prevention of Pain. Indian J Anesth Analg. 2019;6(4):1333-.

Introduction

Intravenous induction is the most commonly used method for induction of general anesthesia. An ideal intravenous anaesthetic agent should provide hypnosis, amnesia and analgesia without undesirable cardiac and respiratory side effects. Commonly used intravenous anaesthetics are barbiturates (thiopentone) and non-barbiturates (propofol, etomidate, ketamine).

Propofol has a rapid onset (15–45 seconds) and short duration of action (5–10 minutes). Its attractive kinetic properties like titrable level of anesthesia, absence of cumulation, rapid and clear headed recovery, less postoperative nausea and vomiting, greater depression of laryngeal reflexes than other

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Received on 19.05.2019, **Accepted on** 19.06.2019

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commonly used anaesthetic agents[1] and minimal side effects makes it an ideal agent for induction of anesthesia.[2]

Propofol is known to cause severe, sharp, stinging or burning pain on injection, especially when given in small veins on dorsum of hand. This is clinically unacceptable as it can cause agitation and interfere with smooth induction of anesthesia. The reported incidence varies between 28% and 90% in adults when a vein on dorsum of hand is used.[3] It can be immediate or delayed in nature. The immediate pain probably results from direct irritant effect whereas delayed pain results from indirect effect via the kinin cascade which occurs 10–20 seconds later.[4] Nafamostat mesilate, a kallikrein inhibitor, is effective in decreasing pain on injection of propofol. Its effectiveness has been attributed to the activation of kallikrein- kinin system as the propofol emulsion contacts free nerve endings in the vein. Factor XII is activated which converts prekallikrein to kallikrein, which then cleaves high-molecular weight kininogen to release bradykinin. Bradykinin causes vasodilatation and increased permeability of vein, increasing contact between aqueous phase of propofol and free nerve endings of vein. This will manifest as pain.[5,6]

Drugs like lignocaine, opioids like fentanyl, morphine and butarphanol, magnesium sulphate, paracetamol, ephedrine, metoclopramide and many more have been tried to reduce this pain. Of these the most commonly used methods are pre-treatment with IV (intravenous) lignocaine or IV fentanyl.

Lignocaine reduces pain due its local anaesthetic action,[7] fentanyl, has some peripherally mediated analgesic action within the clinical dosage range,[8] ondansetron[9] due to its multifaceted action as Na channel blocker, a $5HT_3$ receptor antagonist and μ-opioid agonist, can be used to alleviate pain produced by propofol. However the efficacy of ondansetron has never been compared with drugs like lignocaine and fentanyl.

Our aim is to compare the efficacy of lignocaine, ondansetron and fentanyl in reducing pain on injection of propofol, to detect an agent with minimal side effects and the hemodynamic changes due to these drugs.

Materials and Methods

After approval by the Hospital Ethics Committee, we studied 150 patients of either sex, aged 20-60 years, scheduled for elective surgery under general anesthesia.

All patients who belong to the ASA physical status class I and II were enrolled for this prospective randomized, double-blind study. Patients were not included if they refused to participate in the study, a history of allergy to the study medications, hemodynamically unstable patients, presence of infection on the dorsum of hand, difficult IV cannulation. Also excluded were patients of ASA physical status III and IV, pregnant and diabetic patients, patients with pre-existing cardiac conduction defects, patients receiving analgesics and patients with difficulty in communication.

In a pilot study on 20 patients we found that all patients complained of pain during propofol injection. The incidence of moderate to severe pain was highest at 15 seconds. So the number needed to bring down the incidence of pain by 50%, keeping the type I error at 5% and power of study at 95% was 44. We used a web based sample size calculator. To round it off we have taken the number of patients in each group as 50.

Randomization list was generated by random number function using the Microsoft Excel 2003 spreadsheet, resulting in a list of 150 assigned to participants receiving the drugs. Randomization was conducted using sequentially numbered, opaque and sealed envelope. Patients were divided in three groups, 50 patients in each group.

Group A: IV Lignocaine 42 mg (2 ml) diluted to 5 cc.

Group B: IV Ondansetron 4mg diluted to 5cc.

Group C: IV Fentanyl 100 mcg diluted to 5cc.

The study drug was prepared in identical looking (5ml) coded syringes by an anaesthesiologist not involved in the study. The drug administrator and the person making the observations were blind to the study drug.

A complete pre-anaesthetic evaluation was done. After explaining the anaesthetic procedure to the patients, written informed consent was taken to include them in the study. They received the study medication as per randomization. During the preoperative rounds all patients were explained about the pain scoring method advocated by Mc Crirrick and Hunter*.

All patients were kept fasting 6 hours before surgery. They were advised to take tablet alprazolam 0.5 mg and tablet ranitidine 150 mg night before surgery. In the operating room,

non-invasive blood pressure, electrocardiogram and pulse oximeter were attached and baseline vital parameters were noted. Intravenous access was established with an 18-G cannula on the dorsum of the non-dominant hand. No analgesic or sedative drugs were given before induction. Venous occlusion of the arm proximal to the puncture site was maintained with a blood pressure cuff inflated to 40 mmHg. The study drugs were injected over 30 seconds and venous occlusion was released after 1 min of completion of study drug injection. Propofol (2 mg/kg) was administered through the intravenous cannula. During the first 25% of the calculated propofol dose, the patient was assessed according to four- point pain score at 0, 5, 10, 15 and 20 seconds. Following which, general anesthesia was continued with the remainder of the calculated dose of propofol. Vecuronium 0.1 mg/kg intravenous was used to facilitate tracheal intubation. Anesthesia was maintained with isoflurane 1% and 60% nitrous oxide with oxygen on controlled ventilation with intermittent bolus of vecuronium.

Intraoperative analgesia was maintained with incremental doses of intravenous fentanyl 50 mcg. At the end of surgery, inhalational agents were discontinued and neuromuscular blockade was reversed with neostigmine 0.5 mg/kg with glycopyrrolate 0.1 mg/kg intravenously. The participants were extubated and transferred to the recovery area after confirmation of satisfactory recovery criteria. All observations were recorded by an anaesthesiologist not involved in the study.

Mc Crirrick and Hunter scale of pain assessment on injection with propofol

Pain score	Degree of pain	Response
0	None	Negative response to questioning
1	Mild	Pain reported in response to questioning only, without any behavioral signs
2	Moderate	Pain reported in response to questioning and accompanied by a behavioral sign or pain reported spontaneously without questioning
3	Severe	Strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears

The following observations were made:

Age, sex, ASA grade, body mass index (BMI).

Pain scores at 0, 5, 10, 15 and 20 seconds after propofol injection.

Heart rate and oxygen saturation was monitored continuously, recorded at baseline, 0, 5, 10, 15 and 20 seconds after propofol injection.

Mean arterial blood pressure at baseline, after 20 seconds, 5, 10, 15 and 20 minutes.

Any adverse effects.

Statistics Analysis

Data represented as mean ± SD (n = 50). All the results were analyzed statistically by one-way and two-way ANOVA with Dunnett's post hoc test and Chi square test by using Graphpad Prism 7.0 (GraphPad Software, Inc., CA, USA). P <0.05 was considered as significant.

Results

All the three groups were comparable (p > 0.05) with respect to demographic parameters and ASA Physical Status class as shown (Fig. 1 and 2).

There was no statistically significant difference in the mean pulse rate recorded at baseline and at 0 seconds but a statistically significant difference was noted at 5, 10, 15 and 20 seconds when compared with baseline pulse rate (p < 0.05) (Table 1, Fig. 3) There was a statistically significant difference in the mean blood pressure recorded at baseline and that recorded after 20 seconds, 5, 10, 15 and 20 minutes (p < 0.05) (Table 2, Fig. 4).

No significant changes were noted in the SpO_2 between the studied groups (p > 0.05) (Fig. 5).

The incidence of pain when compared amongst the groups was statistically insignificant (Table 3, Fig. 6). Chi – square test {χ^2 – Test} was used for the comparison of incidence of pain. Comparison of Group A with Group B and Group C gives p value as 0.0956 and 0.514 respectively, while comparison of Group B with Group C gives p value as 0.1333 which is statistically insignificant.

After administration of drug, 48 (96%) patients in Group A, 49 (98%) patients in Group B and all patients [50 (100%)] in Group C experienced pain (p=0.7675) (Table 4). Pain score was compared in all the groups at 0, 5, 10, 15 and 20 seconds (Table 5, Fig. 7).

The mean pain score (MPS) in Group A, B and C was 1.46 ± 0.61, 1.42 ± 0.53, 1.48 ± 0.50 respectively (Fig. 8). Chi – square test was used for the comparison of pain scores in the study groups (Fig. 9). Comparison of 'MPS 0'(no pain) in Group A with Group B and C gives P value as 2.037 and

0.555 respectively, while comparison of Group B with Group C gives *p* value as 0.0964 which is statistically insignificant.

Comparison of 'MPS 1'(mild pain) in Group A with Group B and C gives *p* value as 0.036 and 0.015 respectively which is statistically significant while comparison of Group B with Group C gives *p* value as 0.534 which is statistically insignificant.

The 'MPS 2' (moderate pain) in Group A when compared with Group B ($p = 0.074$) was statistically insignificant and that with Group C ($p = 0.0005$) was significant while comparison of Group B with

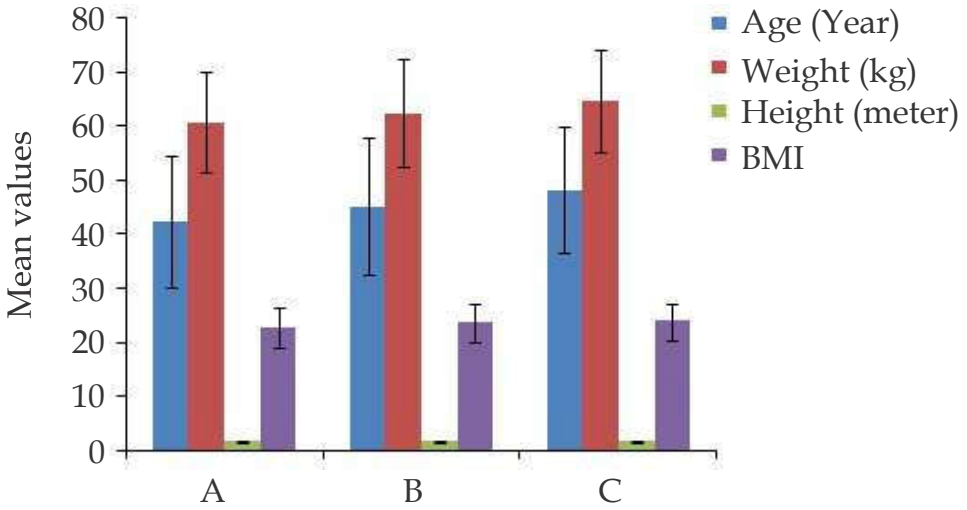

Fig. 1: Graphical representation of average age, weight, height and BMI of the patients in different drug treated group [Mean ± SD (n=50)]. Column width.

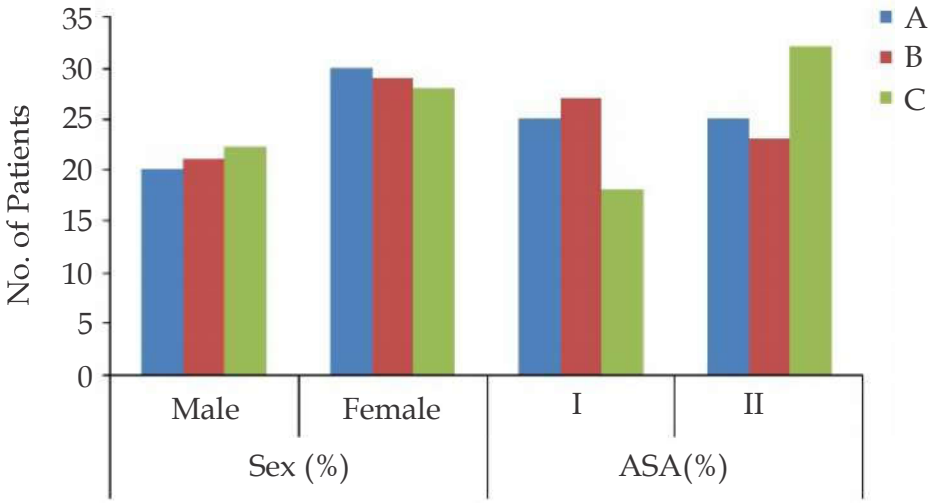

Fig. 2: Graphical representation of Gender and ASA stage wise distribution of patients in different drug treated group [Data represented as n (%). Statistical analysis for the Gender of patients $X^2=0.1642$, $p = 0.9212$.Statistical analysis for ASA Physical Status $X^2=3.589$, $p = 0.1662$. Chi square test was performed for the statistical analysis]. Column width.

Table 1: Effect of different drug treatment on the pulse rate at different time interval after the administration of drug

Group	Pulse rate (Beats/min)					
	Baseline	0 Sec	5 Sec	10 Sec	15 Sec	20 Sec
A	89.3 ± 14.3	89.7 ± 14.5	94.2 ± 14.8	98.7 ± 14.8##	102.6 ± 15.7##	106.5 ± 16.4##
B	88.3 ± 9	88.1 ± 9.2	94.1 ± 9.5#	101.2 ± 9.8##	106.7 ± 9.61##	112.2 ± 10.6##
C	87.5 ± 9.1	87 ± 9.2	90.9 ± 9.5	102.7 ± 9.5##	112.4 ± 9.2##	123.63 ± 8.7##

Mean ± SD (n=50), ##*P*<0.01 compared to baseline

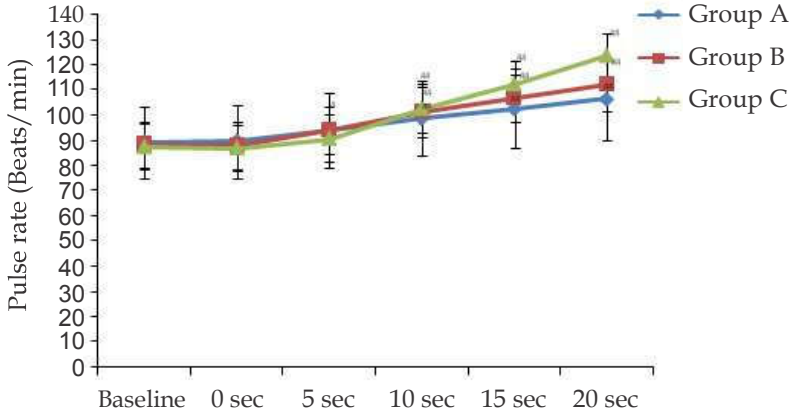

Fig. 3: Effect of different drug treatment on the pulse rate at different time interval after the administration of drug [Mean ± SD (n=50), ## p <0.01 compared to baseline]. Column width.

Table 2: Effect of different drug treatment on the mean blood pressure at different time interval after the administration of drug

Group	Mean blood pressure (mm Hg)					
	Baseline	**20 Sec**	**5 min**	**10 min**	**15 min**	**20 min**
A	101.88 ± 9.62	93.48 ± 7.05##	92.33 ± 7.18##	94.05 ± 7.11##	93.25 ± 7.18##	93.18 ± 9.97##
B	99.14 ± 10.06	92.5 ± 6.63##	91.86 ± 6.61##	94.08 ± 6.33##	92.95 ± 6.24##	93.3 ± 8.69##
C	102.14 ± 7.71	93.25 ± 7.41##	91.37 ± 7.24##	93.99 ± 6.73##	92.2 ± 7.18##	92.81 ± 9.19##

Mean ± SD (n=50), ##P <0.01 compared to baseline

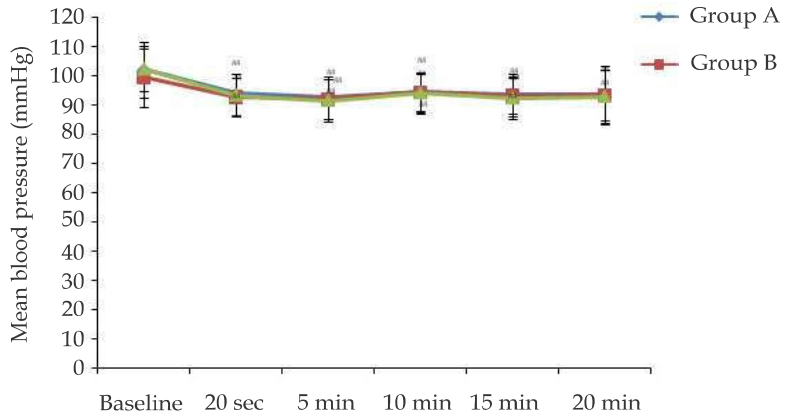

Fig. 4: Effect of different drug treatment on the mean blood pressure at different time interval after the administration of drug [Mean ± SD (n=50), ## p <0.01 compared to baseline] Column width.

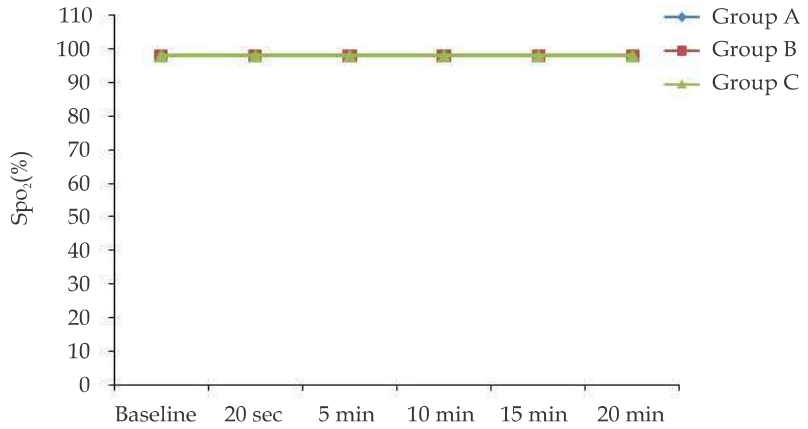

Fig. 5: Effect of different drug treatment on the percentage of SpO_2 at different time interval after the administration of drug [Mean ± SD (n=50)] Column width.

Table 3: Effect of different drug treatment on the incidence of pain at different time interval after the administration of drug

Group	Incidence of Pain n (%)				
	0 Sec	5 Sec	10 Sec	15 Sec	20 Sec
A	0 (0)	7 (14)	24 (48)	45 (90)	48 (96)
B	0 (0)	1 (2)	35 (70)	49 (98)	49 (98)
C	0 (0)	0 (0)	17 (34)	46 (92)	50 (100)

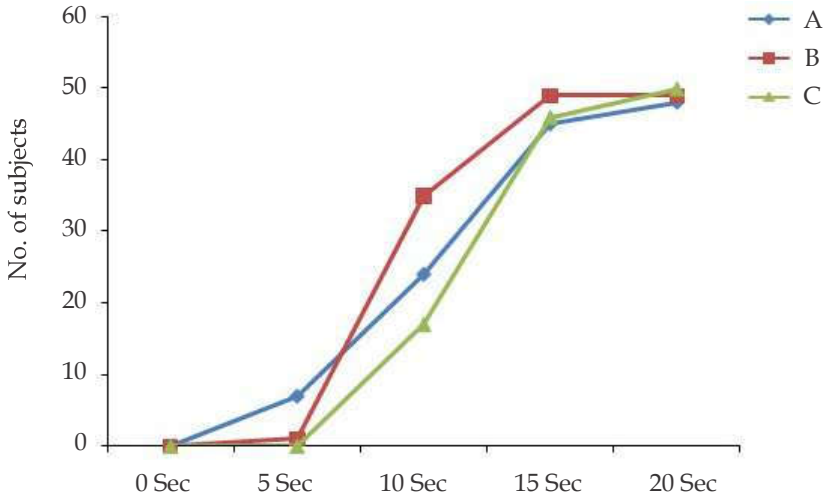

Fig. 6: Effect of different drug treatment on the incidence of pain at different time interval after the administration of drug. Column width.

Table 4: Number of patients experiencing pain after the administration of drug

Sr. No.	Group	Number of patients complaining of pain n(%)	Number of patients free from pain n(%)
1	A	48 (96)	2 (4)
2	B	49 (98)	1 (2)
3	C	50 (100)	0 (0)
	p Value	0.7675	
	X^2 value	0.5292	

Data represented as n (%), X^2=0.5292, p = 0.7675
Chi square test was performed for the statistical analysis

Table 5: Number of patients experiencing different levels of pain at different time interval after the administration of drug

Sr. No.	Group	Pain Level	No. of patients complaining of pain at different time interval n(%)				
			0 Sec	5 Sec	10 Sec	15 Sec	20 Sec
1	A	Mild	0 (0)	7 (14)	18 (36)	28 (56)	24 (48)
		Moderate	0 (0)	0 (0)	6 (12)	17 (34)	23 (46)
		Severe	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)
2	B	Mild	0 (0)	1 (2)	35 (70)	37 (74)	27 (54)
		Moderate	0 (0)	0 (0)	0 (0)	12 (24)	22 (44)
		Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
3	C	Mild	0 (0)	0 (0)	17 (34)	45 (90)	26 (54)
		Moderate	0 (0)	0 (0)	0 (0)	1 (2)	24 (48)
		Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Data represented as n (%)
Statistical analysis for mild pain level on 10, 15 and 20 sec X^2=7.399, p= 0.1162
Statistical analysis for moderate pain level on 10, 15 and 20 sec X^2=19.87, p= 0.0005
Chi square test was performed for the statistical analysis

Group C (p = 0.010) was statistically significant. Only one patient (2.08%) had 'MPS 3' (severe pain) in Group A which is statistically insignificant.

There were few adverse events observed in all the groups during the study period [Table 7].

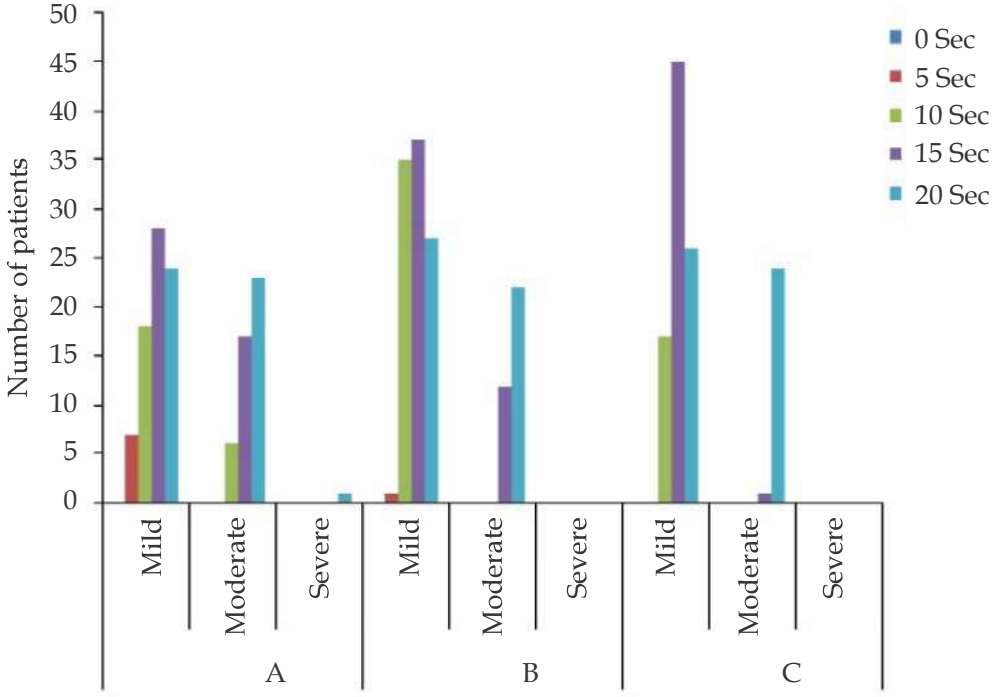

Fig. 7: Number of patients experiencing different level of pain at different time interval after the administration of drug. Column width.

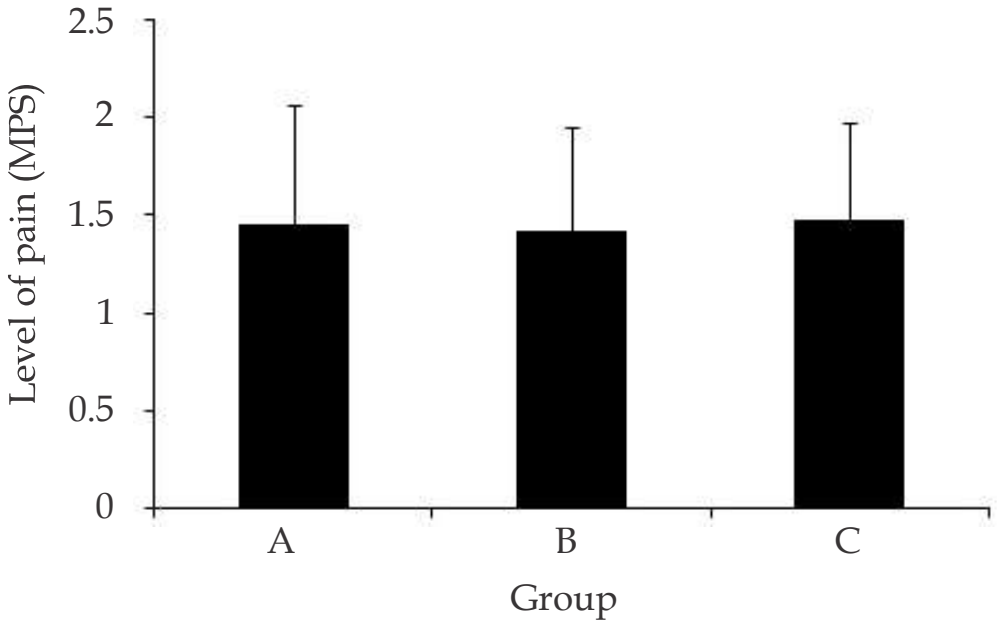

Fig. 8: Effect of different drug treatment on the level of mean pain score [Mean ± SD (n=50)]. Column width.

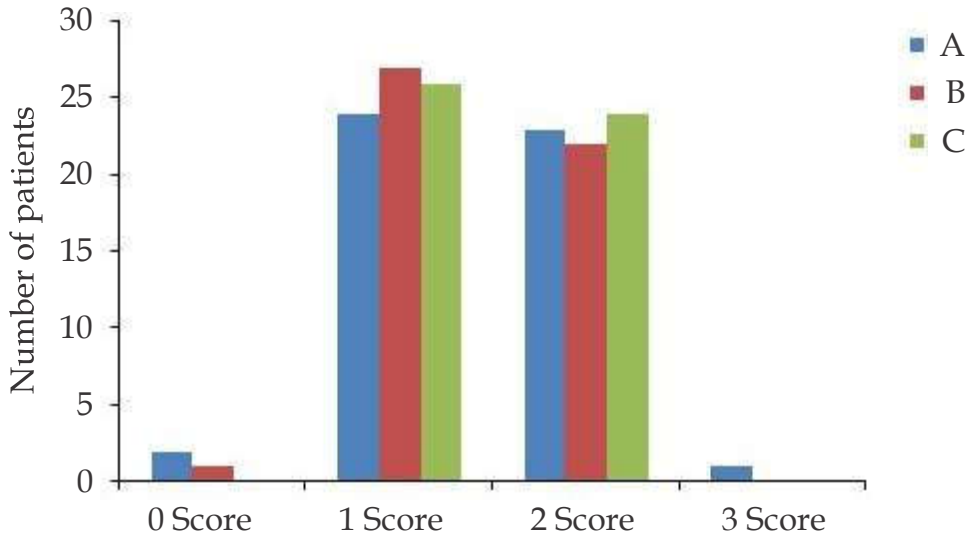

Fig. 9: Number of patients experiencing different level of pain after the drug administration [Data represented as n (%). X^2=4.269, p = 0.6404. Chi square test was performed for the statistical analysis]. Column width.

Table 6: Number needed to treat (NNT)

Groups	NNT	ARR	RRR
Lignocaine	4.5	0.22	0.31
Ondansetron	4.1	0.24	0.34
Fentanyl	4.5	0.22	0.31

ARR: Absolute Risk Reduction, RRR: Relative Risk Reduction

Table 7: Adverse events during the study

	Groups			
Adverse event	A	B	C	*p* value
Redness	1	0	0	>0.05
Hypotension	0	0	0	
Wheal	0	0	1	
Pruritus	0	1	0	

Discussion

All the three groups were comparable with respect to demographic parameters and ASA Physical Status ($p > 0.05$) [Figs. 1, 2].

Lignocaine has been extensively used, either separately or as preformed mixture to alleviate pain on propofol injection. Picard *et al.*[10] in a meta-analysis have found the NNT (number needed to treat) of 40 mg of lignocaine to be 1.6. Lignocaine in a dose of 0.5 mg/kg was effective in reducing pain in 60% cases when administered with a rubber tourniquet on the forearm 30-120 seconds before the injection of propofol. Fentanyl (100 mcg) has been shown to provide more analgesia than placebo.[11] Ondansetron has provided results comparable to tramadol 50 mg.[12] Since fentanyl and ondansetron are the two drugs routinely used in our set up for all the surgeries done under general anesthesia, we felt the necessity of testing their ability to attenuate pain from propofol injection and comparing its efficacy with that of lignocaine. This would save us from using a separate drug which will avoid the expenses and adverse effects as well. The doses fentanyl, lignocaine and ondansetron have been the same as used by Pang *et al.*[8] and Zahedi *et al.*[13]

We have chosen the dorsum of the non-dominant hand for the injections. Although Kang *et al.*[14] have shown that injection in the vein on dorsum of hand was more painful (61.2%) than in antecubital fossa (22.5%) ($p < 0.01$), we have still chosen this site in our study as it was not possible to attach the tourniquet with the IV line at any other site. However, since we did not take any placebo group the decision was not of ethical concern.

We have observed changes in the pulse rate and SpO_2 at the baseline, at the start of propofol injection and thereafter at 5, 10, 15 and 20 seconds during propofol injection. However recording of blood pressure with non-invasive method was not possible at the above mentioned intervals. So we have taken the baseline reading (before starting of propofol injection) and thereafter at the end of 20 seconds, 5, 10, 15 and 20 minutes. Following which changes in the heart rate and blood pressure would be construed as resulting from pain.

Baseline mean pulse rate was comparable between the three groups. The intra-group analysis of pulse rate showed a significant increase in the pulse rate at 5, 10, 15 and 20 seconds of propofol injection in all the groups compared to baseline ($p < 0.05$) [Table 1, Figure 3]. This could have been a response as a result of pain on injection of propofol despite of pre-treatment with lignocaine, ondansetron and fentanyl. However the mean pulse rate was comparable between the three groups at 5, 10, 15 and 20 seconds ($p > 0.05$). Similarly, there was a statistically significant increase in the mean blood pressure recorded at baseline and that recorded after 20 seconds, 5, 10, 15 and 20 minutes of propofol injection ($p < 0.05$) [Figure 4]. No significant changes were noted in S_pO_2 over the baseline reading [Fig. 5]. In the earlier studies many authors have not commented on hemodynamic changes during propofol injection. Ray *et al.*[15] in their study have observed hemodynamic changes, but have not commented on their trend. Mahmood *et al.*[16] and Canbay *et al.*[17] found no significant changes in hemodynamic parameters. They have used ketamine, dexamethasone and lignocaine as their study drugs.

All patients in Group C experienced some form of pain at some time during the study period. However two patients in Group A and one patient in Group B did not experience any pain during any time of the observation period (Table 4). There was no statistically significant difference in the incidence of pain in the three groups. Therefore it is not possible for us to comment on the superiority of one drug over the other as far as the incidence of pain is concerned. Ray *et al.*[15] in their study have documented a significant difference in the incidence of pain between the lignocaine and fentanyl pre-treatment group (14.3 vs. 42.9). They have calculated the NNT (number needed to treat) for fentanyl and lignocaine to be 4 and 2 respectively.

The incidence of 'MPS 1' (mild pain) increased with time, with peak at 15 seconds and then declining at 20 seconds. [Table 5] There was a statistically significant difference in the incidence of 'mild pain' at 15 seconds in Group A and Group B ($p = 0.0362$), so also in Group A and Group C ($P = 0.0156$). Incidence of mild pain in Group B and C was comparable. The incidence of 'MPS 2' (moderate pain) at 15 seconds was comparable between Group A and Group B ($p = 0.0742$) however the same in group C was significant ($p = 0.0005$) when compared with the other two groups. No patient in Group B and C had severe pain at any time period.

Our study cannot be compared with the other studies with regard to severity of pain, since they have taken pain as an all or none phenomenon. We have taken a four point verbal categorical scoring system in accordance with the study of Mahmood *et al.*[16] as it was simple to use by the patients. Visual analogue scale (VAS) was not appropriate to the present study as appropriate hand-eye coordination might not be present in all patients during the rapidly changing state of consciousness of anesthesia induction.

The incidence of moderate and severe pain in our pilot study was 100% at 15 seconds. We aimed at 50% reduction in its incidence with our test drugs. All the three drugs were able to successfully attenuate moderate and severe pain due to propofol injection but not mild pain, which means patients did not remain completely pain free.

The mechanism of pain produced by propofol has been shown to be the high concentration of free propofol in the aqueous phase[18,19] of an emulsion and the lipid carrier.[20] A kinin cascade has been suggested which describes a slight delay before pain is experienced. We have experienced this phenomenon in our patients where maximum pain has been experienced at 15 seconds. The immediate pain which is due to the local irritant action of the drug on vein has not been inhibited by these drugs. Whereas the delayed effect, which is due to the kinin cascade, was effectively attenuated.

Our study was powered to find a 50% reduction in the incidence of pain at 15 seconds. So, all our study drugs have successfully achieved reduction in the pain induced by propofol at 15 seconds to < 50% (34%, 24%, 2% respectively in Group A, B & C for moderate pain at 15 seconds and 0% severe pain in all the groups at 15 seconds). The NNT (number needed to treat) for the three drugs were found to be 4.5, 4.1 and 4.5 respectively for lignocaine, ondansetron and fentanyl [Table 6]. Number needed to treat (NNT) of 4 means 4 out of 10 patients will benefit from treatment to be an effective drug. The expected NNT is < 2. However, since our study was powered to detect 50% reduction only, we cannot comment on the efficacy of drugs based on NNT.

One patient in the Group A had redness at the site of drug injection, one patient had pruritus in Group B and one had a wheal in the Group C. Overall these were very mild reactions and did not need any form of intervention.

Conclusion

We conclude that pre-treatment with the three drugs Lignocaine 42 mg, Ondansetron 4 mg and Fentanyl 100 mcg effectively decreased the incidence of pain on propofol injection at 15 seconds. However the superiority of one drug over the other cannot be commented. All the three drugs were comparable with respect to hemodynamic changes and adverse effects.

Key message: Propofol, an ideal intravenous anaesthetic agent causes pain on injection which interferes with smooth induction of anesthesia. Fentanyl and Ondensetron were compared with Lignocaine to test their ability to attenuate pain from propofol injection. All the three drugs effectively reduced pain on propofol injection but none was found superior over other.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1343-1346
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.39

Dexmedetomidine is a Better Adjuvant than Clonidine, with Ropivacaine in Supraclavicular Brachial Plexus Block

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Abstract

Regional anesthesia has some advantages over general anesthesia such as it can be used in outpatient anesthesia, for patients with full stomach, for diabetic patients, associated cardiac, pulmonary, hepatic or renal damage and poly-trauma. Alpha-2 agonists added to local anaesthetic drugs increases the duration of painless period during and after surgery. Here we elicit the clinical Performance of this two drugs dexmedetomidine and clonidine as an additive agent to local anaesthetics like ropivacaine in blocking the brachial plexus by supraclavicular method. The clinical parameters we study here are onset, duration of Duration of blockade (both S and M) and analgesia time and hemodynamic stability. *Material and Methods:* Prospective study was done on patients undergoing upper arm surgeries under brachial block were split into two equivalent groups. D-group received 0.375% ropivacaine (30 ml) plus one mcg/kg dexmedetomidine, C- group received 0.375% ropivacaine (30 ml) plus one mcg/kg clonidine. *Results:* Statistical analysis shows significant difference in onset of sensory (S) and motor (M) blockade, highly significance in duration of sensory and motor blockade between D and C groups (p=0.0001). High Statistical significance was seen analgesia duration (p=0.0001) and number of rescue analgesics used (p=0.0001) among D and C groups. *Conclusion:* Dexmedetomidine has more additive benefits than clonidine when combined with ropivacaine by making the onset of clinical effect earlier, prolonging the blockade extent (both S and M) and painless period during post surgery with fewer requirements of rescue analgesics after arm, forearm and hand surgeries.

Keywords: Ropivacaine; Clonidine; Dexmedetomidine; Sensory blockade (S); Motor blockade(M); Local anaesthetic.

How to cite this article:

Gunaseelan Sivasamy, Priyanka Selvam, Thirunavukkarasu M *et al.* Dexmedetomidine is a Better Adjuvant than Clonidine, with Ropivacaine in Supraclavicular Brachial Plexus Block. Indian J Anesth Analg. 2019;6(4):1343-1346.

Introduction

Surgerie's done for arm, forearm and hand under peripheral nerve block provides excellent intra-operative analgesia and prolongs the post-operative analgesia duration with least complications[1]. Pain transferred by nerve fibers is the basis for regional block working mechanism and the transfer of pain can be interrupted along their pathway. Other important advantages are postoperative analgesia, early ambulation, no airway manipulation, early feed intake by oral route and lesser incidence of postoperative respiratory, gastric, intestinal and thrombo-embolic complications.[2] Regional

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Received on 24.04.2019, **Accepted on** 22.05.2019

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anesthesia provides better operating conditions, good muscle relaxation and better hemodynamic stability after nerve block. Using supraclavicular nerve block anesthesia can be given to forearm and arm procedures using LA (Local anaesthetic).[3] Initial and earliest supraclavicular block was clinically done by Kulen Kampff[4] in 1912, and Pearson in 1955 clinically performed the use of electrostimulation to find out nerves,[5] nerves stimulator was first use in anaesthesiology by Greenblatt and Denson[6] in 1962 that introduced the nerve stimulator into anaesthesiology clinical practice. Even though they have pharmacological similarity with bupivacaine, extent of ropivacaine action is very longer and very huge margin of safety.[7-8] Ropivacaine is a amide local anaesthetic which has less cardiovascular and CNS toxic effects than bupivacaine.[9] Simultaneous administration of Alpha-2 adrenergic agonists enhances the clinical performance of LA solutions. Alpha 2 receptor activity is highly is highly selective for dexmedetomidine and higher binding effect to alpha 2 adrenoceptor than affinity for clonidine. With ropivacaine, by increasing the dose of the drug results in enhanced duration of blockade(both S and M).[10,11,12,13]

Materials and Methods

This study was conducted in Sri Venkateshwara Medical College Hospital & Research Centre after approval of the medical college ethical board and informed written consent was taken from all patients. A double blinded randomised clinical study was performed on sixty male and female adults patients (ASA-1 & 2), posted for upper limb surgeries during the period of December 2016 to January 2018. The randomization was made by envelope technique which was sealed one. Analysis of statistics was done with software SPSS V(23) and *T*- test was used for comparing and computing $\overline{X} \pm \sigma$ for continuous variables. We used 95% CI and the results were accepted as statistically significant if p<0.001. Prospective study by blinding both study performer and patients was done and patients undergoing upper arm surgeries under brachial block were split into two equivalent groups. D-group received 0.375% ropivacaine (30 ml) plus one mcg/kg dexmedetomidine, C- group received 0.375% ropivacaine (30 ml) plus one mcg/kg clonidine. Following parameters including onset, duration of blockade (both S and M) and duration of painless period after surgical operation were record. SBP, DBP, Heart rate, SpO_2 were recorded.

Results

Statistical analysis shows significant difference in onset of S & M blockade (Table-1), highly significance in duration of S & M blockade between D and C groups (p=0.0001) (Table-2). High Statistical significance was seen analgesia duration (p=0.0001) and number of rescue analgesics used (p=0.0001) among D and C groups (Table-3) this values are shown in tables below. Non significant difference in HR, SBP, DBP (p>0.05) among both groups.

Table 1: Onset of sensory and motor block in two groups (Minutes)

Onset	Group (D)	Group (C)	*p*
S-Block	9.17 ± 2.37	11.27 ± 2.66	0.002
M-Block	12.97 ± 2.76	14.57 ± 3.25	0.04

S: Sensory, M: Motor.

Table 2: Sensory and motor block duration in two groups

Duration	Group (D)	Group (C)	*p*
S-Block	500.57 ± 46.28	313.3 ± 48.94	0.0001
M-Block	476.17 ± 45.67	290.43 ± 65.64	0.0001

Table 3: Duration of analgesia and Rescue analgesics among two groups

Duration	Group (D)	Group (C)	*p*
Duration of Analgesia	592.93 ± 45.95	441.53 ± 18.19	0.0001
No of rescue analgesics	2.13 ± 0.63	3.53 ± 0.82	0.0001

Discussion

The supraclavicular approach is considered to be the easiest and most effective approach for anesthesia of forearm and arm procedures. The classical approach using the anatomical Ultrasonography (USG) guidance and peripheral nerve stimulator (PNS) have improved the success rates and safety margin.benefits of this block include quick onset, expected and deeper anesthesia with maximum success. Main disadvantage of using local anaesthetics along is delayed on setoff block, short duration of block and shorter duration of analgesia after surgery to compensate this deficiency many additives like alpha 2 agonists, steroids like Dexamethasone, benzodiazepines, anti-cholinesterase's etc., are being commonly added to local anaesthetics and used. We consider this presently done study to evaluate the effect of clonidine and dexmedetomidine which is added to local anaesthetic ropivacaine as additive in brachial nerve block done over supra-clavicular region

mainly in the limb operations of arm and forearm. Duration of S and M blockade was significantly extended in study done by Don Sebastian et al[14], Vania k *et al.*[15], Kamlesh k *et al.*[16], Saritha S swami *et al.*[17], Chaudhary *et al.*[18] (p=0.01, p=0.0001, p=0.001, p=0.001, p=0.001) with high statistical significance. Duration of painless period was extended in Don Sebastian *et al.*[14], Kamlesh k *et al.*[16], Saritha S swami *et al.*[17], and statistically significant.

In our current study onset of S & M block (p=0.002), (p=0.04) were slower in clonidine group of patients and faster in group of patients receiving dexmedetomidine. Duration of sensory block (p=0.0001), motor block (p=0.0001) were longer in dexmedetomidine group and highly significant statistically. Duration of analgesia (p=0.0001) is longer and number of rescue analgesics (p=0.0001) used were lesser in dexmedetomidine group and statistically highly significant in comparison with clonidine group. Hence the result of this present study has correlated with Sarita S Swami[17], Chaudhary *et al.*[18],Vania k *et al.*[15], and Don sebastin[14] study by extending the duration of S & M block, duration of painless period and decreased need for extra dose of analgesics.

Dexmedetomidine action is mainly through the alpha 2 receptor which is adrenergic in nature the selectivity to this receptor is very high and acts as agonist. The activity at alpha 1 recepyor and alpha 2 receptor is 1:220 times for clonidine and 1:1620 times for dexmedetomidine. Following are the mechanisms of action at alpha 2 receptor level as agonist (1) analgesia is provided mostly by central action (2) by acting over the peripheral nerve directly (3)vaso-constriction mediated by receptors (4) knocking off the inflammatory mechanism. Extended duration of action is due to the peri-neural administration of alpha 2 receptor agonist as additive to local anaesthetics.[19]

Nerve hyperpolarisation is the mechanism for extending the painless period. it is brought about by blocking the cation Ih current in the nerve. This blocking also results in prolonged action over C fibers (pain) than in A alpha fibers (motor). Action potential is inhibited at higher level by dexmedetomidine than clonidine. Loss of pain and sedation mechanism by blocking the release of pain producing substance P at the level of dorsal root and by stimulating the alpha 2 receptors belonging to the adrenergic group at L. coerleus. Other mode is by blocking the noci-ceptive neurotransmission of the nor-adrenergic system at the descending pathway. Clonidine by producing alpha one mediated vaso-constriction and decreases the uptake of clonidine-local anesthesia mixture and reduces the uptake into the circulatory system,whereas dexmedetomidine has limited action on alpha one receptors.[19]

Experimental studies done on rats especially by brumett and his team have proved that alpha 2 agonists in large doses have extended the time of nerve blocks done on sciatic nerve when added to local anaesthetics. On examination done on histopathology of sciatic nerve, it has been found that myelin sheath of the nerve and axon were not affected by the perineural alpha 2 agonists mainly dexmedetomidine. There was increase in cytokines numbers at the site of nerve damage.this is the main reason for the use of alpha 2 agonists as additives to local anaesthetics and a concrete evidence for the neuro protective effect produced by dexmedetomidine. High safety margin of this drugmakes it abetter choice for intrathecal use. In addition it produces glomerular filtration enhancement, enhancement of threshold for seizures, reduces salivary secretion and IOP (intra ocular pressure).[19]

Conclusion

Dexmedetomidine has more additive benefits than clonidine when combined with ropivacaine by making the onset of clinical effect earlier, prolonging the blockade extent (both S and M) and painless period during post surgery with fewer requirements of rescue analgesics after arm, forearm and hand surgeries.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1347-1353
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.40

A Prospective Randomised Controlled Study of Pre-Emptive Oral Flupirtine on Postoperative Analgesia in Patients Undergoing Abdominal Surgeries Under General Anesthesia

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Abstract

Introduction: Flupirtine is non-opioid, non-NSAID, centrally acting indirect NMDA receptor antagonist. It's analgesic effect is equivalent to NSAIDs and opioids with devoid of their side effects. Abdominal surgeries are the most painful surgeries amongst the surgical procedures. *Aim:* To evaluate the pre-emptive analgesic effect of flupirtine for postoperative pain relief in patients undergoing abdominal surgeries. *Methods:* 60 patients of either sex posted for elective abdominal surgeries were included in this study. These patients were aged between 18 and 60 years with ASA physical status I and II. They were randomly divided into two groups, named group A and group B. Patients in group A received 2 oral placebo capsules and group B patients received 2 flupirtine 100 mg capsules orally. Both drugs were administered two hours before the surgery. All patients underwent abdominal surgeries under general anesthesia. In the postoperative period patients were assessed for the intensity of pain using Numerical rating scale, Time to first rescue analgesia, Ramsay sedation score and side effects in the first 24 hours postoperative period. If NRS score ≥ 4, rescue analgesic tramadol 50 mg iv was given at 6 hours interval. *Results:* The mean NRS score was significantly decreased (p = 0.00) in group B patients for the first 3 hours. The time to first rescue analgesia was significantly high (p = 0.00) in group B patients. 60% of patients in group A received rescue analgesia in the first hour of the postoperative period. The mean RSS score was high in group B patients in the first 3 to 5 hours. The side effects were less in both groups. *Conclusion:* This study concludes that pre-emptive administration of oral flupirtine 200 mg provides effective analgesia in the first 2 to 3 hours of the postoperative period in patients undergoing abdominal surgeries with mild to moderate sedation.

Keywords: Pre-emptive analgesia; Flupirtine; Abdominal surgeries.

How to cite this article:

Ilango Ganesan, C Manikandan. A Prospective Randomised Controlled Study of Pre-Emptive Oral Flupirtine on Postoperative Analgesia in Patients Undergoing Abdominal Surgeries Under General Anesthesia. Indian J Anesth Analg. 2019;6(4):1347-1353.

Introduction

Pain from surgery occurs as a result of tissue trauma and results in physical and psychological discomfort to the patients. There is a relationship between perioperative tissue damage and postoperative pain.[1] Acute and sustained release of chemical mediators during perioperative period leads to central sensitization. This causes acute pain to become chronic pain. Avoiding the central sensitisation will help in decreasing the intensity of acute pain and in preventing this acute pain from becoming chronic.[2] Pre-emptive analgesia is a treatment strategy that starts before the surgery

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Received on 29.04.2019, **Accepted on** 08.06.2019

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to prevent the establishment of central sensitization due to incisional and inflammatory injuries. The concept of pre-emptive analgesia was practiced by George Washington Crile in the early 1900s. He stated that trauma caused by surgery produced a "shock and exhaustion" to the central nervous system. Washington Crile advocated pre-incisional local anaesthetic infiltrations combined with general anesthesia. By this way noxious stimuli were prevented from reaching the brain.[3]

A wide range of medications have been examined for their possible pre-emptive analgesic effects, including opioids and nonsteroidal anti-inflammatory drugs (NSAIDS), through systemic or oral route.[4,5] The choice of analgesic depends upon its efficacy, pharmacokinetics, complications, and cost-effectiveness.

Flupirtine is a non-opioid, non-NSAID, centrally acting analgesic, with N-methyl-D-aspartate (NMDA) receptor antagonistic properties. Its relative advantages are preservation of respiratory functions and better gastric tolerability profile. Various studies have investigated its analgesic effect on acute as well as chronic pain. However, its efficacy as a pre-emptive analgesic has not been the primary stand point in any trial.[6]

Abdominal surgeries are the most painful procedures amongst surgical procedures.[7] Pain is a uniquely individual experience and subjective. Patients who undergo abdominal surgeries will have hypoventilation, due to pain from the surgical incision. This hypoventilation in turn will lead to postoperative hypoxia and result in increased morbidity.

Aim

To Study the Efficacy of Pre-Emptive Oral Flupirtine on Postoperative Analgesia in Patients Undergoing Abdominal Surgeries under General Anesthesia

Materials and Methods

This Prospective randomized controlled study was conducted between June 2015 and May 2016 in the Department of Anaesthesiology, in a medical college in South India. The study was approved by the institutional ethical committee. Sixty patients scheduled for abdominal surgeries were included in this study. After getting departmental approval and informed written consent from study patients, this study was started.

Inclusion criteria

1. Patients aged between 18–60 years of either sex with weight 50 to 90 kg
2. American Society of Anaesthesiologist physical status I and II
3. Patient scheduled for elective abdominal surgeries

Exclusion criteria

1. Consent not given
2. History of drug allergy
3. Chronic alcoholism
4. History of psychiatric disorder
5. History of analgesic or opioid usage within one month
6. Pregnancy
7. Liver and renal dysfunction

All patients were nil per oral for 8 hours before the procedure. Aspiration prophylaxis was followed with Injection ranitidine 50 mg iv plus Injection metoclopramide 10 mg IM in all patients. 60 patients posted for abdominal surgeries under general anaesthesia were divided into two groups, 30 patients in each group. When patients arrived in the pre-anaesthetic room all patients were explained about the interpretation of the numerical rating scale (NRS) to assess the postoperative pain intensity. 18 gauge venflon was started. A maintenance fluid Ringer Lactate/ Normal Saline at 100 ml /hr. was given. In the pre-anesthetic room, baseline pulse rate, blood pressure and oxygen saturation were recorded. Then patients in Group A received 2 placebo capsules resembling flupirtine 2 hours before surgery. Patients in Group B received 2 capsules of 100 mg flupirtine 2 hours before surgery. Both groups of patients were monitored with pulse oximetry for pulse rate and oxygen saturation at 15 minutes interval for 2 hours, until being shifted to the operating room. Injection Glycopyrrolate 5 mcg/ kg, injection Midazolam 0.03 mg/kg and injection Fentanyl 2 mcg/kg were given intravenously as premedication. Patients were preoxygenated with 6 l/min of 100% O2 through facemask for 5 mins. Patients were induced with injection Propofol 2 mg/kg IV. Intubation was facilitated with injection Vecuronium 0.1 mg/kg iv, then using direct laryngoscopy endotracheal intubation was done. Anaesthesia was maintained with oxygen and nitrous oxide in a concentration of 66%:33% ratio and sevoflurane at 1%. Injection vecuronium 0.02 mgkg/iv was repeated as the patient recovered from

relaxant effect. Injection Fentanyl 25 mcg iv was given if baseline blood pressure increased above 20%. After the procedure was completed, residual paralysis was reversed with injection Neostigmine 0.05 mg/kg and injection Glycopyrrolate 0.01 mg/kg iv. After achieving adequate recovery, the patient was extubated and shifted to the post anaesthesia care unit (PACU). In PACU, patients were monitored for postoperative pain using NRS score and sedation was assessed by using Ramsay sedation score. The data were analyzed using SPSS (Statistical Package for Social Science) software Version 16.01. The data collected were scored and analyzed, Continuous variables were presented as means with Standard deviation (sd). Categorical variables were presented as frequency and percentages. Student t-test was used for testing the significance of all the variables mean and standard deviation in groups. Chi-square test was used to compare proportions. All the Statistical results were considered significant at p value ≤ 0.05.

Results

Group A and Group B were comparable with respect to gender distribution. Males and females were equally distributed in both groups and statistically insignificant (p=0.61) (Table 1).

Maximum age in both groups was between 31 -40 years of age. Age was comparable in both groups with a p value of 0.86. In respect to weight group A and group B were comparable with each other (p=0.15). With respect to American society of anaesthesiologist physical status both groups were comparable. In both groups a maximum number of ASA 1 patients were included in this study. (Table 2).

The types of surgery performed in both groups were equally distributed in group A and group B. The most common surgery performed in both groups was incisional hernia repair under general anesthesia (Table 3).

Table 1: Gender Distribution

Gender	Group A		Group B		Total	
	Number of patients	%	Number of patients	%	N	%
Male	17	56.67%	15	50.00%	32	53.33%
Female	13	43.33%	15	50.00%	28	46.67%
Total	30	100%	30	100%	60	100%

Table 2: Age Distribution

Age (in years)	Group A		Group B	
	N	%	N	%
≤ 19	2	6.67%	2	6.67%
20–30	3	10.00%	6	20.00%
30–40	8	26.66%	11	36.67%
40–50	17	56.67%	6	20.00%
50–60	0	0%	5	16.67%
Total	30	100%	30	100%

Table 3: Type of Surgery

Surgery	Group A		Group B	
	N	%	N	%
Incisional Hernia	20	66.67%	19	63.34%
Para Umbilical Hernia	5	16.67%	6	20.00%
Appendectomy	4	13.33%	4	13.33%
Open Cholecystectomy	1	3.33%	1	3.33%
Total	30	100%	30	100%

Pulse rate and oxygen saturation were not significantly changed after giving the study drugs. The mean value of pulse rate after drug administration was graphed in a line diagram. No significant change in the pulse rate was observed after drug administration. There were no significant changes in pulse rate, systolic blood pressure and diastolic blood pressures in group B during the surgery and postoperative period. (Fig. 1).

Both groups were comparable in the duration of surgery. It was statistically not significant (p=0.71). The mean duration of surgery in group A and group B was 123.67 minutes and 121.17 minutes respectively (Fig. 2).

The mean numerical rating scale scores were initially lower in Group B patients than Group A for first 3 hours. Of these, the first 2 hours of postoperative analgesia were statistically significant. The mean value of NRS score in group B was initially less than three for the first 3 hours. Higher values were noted between the 4-6th hour of the postoperative period (Fig. 3).

Sixty percent of the patients in group A asked rescue analgesia in the first hour of the postoperative period. But only 3.3% of patients in group B asked rescue analgesia in the first hour. 81% (13% in the 2nd hour, 46% in a 3rd hour) of patients in group B required rescue analgesia after 3rd hour of the postoperative period. This difference was significant (Fig. 4).

There was a statistically significant change noted in Ramsay sedation score (RSS) for the first 5 hours of the postoperative period. The patients in the flupirtine group exhibited more sedation, but remained responsive to commands (Fig. 5).

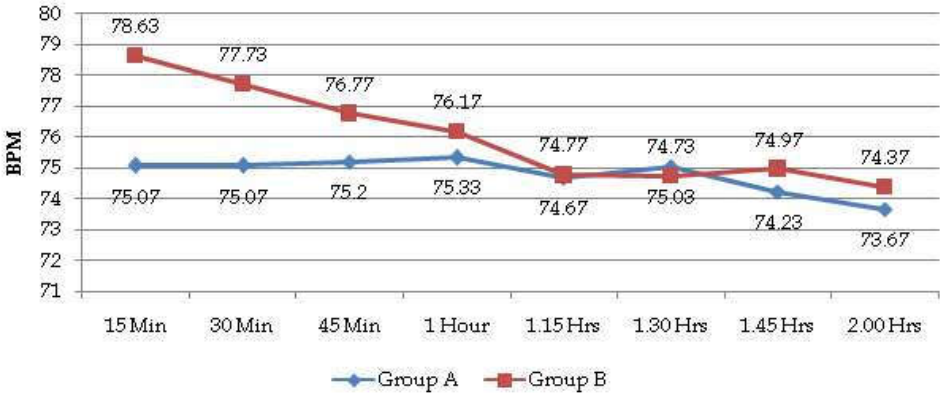

Fig. 1: Pulse Rate after Drug (Placebo/Flupirtine) Administration

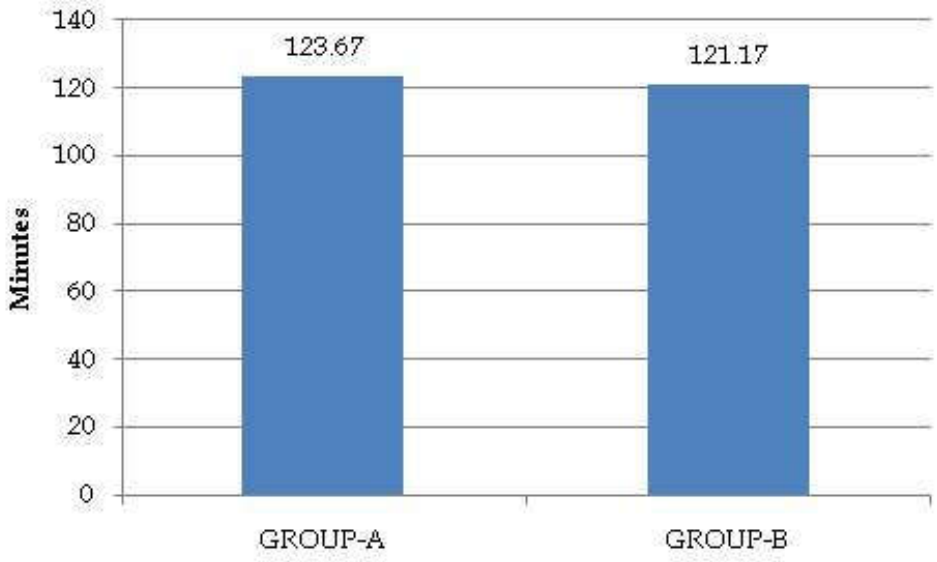

Fig. 2: Duration of Surgery (in Minutes)

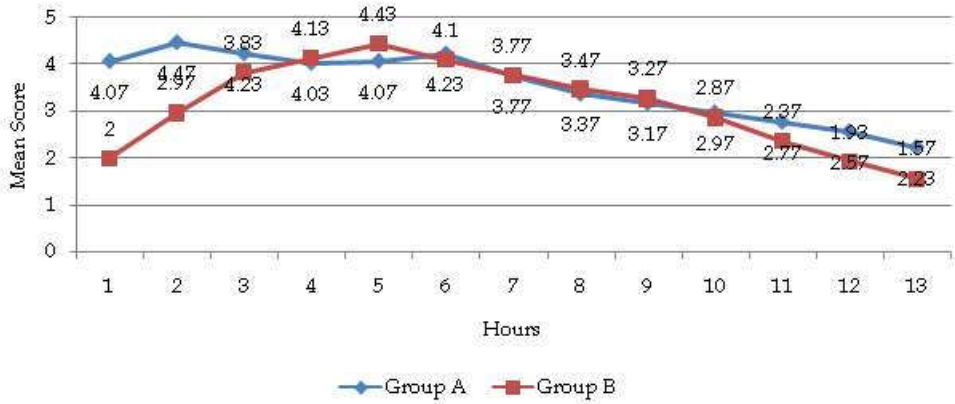

Fig. 3: Numerical Rating Scale

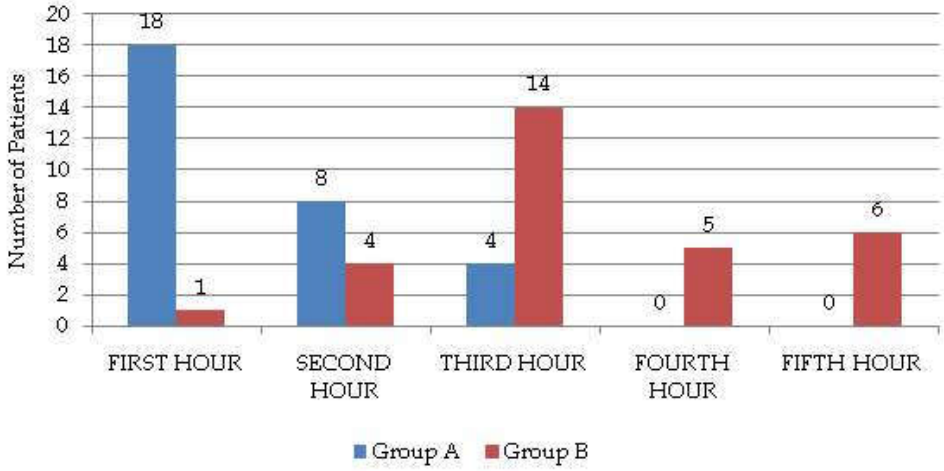

Fig. 4: Time to Rescue Analgesia

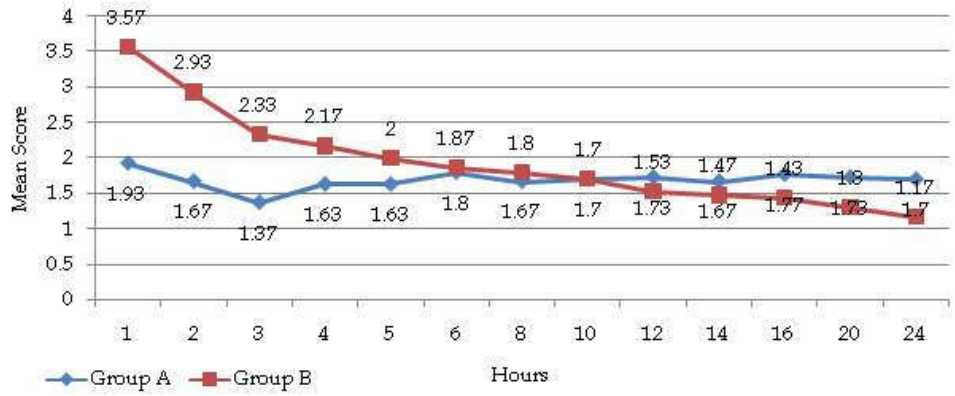

Fig. 5: Ramsay Sedation Scale

Table 4: Side Effects

Side Effects	Group A		Group B	
	No	%	No	%
Nil	29	96.67%	23	76.67%
Bradycardia	0	0%	1	3.33%
Retrosternal Discomfort	0	0%	1	3.33%
Nausea	0	0%	2	6.67%
Vomiting	1	3.33%	1	3.33%
Giddiness	0	0%	2	6.67%
Total	30	100%	30	100%

Seven patients in group B experienced side effects like bradycardia, retrosternal chest discomfort, nausea, vomiting and giddiness. Only one patient in group A experienced vomiting (Table 5).

Discussion

Pre-emptive analgesic modalities can be used as single or in combination. Many studies have been done to evaluate the pre-emptive analgesic effect of opioids and NSAIDs. Ong CK-S *et al.*[8] performed a meta-analysis and demonstrated that the ability of pre-emptive analgesic interventions to decrease the postoperative pain scores, prolong the time to first rescue analgesia and decrease postoperative opioid requirement. Using these measures pre-emptive analgesia showed a beneficial effect after epidural analgesia, local infiltration, and NSAIDs drug administration. Pre-incisional analgesic drug administration showed more effectiveness in decreasing the postoperative pain by protecting the CNS from noxious stimuli induced delirious effect, and which may lead to increased pain and hyperalgesia.

Flupirtine, an indirect acting NMDA receptor antagonist, has a beneficial effect in controlling acute and chronic pain like trauma, migraine, cancer pain and low backache. Its muscle relaxant and the neuroprotective effects are additionally beneficial.

In this study group A and group B patients were comparable with respect to gender distribution, age, weight, height, ASA physical status, types of surgery performed and duration of surgery. Flupirtine attained the peak plasma concentration in about 1.6 to 2 hours when given through oral route. Many studies showed that flupirtine analgesic effect was dose-dependent. Previous studies done with 200 mg flupirtine revealed effective analgesia in controlling postoperative pain in their studies. Further increase of flupirtine dose may lead to side effects like sedation, giddiness, drowsiness in the postoperative period so we choose 200 mg of oral flupirtine to achieve effective analgesia with fewer side effects.

In this study pre-emptively given oral flupirtine 200 mg provides effective analgesia for the first 2 to 3 hours of the postoperative period. Of these first 2 hours of postoperative analgesia were statistically significant (p<0.001, p<0.001). Thereafter a patient experienced only mild pain for the entire postoperative period. This is most convincingly shown by the numerical rating scale score as it was initially low in the first 3 hours of the postoperative period. After that the numerical rating scale score, has shown lower values in the study group than the control group for the remaining postoperative period. Patients were followed up for 24 hours postoperatively. S.M. Abrams *et al.*[9] stated that, flupirtine when given orally, it attained peak plasma concentration at 1.5 to 2 hours and the analgesic effects lasted for 6.5 to 8 hours. Hence it is assumed that, in our study flupirtine attained peak plasma concentration during the intraoperative period and provided adequate analgesia during that period. This was indicated by stable vitals which were noted, till the early postoperative period. But there was not much statistically significant difference noted in the late postoperative period. The time to first rescue analgesia was longer in duration in group B patients (p=0.00). It was comparable to studies done by Vanitha Ahuja and Ambarish Sharma. Ahuja V *et al.*[10] conducted a study to compare the pre-emptive analgesic effect of 100 mg of flupirtine with ibuprofen in gynaecological ambulatory surgeries. Their study showed VNRS score was lower in the 2nd hour of the postoperative period in flupirtine groups. Ambrish Sharma *et al.*[11] conducted a study to compare the analgesic effect of flupirtine with piroxicam in low backache patients. Their study revealed flupirtine has an analgesic effect similar to the piroxicam with better tolerability.

In this study Ramsay sedation score was statistically significant in the first 5 hours of postoperative period (p=0.00, p=0.00, p=0.00, p=0.01 and p=0.04). The mean value of RSS for the first five hours in group B patients were 3.57, 2.93, 2.33,2.17 and 2.0 respectively. The mean value of RSS in group A patients were 1.93, 1.67, 1.37, 1.63 and 1.63 respectively. Patients in group B experienced mild to moderate sedation in the first 3 hours of the postoperative period. Yadav G *et al.*[12] conducted a study to assess the pre-emptive analgesic effect of flupirtine in patients undergoing laparoscopic cholecystectomy. They showed that flupirtine effectively controlled postoperative pain in the first 4 hours of postoperative period,

with higher sedation in flupirtine groups. Yadav G *et al*.[12] done a study in post-craniotomy patients to compare the analgesic effect of flupirtine with diclofenac sodium. Their study showed flupirtine provided analgesia which is equivalent to that of diclofenac sodium, with moderate sedation. But in our study, patients in the study group experienced mild to moderate sedation in the first 3 hours of the postoperative period. In the entire study period, all patients in group A and group B maintained oxygen saturation above 96%. There was no incidence of hypoxia noted in the study period.

Even though the side effects were not statistically significant in this study, 23.3% of group B patients experienced few side effects which include nausea, giddiness, vomiting, retrosternal discomfort and bradycardia. Of this nausea and giddiness were frequently experienced. In contrast, only one patient had vomited in the control group.

Conclusion

This study concludes that pre-emptive administration of oral flupirtine 200 mg provides effective analgesia in the first 2 to 3 hours of the postoperative period in patients undergoing abdominal surgeries with mild to moderate sedation effects. Thereby it prevents pulmonary complications also.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1355-1360
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.41

A Comparison of Dexmedetomidine with Thiopentone Sodium Versus Esmolol with Thiopentone Sodium to Attenuate the Hemodynamic Stress Responses after Electroconvulsive Therapy

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Abstract

Modified electroconvulsive therapy (ECT) under anesthesia is an important in the treatment of severe, persistent depression; bipolar disorder and schizophrenia; especially resistant cases. However, it is commonly associated with acute hyper dynamic responses. *Aims:* To compare the effects of dexmedetomidine and esmolol on patients' haemodynamics, motor seizure duration, and recovery times following ECT. *Study Design:* Randomised Prospective Double Blinded Study. *Materials and Methods:* 90 cases aged between 18 to 50 years belonging to ASA grade I and II were randomly divided into three groups with 30 each. Group A received normal saline (placebo), Group B received dexmedetomidine 1 µg/kg, and Group C received esmolol 1 mg/kg; before induction with thiopentone sodium 2 mg/kg and muscle relaxation with succinylcholine 0.75 mg/kg. Hemodynamic parameters were recorded at different time intervals. The seizure duration using arm isolation method and recovery times using post-anesthesia discharge scoring system (PADSS) were noted. *Analysis:* Data analysis was done using SPSS (Statistical product and service solutions) software trial version 21 for windows. Results were expressed as mean ±SD, proportions and percentages. One way ANOVA test was used to assess the significant differences between groups. *Results:* PostECT rise in hemodynamic parameters was significantly less in dexmedetomidine group as compared to esmolol and control group at 2, 4, 6, and 8 min using ANOVA test. There was no significant difference in seizure duration, emergence, and recovery among the three groups. *Conclusions:* Both drugs reduce the hyperdynamic response to ECT without affecting the seizure duration, but dexmedetomidine has more favourable response in view of stable vitals, smooth emergence and no adverse effect on recovery duration.

Keywords: Dexmedetomidine; Esmolol; Modified electroconvulsive therapy.

How to cite this article:

B Krishna Chaitanya, A Prashanth, Shaik Hala. A Comparison of Dexmedetomidine with Thiopentone Sodium Versus Esmolol with Thiopentone Sodium to Attenuate the Hemodynamic Stress Responses after Electroconvulsive Therapy. Indian J Anesth Analg. 2019;6(4):1355-1360.

Introduction

Electroconvulsive therapy (ECT) is a well known treatment for severe depression in patients who are resistant to pharmacotherapy. Nowadays, almost all the ECT procedures are performed under general anesthesia; also known as modified ECT. However, it is commonly associated with acute hyper dynamic responses, including initial parasympathetic response followed by transient hypertension and tachycardia due to catecholamines release in the body**.** During the sympathetic stimulation**,** systolic blood pressure may increase by 30%–40% and heart

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Received on 07.05.2019, **Accepted on** 08.06.2019

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rate (HR) may increase by 20% (or more**)**.[1] These responses may be harmful to patients with ischemic heart disease, hypertension, and cerebrovascular disease. To decrease this Sympathetic stress response many pharmacological agents like beta blockers, calcium channel blockers, α2 agonists, direct acting vasodilators, and local anaesthetics were tried.[2-6]

Dexmedetomidine is a centrally acting α agonist having high affinity for α-2 receptors with α_2:α_1 binding selectivity ratio of 1620:1 as opposed to to 220:1 for clonidine. The intravenous (IV) dexmedetomidine used as a premedicant in anesthesia as it provides sedation, analgesia, anxiolysis, and improved hemodynamic stability. It also effectively reduces the requirement of anaesthetics.[7] Esmolol hydrochloride is an ultra short acting cardio selective β1 adrenergic receptor antagonist having a rapid onset of action which is administered through intravenous route only and has a distribution half life of 2 min and an elimination half life of 9 min. After an initial dose of 0.5 mg/kg intravenously; over 60 sec, its full therapeutic effect comes in 5 min, and its action ceases within 10–30 min following the discontinuation of drug. Thus use of esmolol appears suitable to reduce short lived stress response associated with laryngoscopy, tracheal intubation, or ECT. As per psychiatry point of view, an adequate motor seizure is defined as the one that lasts more than 25–30s. The objectives of anesthesia to be kept in mind for modified ECT include rapid loss of consciousness, attenuation of hemodynamic responses, avoidance of gross movements, minimal interference with seizure, prompt, smooth and early recovery of spontaneous ventilation and consciousness. Furthermore, early ambulation and discharge to home should be considered. This study was attempted to compare the effects of dexmedetomidine and esmolol after induction with Thiopentone sodium and muscle relaxation by succinylcholine in controlling the hemodynamic stress responses, motor seizure duration and time for recovery in patients who were administered ECT.

Materials and Methods

After ethical committee clearance 90 cases, belonging to the American Society of Anaesthesiologists Classes I and II, aged 18–50 years diagnosed with major depressive disorder (suicidal patients), schizophrenia, catatonia (in which first line treatment failed), or bipolar disorder were included in the study. Patients with atrio-ventricular conduction block greater than first degree, history of major illness such as tuberculosis, bronchial asthma, hypertension, recent history of stroke, acute respiratory disorders, raised intracranial tension from any cause, systolic blood pressure (SBP) < 90 mmHg, Heart rate < 50 bpm or history of drug allergy to interventional drugs and pregnant females were excluded from the study. The study population was randomly divided into three groups (Groups A, B, and C) with thirty cases in each group. Pre-anaesthetic evaluation was done thoroughly. Airway assessment using Mallampati grading; eye examination to rule out any signs of raised intracranial tension (papilledema) and other routine investigations were done. Chronic anti depressant medications were continued on the day of surgery. The patient was kept nil per oral for 6 h. In the ECT suite, 20 G cannula was inserted, and normal saline infusion was started. Multi parameter monitors were attached to record HR, non-invasive measurements of SBP, diastolic blood pressure (DBP), mean arterial blood pressure (MAP), SPO_2 and electrocardiogram. Baseline vitals were taken after giving 5 min for stabilizing the patient. Group A (n=30) received normal saline (placebo); Group B (n=30) received Dexmedetomidine 1 μg/kg (total volume of 20 ml over a period of 10 min); and Group C (n=30) received Esmolol 1 mg/kg (total volume of 20 ml over a period of 3 min) before induction using syringe pumps. Preoxygenation was done for 3 min through face mask with Bain's circuit. General anesthesia was induced with IV Thiopentone Sodium 2 mg/kg until eyelash reflexes lost**.** Then, after inflating tourniquet of the other arm, succinylcholine 0.75 mg/kg IV was administered. When the fasciculations subsided, and adequate muscle relaxation was obtained, an oral soft bite block was placed in the mouth.

Psychiatrist was allowed to place bi-fronto temporal electrodes over forehead and a brief pulse stimulus of 90–120 volts maintenance electroconvulsive therapy current for 1 millisecond was given to produce seizures. The effectiveness of ECT current was determined by the appearance of tonic–clonic seizures.The ventilation was assisted with 100% O_2, until the patient resumed adequate spontaneous breathing. Following the ECT current, the Heart rate, Systolic BP, Diastolic BP, and Mean arterial pressure were recorded at 0, 2, 4, 6, 8, 10 min, and thereafter every 5 min till 30 min and then every 15 min. The duration from the begining of stimulus (ECT) to the cessation of clonic tonic motor activity in the isolated arm was recorded using clinical method. The duration of recovery from the succinylcholine especially

spontaneous breathing was recorded. Patients were assessed for side effects such as nausea, vomiting, hypotension/hypertension, respiratory depression after the electrical stimulus and were discharged from the post-anesthetic care unit to the psychiatry department according to postanesthesia discharge scoring system (PADSS) criteria.

Analysis

Data analysis was done using SPSS (Statistical product and service solutions) software trial version 21 for windows. Results were expressed as mean ± standard deviation, proportions and percentages. One way ANOVA test was used to assess the significant differences between groups. For all statistical analysis $p< 0.05$ was considered as statistically significant.

Results

There was no significant difference in the baseline variables like heart rate and mean arterial pressure among the three groups ($p>0.05$). (Table 2) There was also a significant increase in the heart rate and MAP while immediately after giving ECT and up to 2nd and 4th minute in the groups A and C ($p<0.05$) unlike Group B which showed no significant change in the HR and MAP throughout the observation period ($p>0.05$) (Tables 3 and 5).

Post Hoc tests showed that there was a significant difference ($p<0.05$) in the heart rate and MAP between Group A and B and Group A and C during infusion of the drug and at 2, 4, 6 and 8 minutes. A comparison between Group B and group C revealed significant difference regarding HR and

Table 1: Shopwing the Demographic data

	Group A (control) Mean ± SD	GroupB (dexmedetomidine) Mean ± SD	Group C (esmolol) Mean ± SD
Age (years)	33.4 ± 9.05	34 ± 8.21	34.2 ± 8.41
Sex ratio (male:female)	20:10	21:9	19:11
Weight (kg)	56.12 ± 14	55.2 ± 5.12	56.5 ± 7.16

SD- *standard deviation*

Table 2: Showing The intergroup comparison of baseline vitals

Baseline	Group A (control) Mean±SD	Group B (dexmedet-omidine) Mean±SD	Group C (esmolol) Mean±SD
HR (/min)	76.5 ± 4.52	77.03 ± 3.84	76.2 ± 4.10
SBP (mmHg)	119.93 ± 3.77	121.0 ± 3.29	120.26 ± 3.53
DBP(mmHg)	76.4+3.51	76.93 ± 3.08	77.26 ± 2.75
MAP(mmHg)	90.86 ± 3.06	91.6 ± 2.44	91.53 ± 2.36
SpO_2(%)	98.93 ± 0.77	98.86 ± 0.80	98.86 ± 0.76

HR – Heart rate; SBP – Systolic blood pressure; MAP – Mean arterial pressure; DBP – Diastolic blood pressure; SpO_2 – Oxygen saturation

Table 3: showing the Post electroconvulsive therapy changes in heart rate in Group A, B, and C at different time interval

Time(min)	Group A (beats/min)	Group B (beats/min)	Group C (beats/min)
Infusion	79.60	83.43	80.53
Induction	76.93	72.17	78.43
0	108.97	76.03	92.83
2	106.03	81.17	94.53
4	98.80	80.63	86.87
6	89.23	81.43	82.87
8	80.10	81.80	81.33
10	80.03	81.80	81.33
15	80.10	81.80	81.33
20	80.03	81.80	81.33
25	80.10	81.80	81.33
30	80.03	81.80	81.33

HR of three groups with time.

Table 4: Showing the comparison of HR among the Groups.

Time	Group A versus Group B (P value with significance)	Group A versus Group C (P value with significance)	Group B versus Group C (P value with significance)
Baseline	0.63 (NS)	0.30 (NS)	0.63 (NS)
After study drug infusion	<0.001 (HS)	<0.001 (HS)	0.06 (NS)
After induction	0.08 (NS)	0.92 (NS)	0.18 (NS)
After ECT			
0 min	0.001 (HS)	0.280 (NS)	0.000 (HS)
2 min	0.000 (HS)	0.000 (HS)	0.000 (HS)
4 min	0.000 (HS)	0.000 (HS)	0.000 (HS)
6 min	0.000 (HS)	0.000 (HS)	0.000 (HS)
8 min	0.000 (HS)	0.000 (HS)	0.349 (NS)
10 min	0.224 (NS)	1.388 (NS)	0.738 (NS)
15 min	1.383 (NS)	1.383 (NS)	1.383 (NS)
20 min	1.383 (NS)	1.383 (NS)	1.383 (NS)
25 min	1.383 (NS)	1.383 (NS)	1.383 (NS)
30 min	1.383 (NS)	1.383 (NS)	1.383 (NS)

(S – Significant (p<0.05); NS – Nonsignificant (p>0.05); HS – Highly significant (p<0.001). ECT – Electroconvulsive therapy)

Table 5: Showing Postelectroconvulsive therapy changes in MAP in Group A, B, and C at different time interval MAP 3 groups

Time(min)	Group A (mm of Hg)	Group B (mm of Hg)	Group C (mm of Hg)
infusion	93.87 ± 3.27	93.77 ± 6.50	92.73 ± 5.90
induction	89.40 ± 3.28	89.83 ± 6.40	90.53 ± 5.87
Ect	119.40 ± 3.50	92.97 ± 8.33	104.70 ± 6.59
2	117.27 ± 3.62	94.70 ± 7.78	102.73 ± 6.48
4	109.57 ± 3.29	92.43 ± 7.23	97.00 ± 6.22
6	99.47 ± 3.41	91.97 ± 6.59	93.20 ± 6.42
8	93.60 ± 3.21	93.50 ± 5.69	92.93 ± 6.11
10	93.60 ± 3.21	93.17 ± 6.06	92.93 ± 6.11
15	93.60 ± 3.21	93.17 ± 6.06	92.93 ± 6.11
20	93.60 ± 3.21	93.17 ± 6.06	92.93 ± 6.11
25	93.60 ± 3.21	93.17 ± 6.06	92.93 ± 6.11
30	93.60 ± 3.21	93.17 ± 6.06	92.93 ± 6.11

Table 6: Showing comparison of MAP among the 3 groups

Time	Group A versus Group B (P value with significance)	Group A versus Group C (P value with significance)	Group B versus Group C (P value with significance)
After study drug infusion	<0.001 (HS)	<0.001 (HS)	0.06 (NS)
After induction	0.08 (NS)	0.92 (NS)	0.18 (NS)
After ECT			
0 min	0.756	0.417	0.616
2 min	0.000	0.000	0.000
4 min	0.000	0.000	0.000
6 min	0.000	0.000	0.003
8 min	0.000	0.000	0.402
10 min	0.940	0.619	0.672
15 min	0.753	0.628	0.865
20 min	0.753	0.628	0.865
25 min	0.753	0.628	0.865
30 min	0.753	0.628	0.865

(S – Significant (p<0.05); NS – Nonsignificant (p>0.05); HS – Highly significant (P<0.001). ECT – Electroconvulsive therapy)

MAP at 2, 4 and 6 minutes only. There was no significant difference between among the 3 groups after 8 minutes.

Discussion

ECT induces generalized tonic–clonic epileptic seizure. The patients undergoing for ECT might be on a number of anti psychotic medications which can cause exaggerated cardiovascular responses. In our study, postECT hyper dynamic responses were significantly less in the dexmedetomidine group at 0, 2, 4, 6, and 8 min as compared with Group A and Group C. similar observations were noted by Shams and ElMasry[7] and Begec *et al*.[8]. Although, Fu and White[9] have found that dexmedetomidine extended the seizure activity duration during ECT, Shams and ElMasry,[7] Mizrak *et al*.,[10] Cohen and Stewart,[11] and Dodawad[12] have found that there was no significant differences in the duration of seizure activity when using dexmedetomidine with the control population, Similar findings were noted in our study. Saito *et al*.,[13] Howie *et al*.[14] and Weinger *et al*.[15] found no significant differences in the duration of seizures, when comparing esmolol versus control group before ECT which was similar in our group. Motor seizure duration and recovery from anesthesia were similar in all the groups. In our study we observed that dexmedetomidine reduced emergence agitation following recovery from anesthesia for ECT, in contrast the recovery was smooth.

The duration of Motor seizure activity was not effected and recovery was not delayed. There were no side effects such as headache, respiratory depression, hypoxemia, bradycardia, hypotension, jaw pain, and muscle spasms. Esmolol has a very fast onset of action (2 min) while dexmedetomidine has a little delayed onset of action and has to be given by infusion. To make double blinding possible, we have given esmolol also in same fashion as dexmedetomidine, but this may reduce the efficacy of esmolol as it is rapidly eliminated from the body. To avoid this bias and rather than making esmolol less effective, we have changed the anaesthesiologist, after giving esmolol in bolus form and dexmedetomidine in an infusion, which is a preferred technique.[16] As ECT procedures are performed frequently in the outpatient setting, the anaesthetic agents used for these procedures should have rapid recovery profiles. In the our study, none of these two drugs (esmolol and dexmedetomidine) prolong the recovery times. These drugs may be superior to other drugs for ECT because of their short halflife and wide therapeutic indices. However, the implications of these findings require further investigation.

Conclusion

Both esmolol and dexmedetomidine attenuate the hyper dynamic response to ECT without affecting the seizure duration, but dexmedetomidine has a more favourable response in view of stable vitals, smooth emergence, and no adverse effect on recovery duration.

Limitations

The monitoring of seizure duration by observing tonic–clonic activity and not using electroencephalogram (EEG) was a limitation of our study because EEG seizure duration activity may be longer than motor seizure activity.

Financial Support and Sponsorship: Nil.

Conflicts of Interest: There are no conflicts of interest.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1361-1366
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.42

Comparison of Low Dose Fentanyl with Low Dose Dexamethasone as an Adjuvant to 0.5% Bupivacaine in Supraclavicular Block via Multipoint Injection Technique under Sonographic Guidance

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Abstract

Background: To see effect of low dose fentanyl vs low dose dexamethasone in ultrasound guided supraclavicular block via multipoint injection technique. *Methods:* This double blinded randomized controlled study was carried out on 60 patients belonging to ASA grade I and II, undergoing surgeries of the upper limb under USG guided supraclavicular block via multipoint injection technique. Group I (NS) received 20 ml 0.5% bupivacaine with 1 ml normal saline. Group II (Fenta) received 20 ml 0.5% bupivacaine with 10 µg (1 ml) fentanyl. Group III (Dexa) received 20 ml 0.5% bupivacaine with 4 mg (1 ml) dexamethasone. *Results:* The onset of sensory blockade in group 1 (NS) was 9.6430 ± 1.19025 min, in group 2 (Fenta) it was 10.3395 ± 0.59338 min, whereas in group 3 (Dexa) it was 3.9735 ± 0.41802 min. The onset of motor blockade was 17.9025 ± 1.13816 min in group 1 (NS), 17.9530 ± 0.85577 min in group 2 (Fenta), 8.6145 ± 1.15154 min in group 3 (Dexa). The mean duration of sensory blockade in group 1 (NS) was 259.200 ± 36.3544 min, in group 2 (Fenta) it was 406.350 ± 20.1240 min, whereas in group 3 (Dexa) it was 1031.500 ± 173.8676 min. The mean duration of motor block in minutes was 197.900 ± 31.8878 in group 1 (NS), 339.250 ± 26.2616 in group 2 (Fenta) and 934.950 ± 168.9181 min in group 3 (Dexa). *Conclusion:* The dosage of fentanyl and dexamethasone do not linearly correlate to the degree of blockade. Dexamethasone is superior to fentanyl as an adjuvant in supraclavicular block.

keywords: Bupivacaine; Supraclavicular Block; Dexamethasone.

How to cite this article:

Kunaal Kumar Sharma, Rajesh Kumar Verma, Surinder Singh *et al.* Comparison of Low Dose Fentanyl with Low Dose Dexamethasone as an Adjuvant to 0.5% Bupivacaine in Supraclavicular Block via Multipoint Injection Technique under Sonographic Guidance. Indian J Anesth Analg. 2019;6(4):1361-1366.

Introduction

It is an old belief "to be strong is to never feel pain" Perhaps this is the main reason that through the generations of medical science, pain became the most neglected symptom of all, be it in acute trauma scenario or in chronic debilitating diseases. We should realize that the strongest people are the ones who have felt pain, understood it, accepted it and learned from it. Postoperative pain relief is the core component of rehabilitation programmes and early ambulation. The IASP advocates that relief of pain should be recognized as a human right.[1] The

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Received on 08.05.2019, **Accepted on** 08.06.2019

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supraclavicular approach to the brachial plexus characteristically is associated with a rapid onset of anesthesia and a high success rate. Ultrasound application allows for non-invasive visualization of tissue structures. The ability to image the plexus, rib, pleura and subclavian artery with ultrasound guidance has increased safety due to better visualization of anatomy and needle placement.

The aim of our study was to research about low doses of adjuvants for supraclavicular blocks in this present era of multipoint injection techniques / targeted intracluster injection technique under sonographic guidance for perineural blocks. The use of opioids in medical science has been present since 18th century when Friedrich Wohler discovered alkaloid from coca leaves which alleviated pain. In 1879 Vassily von Anrep recommended cocaine usage for surgical anesthesia. Fentanyl has been used in brachial plexus block for last three decades, and we believe that we are using it in a low dose of 10µg for the very first time. Dexamethasone is a glucocorticoid which exerts its effects on brachial block by a complex action and we used it in a low dose of 4 mg.

Materials and Methods

The study was conducted in a randomized controlled manner in a multispecialty tertiary care centre. The inclusion criteria of our study was met by only 60 out of the total 67 patients enrolled for the study. They underwent surgeries of the upper limb under USG guided supraclavicular brachial plexus block via multipoint injection technique. Patients were divided into three groups of twenty patients each and 21 ml injectant mixture was administered by a 20G needle in an in-plane approach, under direct sonographic visualisation with 6-13 Hz linear probe. Group I (NS) received 20 ml (0.5%) bupivacaine with 1 ml normal saline, group II (Fenta) received 20 ml (0.5%) bupivacaine with 10 µg (1 ml) fentanyl, whereas group III (Dexa) received 20 ml (0.5%) bupivacaine with 4 mg (1 ml) dexamethasone.

Heart rate, mean arterial pressure, respiratory rate and SpO_2 were noted before anesthesia in operation theatre, thereafter at the time of administration of nerve block, and then at 2 min, 5 min, 10 min intervals. Thereafter, the parameters were noted at every 15 min till 180 min. The block parameters like latency, duration, quality, postoperative analgesia and postoperative complications were also recorded. The Quality of block was assessed by four point scale The results were analyzed using IBM-SPSS software by ANOVA and Tukey test.

Results

Demographic distribution: There was no significant difference between the age groups of the patients in the three groups (*p*-value = 0.965157). Also no significant difference was found between the weight of patients in the three groups (*p*-value = 0.313619). (Fig. 1)

Onset of Blockade: The mean onset of sensory block

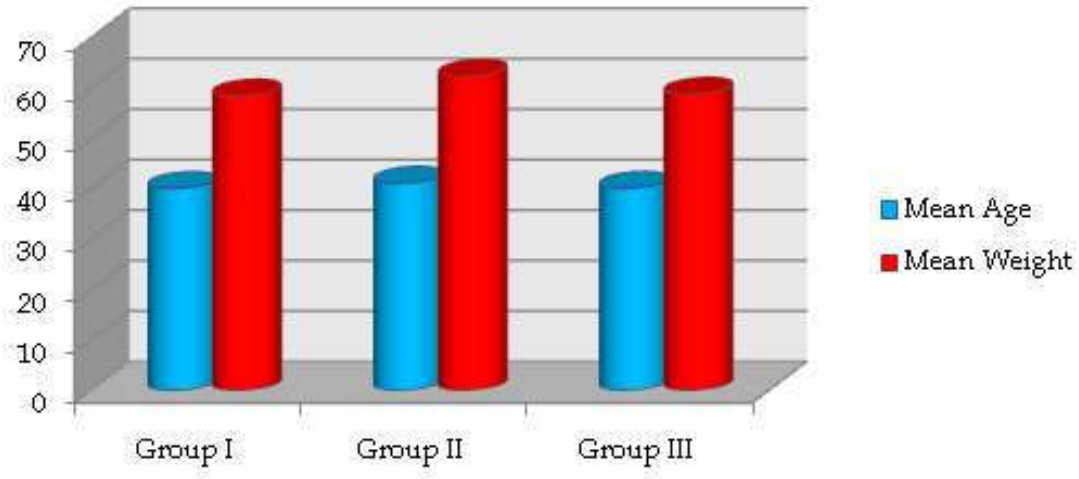

Fig. 1: Mean age and weight distribution

in group 1 (NS) was 9.6430 ± 1.19025 min, in group 2 (Fenta) it was 10.3395 ± 0.59338 min, whereas in group 3 (Dexa) it was 3.9735 ± 0.41802 min. As per post hoc analysis of ANOVA by Tukey test, these results were significant when group 2 was compared with group 1 (*p*-value 0.022), and when group 3 was compared with groups 1 and 2 (*p*-value 0.000). The mean onset of motor block in group 1 (NS) was 17.9025 ± 1.13816 min, in group 2 (Fenta) it was 17.9530 ± 0.85577 min and in group 3 (Dexa) it was 8.6145 ± 1.15154 min. (Fig. 2) As per post hoc analysis of ANOVA by Tukey test, these results were significant.

Duration of blockade: The mean duration of sensory blockade in group 1 (NS) was 259.200 ± 36.3544 min, in group 2 (Fenta) it was 406.350 ± 20.1240 min, whereas in group 3 (Dexa) it was 1031.500 ± 173.8676 min.(*p*-value 0.000). The mean duration of motor block was 197.900 ± 31.8878 min in group 1 (NS), 339.250 ± 26.2616 min in group 2 (Fenta) and 934.950 ± 168.9181 min in group 3 (Dexa). (*p*-value 0.000). (Fig. 3) (Table 1).

The MAP, HR, RR and SpO_2 remained stable throughout the procedure, during the study period. During the postoperative period, mean VAS score at the time of first requirement of rescue analgesic

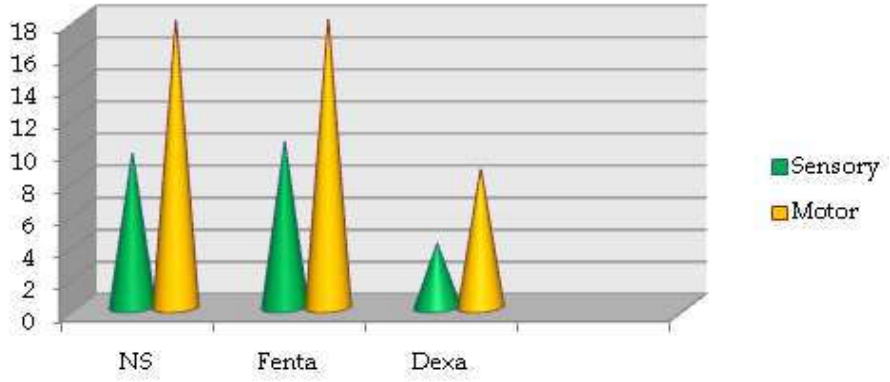

Fig. 2: Onset of blockade

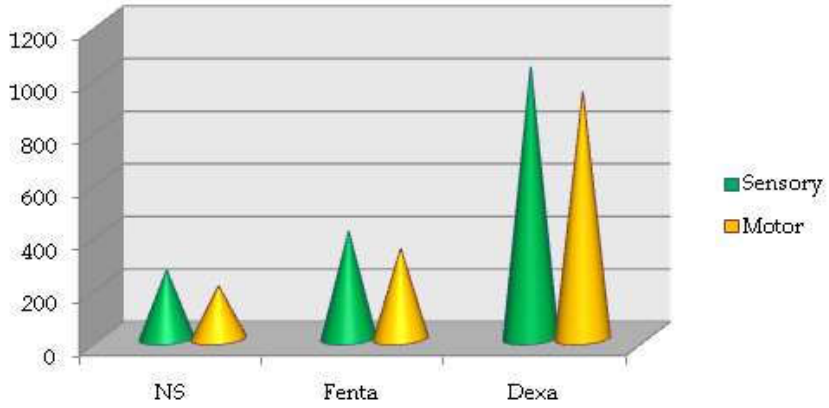

Fig. 3: Duration of blockade

Table 1: Monitored parameters of blockade

Parameters	Group I	Group II	Group III	*p*-value
Mean Sensory onset (in min)	9.6430 ± 1.19025	10.3395 ± 0.59338	3.9735 ± 0.41802	0.000
Mean Sensory duration (in min)	259.200 ± 36.3544	406.350 ± 20.1240	1031.500 ± 173.8676	0.000
Mean Motor onset (in min)	17.9025 ± 1.13816	17.9530 ± 0.85577	8.6145 ± 1.15154	0.000
Mean Motor duration (in min)	197.900 ± 31.8878	339.250 ± 26.2616	934.950 ± 168.9181	0.000
Postoperative VAS score	7.950 ± 0.9445	5.400 ± 0.5982	1.200 ± 1.7045	0.000
Postoperative analgesic consumption (in mg)	221.25 ± 16.7705	127.5 ± 49.271	26.25 ± 36.702	0.000
Quality of block	3.15 ± 0.3663	3.2 ± 0.4104	3.9 ± 0.3078	0.000

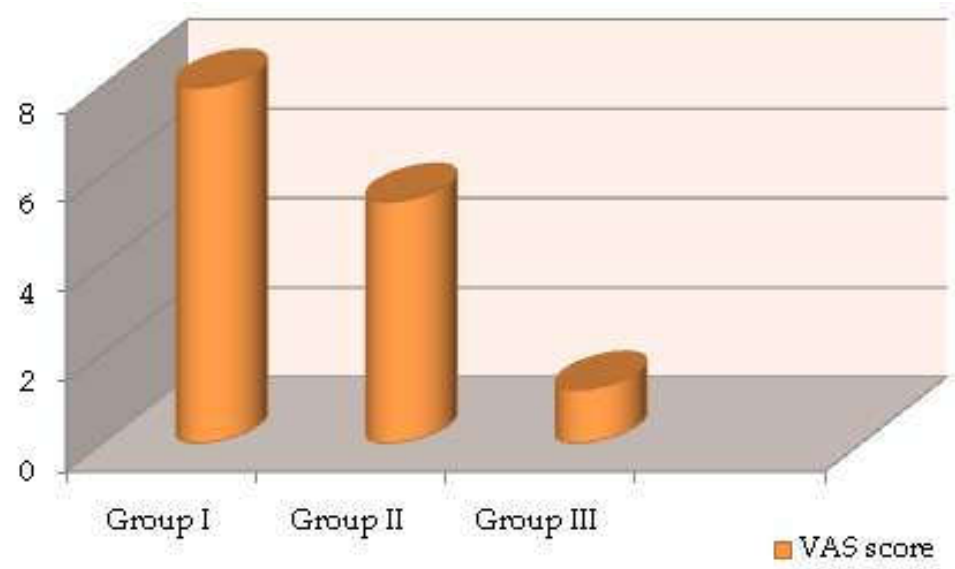

Fig. 4: Postoperative VAS at the time of first requirement of rescue analgesic

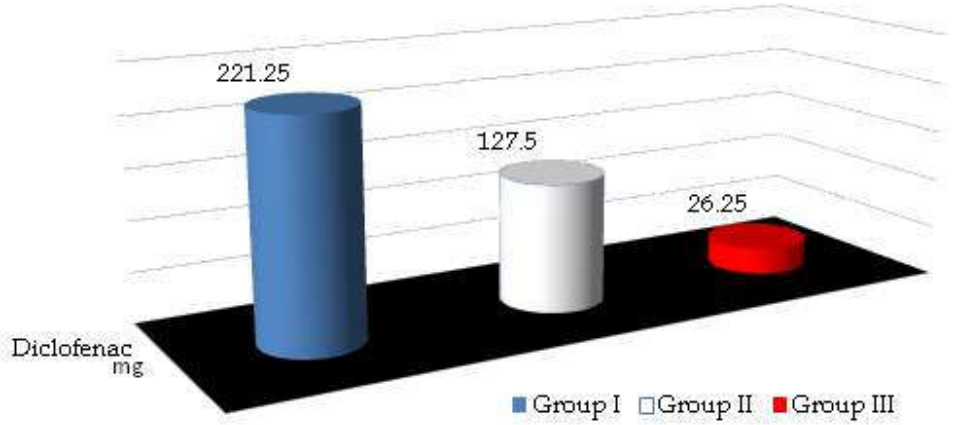

Fig. 5: Postoperative rescue analgesic consumption

(75 mg diclofenac), was least in group III (1.200 ± 1.7045) and maximum in group I (7.950 ± 0.9445). (Fig. 4). These results were highly statistically significant (p = 0.000). The rescue analgesia was given as 75 mg diclofenac intramuscularly. The mean postoperative rescue analgesic consumption (diclofenac) in group I was 221.25 ± 16.7705 mg, in group II it was 127.5 ± 49.271 mg, whereas in group III it was just 26.25 ± 36.702 mg (p = 0.000). (Fig. 5). The mean quality of block was in group III was 3.9 ± 0.30, in group II it was 3.2 ± 0.41 and in group I it was 3.15 ± 0.166.

Discussion

Supraclavicular block for upper extremity surgery anaesthetizes the brachial plexus at its divisions, where it is in its most compact form. Therefore it provides a complete and reliable block for upper extremity surgery.

Attardi *et al.*[2] showed that dexamethasone's mechanism of action in perineural blockade results from decreased nociceptive C-fibre activity via a direct effect on glucocorticoid receptors and inhibitory effect on potassium channels. It is also suggested that by local vasoconstrictive effect there occurs a reduction of local anaesthetic absorption, which leads to quicker onset and prolongation of blockade as demonstrated by Shishido *et al.*[3]. Also, Stan *et al.*[4] showed that glucocorticoids can prolong analgesia period by suppressing the synthesis of inflammatory mediators. Neurotoxicity to perineural corticosteroids is related mainly to the preservative benzyl alcohol,

vehicle polyethylene glycol and the presence of insoluble steroid particulate matter in the injectate. Dexamethasone is non-particulate and we used a preservative-free formulation. In addition, Ma *et al.*[5] have demonstrated neuroprotective effects of perineurally administered dexamethasone in murine studies. Perineural corticosteroid injections are widely used throughout the world. The time of onset of blockade with dexamethasone in our study group III (sensory onset 3.973 ± 0.418 min, motor onset 8.614 ± 1.151 min) was faster than that seen by Parveen *et al.*[6] (sensory onset 28.20 ± 3.02 min, motor onset 38.70 ± 4.25 min) and Alarasan *et al.*[7] (sensory onset 10.36 ± 1.99 min, motor onset 12 ± 1.64 min). Although, Parveen *et al.* and Alarasn *et al.* used a higher dose of dexamethasone (8 mg) in comparison to our dose of 4 mg, we were still able to get faster onset of block in our study group.

We attribute this to the use of multipoint injection technique which resembles the targeted intracluster injection technique of Techasuk *et al.*, in which we injected 11 ml of the injectant mixture at the eight ball corner pocket, followed by injecting 5 ml at the middle trunks and 5 ml at the upper trunks. Techasuk *et al.*[8] have observed better results with targeted intracluster injection technique in comparison to double injection technique in supraclavicular block.

We have used 4 mg dexamethasone and the duration of sensory and motor block in our study is 17.192 ± 2.897 hrs and 15.582 ± 2.815 hrs. This is comparable to the study by El-Baradey *et al.*[9] which however used a higher dose (8 mg) of dexamethasone. We believe that dose of dexamethasone has little to do with prolongation of block duration and analgesia. This is evident in the study by Liu *et al.*[10], in which the addition of 1 mg, 2 mg and 4 mg dexamethasone to the local anaesthetic mixture significantly prolonged the analgesia duration to 22.3 hours, 23.3 hours and 21.2 hours in each of the respective groups which had received USG guided supraclavicular block.

Fentanyl is a proven adjuvant for perineural blockade, but its usage in low doses has not been widely studied. We believe that this is for the first time that fentanyl is being used in such a low dose of 10 µg in 20 ml bupivacaine (0.5%). And on the top of that, significance of prolongation of block even at this low dosage of fentanyl emphasizes the reason for need of more such studies with low dose of fentanyl.

The duration of sensory and motor block in group II (fentanyl) was significantly prolonged in comparison to the control group I (NS). Rajkhowa *et al.*[11] used higher dose (50µg) of fentanyl as adjuvant in supraclavicular block and got sensory and motor block of 7.75 ± 0.47 hrs and 6.56 ± 0.43 hrs duration, while we used 10 µg and obtained comparable result of sensory and motor block of 6.77 ± 0.335 hrs and 5.65 ± 0.437 hrs. We believe that as per the the study by Gissen *et al.*[12], the local anaesthetic properties of fentanyl were responsible for this effect. Also Stein *et al.*[13], have shown that the opioid receptors on the peripheral nerve terminals get up-regulated due to inflammation at the fractured site, thereby cytokines activate the endogenous opioid peptides and cause local analgesia at the site of inflammation. The opioids inhibit neuronal firing and transmitter release, and also inhibit the release of substance-P. We believe that this mechanism also came into play while we used the low dose of fentanyl for supraclavicular block in our study.

The intergroup comparison between the dexamethasone group and fentanyl group showed that dexamethasone is superior to fentanyl in terms of faster onset of blockade, prolonging the duration of block, quality of the block and postoperative analgesia. This deduction is analogous to the study by Yaghoobi *et al.*[14] who although had used higher doses of fentanyl (100 µg) and dexamethasone (8 mg) alongwith larger injectant volume in their study on axillary block.

Conclusion

The use of low dose dexamethasone (4mg) prolonged the duration of block to a far greater extent (sensory 17.192 ± 2.897 hrs, motor 15.582 ± 2.815 hrs) than the use of low dose fentanyl (10 µg), (sensory 6.772 ± 0.335 hrs, motor 5.654 ± 0.437 hrs). The postoperative VAS score at the time of first requirement of rescue analgesia was lowest in the dexamethasone study group. Likewise, the mean postoperative rescue analgesic requirement of diclofenac in dexamethasone group was least among the three study groups. Also, the quality of block was most superior in the dexamethasone group. So we advocate its use over fentanyl in supraclavicular block. Administration of supraclavicular block under sonographic guidance resulted in stable haemodynamics throughout the study period in all the three groups, and no patient developed any adverse effects related to supraclavicular block.

Limitations: The sample size of our study groups was small. We also did not measure the serum concentration and CSF levels of the adjuvants used in our study in order to quantify the systemic absorption of these drugs (if any).

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1367-1372
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.43

A Study of Comparison of Intubating Conditions and Haemodynamic Effects after the Administration of Succinylcholine and Rocuronium Bromide

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Abstract

Background and Aim: Though rocuronium has a rapid onset of neuromuscular blockade like succinylcholine without the latter's adverse effects, its use is limited due to its prolonged action. Present study was performed with an aim to compare the outcome of using Rocuronium and Succinylcholie as muscle relaxant (MR). *Material and Methods:* A single-center, prospective-randomized, blinded study of 60 patients, divided into 2 groups and intubation conditions were evaluated. *Results:* The intubating conditions were scored as excellent in 29 and 26, and Good intubating conditions were observed in 1 and 4 Patients of group I and 2 respectively. *Conclusion:* We conclude that rocuronium, an innovative nondepolarizing MR with a succinct onset of action and transitional duration, but lack of the unpleasant reactions connected with succinylcholine may be a appropriate alternative to succinylcholine for tracheal intubation.

Keywords: Muscle relaxant; Randomized trial; Rocuronium; Succinylcholine.

How to cite this article:

Lovina Neil, Harshil Shah. A Study of Comparison of Intubating Conditions and Haemodynamic effects after the Administration of Succinylcholine and Rocuronium Bromide. Indian J Anesth Analg. 2019;6(4):1367-1372.

Introduction

From the ancient time man has always been in the quest for perfection. Anesthesia has been receptive to new ideas & new discoveries for better patient care. Introduction of newer drugs & techniques have further helped in improvement in anesthesia practice. At present endotracheal intubation is an essential element of organization of general anesthesia throughout surgical procedures to maintain airway, to allow IPPV and to prevent aspiration. Dangerous period for aspiration is the time interval between suppression of protective reflexes & development of satisfactory intubating conditions. Hence this time interval should be as short as possible.[1-5]

Succinylcholine introduced by the Daniel Bovet *et al.* in 1949, revolutionized anaesthetic practice by providing intense neuromuscular blockage of very quick start & very small period of action, and yet relaxant of alternative for habitual intubation and quick succession initiation of anesthesia.[5] Adding up to fasciculation it had numerous adverse effects as well. Therefore the search is on for agent, which

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Received on 07.05.2019, **Accepted on** 08.06.2019

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has quick onset of action, quick revival, and non-cumulative effect, without cvs side effects, with high potency, pharmacologically inactive metabolites, and reversibility with cholinesterase inhibitors.[6-8]

Recently developed neuromuscular blocking drugs are of intermediate duration & to a major extent free of side effects. However even after intubating doses onset of action is relatively slow as compared to succinylcholine. Among the muscle relaxants in current utilize, the transitional acting non-depolarizing muscle relaxants- vecuronium & atracurium besylate are good-looking alternatives.[9-15] However ,neither of them has been demonstrated to have significant shorter onset time as required for quick tracheal intubation as compared to succinylcholine. The use of high initial bolus doses of either atracuruim or vecuronium condensed the beginning time however at the cost of an extended period of action which may be undesirable in certain situations. Rocuronium bromide is a novel aminosteriod neuro-muscular blocking agent linked to vecuronium bromide but has a greater lipophilicity, lesser potency and a very fast onset of action. Good to excellent tracheal intubating condition have been reported with in 60-90 seconds after a dose in a range of 0.6-0.9 mg/kg.[16-21] Several clinical studies conducted by various workers have confirmed the brief onset time of rocuronium bromide. In most studies the timing of tracheal intubation was determined by neuromuscular monitoring or the intubation was done at a prearranged moment in time following organization of neuromuscular blocking drugs. In clinical practice however neuromuscular monitoring and accurate timing are rarely used, and many anaesthesiologists commence laryngoscopy based on clinical assessment.

The aim of the current research is to examine and evaluate the intubating conditions, onset of time, time of action & haemodynamic effects in ASA Gr I/II receiving succinylcholine & rocuronium bromide for quick tracheal intubations.

Materials and Methods

Sixty patients of ASA grade I and II, aged between 20 to 60 years, go through a variety of surgical events were elected for the research. Ethical approval was taken from the institute ethical committee and written informed consent taken from the all participants. Exclusion criteria were: Patients with systemic Disease and those who were not willing to participate in the study.

60 Patients were separated in 2 groups. Group I Patients (n=30) received Inj.Succinylcholine chloride 1.5 mg/kg IV, Group II Patients (n=30) received Inj.Rocuronium Bromide 0.9 mg/kg IV For Tracheal Intubation.

On entrance to the operating room, vital parameters were evaluated and iv admittance was establish. Surface electrodes of neuromuscular monitor were applied to forearm at wrist to stimulate ulnar nerve. Patients were Premedicated with Inj. Glycopyrolate 4 µg/kg IV and Inj. Fentanyl 2 µg/kg IV, 15 min. before induction. After Pre-oxygenation for 3 minutes anesthesia was induced with Inj. Thiopentone 5-7 mg/kg IV till the loss of eye lashes reflex.

Prior to delivery of muscle relaxant the supramaximal stimulus was determined with the help of the peripheral nerve stimulation by observing contraction of adductor pollicis by visual, tactile assessment. After induction, muscle relaxant according to the group given in running IV line. After giving muscle relaxant the single twitch stimulus given all 10 seconds, the time interval from end of injection of muscle relaxant to maximum suppression of control twitch height (we called it onset time) was noted.

An experienced anaesthesiologist, unaware about the muscle relaxant, performed endotracheal intubation. Intubation attempt was tried at 60 seconds following deposition of the muscle relaxant. Intubating conditions were assessed as excellent, good, fair or poor based on jaw relaxation, location and faction of vocal cords and diaphragmatic response to intubation using Copenhagen consensus conference rating scale. If the intubation conditions assessed, not found satisfactory, the intubation stopped and subsequent attempts were made at 30 seconds interval until intubation was achieved with acceptable intubating conditions. Time duration of intubation after muscle relaxant noted at 60 sec, 90 sec, 120 seconds.

Table 1: Copenhagen Consensus Conference Rating Scale Intubating conditions clinically acceptable clinically unacceptable

Variables	Excellent	Good	Poor
1. Laryngoscopy	Easy	Fair	Difficult
2. Vocal Cords			
• Position	Abducted	Intermediate	Closed
• Movements	None	Moving	Closing
3. Reaction to Intubations			
• Movements of Limb	None	Slight	Vigorous
• Coughing	None	Diaphragm	Sustained (>10s)

Anesthesia was then maintained with 50% O_2 + 50% N_2O supplemented with sevoflurane 0.8-1% and rocuronium infusion with controlled ventilation. At impulsive T1 recovery of approximate 25% of control (after intubating dose), rocuronium infusion was started in a dose of 0.3 mg/kg/hr and rate was adjusted to maintain 1 to 2 response to TOF stimuli, if required. Rocuronium infusion was stopped 15-20 minutes prior to probable ending of surgery. At the end of surgery neuromuscular block was assessed by using TOF and when T1 returned to approximately 90% of control patient was reversed by using Inj. Neostigmine 0.05 mg/kg, Inj. Glycopyrolate 0.008 mg/kg. The extubation was performed when the patient was fully awake. The patient was monitored for 24 hrs in post operative period for a residual muscle Paralysis. Any adverse cardiovascular event or allergic reaction to the drug used was noted.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages, means and standard deviations. For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

We have studied 60 ASA Gr. I/II patients undergoing various elective surgeries. The mean onset time for group I was 47.33 ± 9.44 seconds, for group II was 72.67 ± 16.39 seconds. Statistically significant difference was observed between group I and group II (p<0.01). Clinical duration of intubating dose of succinylcholine 1.5 mg/kg was smaller than that of rocuronium 0.9 mg/kg and this difference was statistically significant. The intubating conditions were graded as excellent in 29 (96.7%) and 26 (86.7%) Patients of group I and II correspondingly. The difference was not statistically significant between group I and II (p>0.05). Good intubating conditions were seen in 1 (3.3%) and 4 (13.3%) Patients of group I and 2 respectively (Table 1) but this relationship was not significant.(p>0.05) The alter in Heart Rate and Mean Blood Pressure are described in the charts below. The parameters demonstrate a tendency analogous to each other in both groups (Figs. 1 and 2).

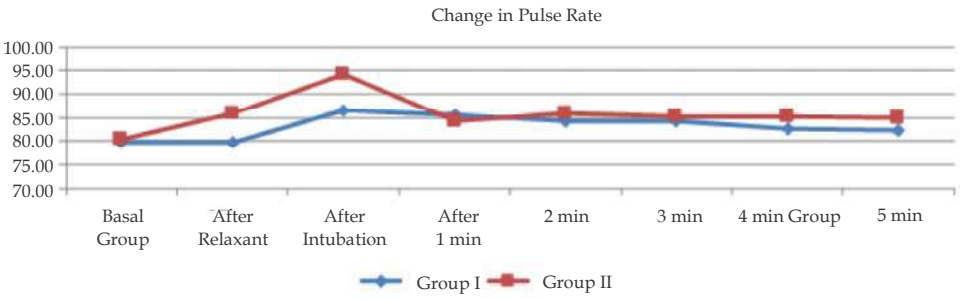

Fig. 1:

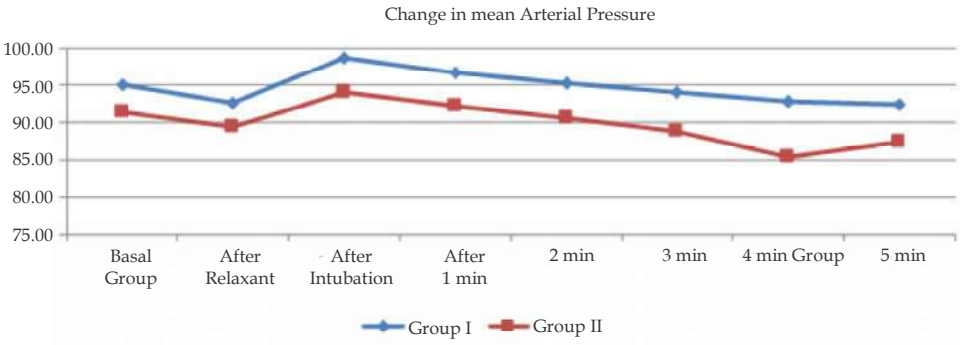

Fig. 2:

Discussion

Traditionally succinylcholine has been the neuromuscular blocking drug of preference for schedule intubations and quick string induction. The smaller onset of action has made it a preferred, except the utilize of succinylcholine can though be connected with many adverse effects as bradycardia, dysrhythmia, hyperkalemia, rise in intra ocular pressure, increase intra cranial pressure, increase intra gastric pressure, post op myalgia. Therefore, a non-depolarising neuromuscular blocker with a quick onset of action, comprising a lesser period of action is desirable.[22,23]

Preliminary studies in animals demonstrated that rocuronium, being a small efficacy compound was connected with a quick onset of outcome contrast to other compounds such as pancronium and vecuronium.[24-27]

Preliminary trials in animal established rocuronium to be 10-20% as powerful as vecuronium and ED doses were set up to be from 0.26 mg/kg to 0.30 mg/kg. Intubating dose of rocuronium utilized in the present study are 0.6 mg/kg and 0.9 mg/kg. Use of superior dose of rocuronium to advance intubating conditions through rapid series intubation and to engrave short the onset time underneath 60 seconds has been advised by a variety of workers but doses superior then 0.6 mg/kg would be connected with a extended duration of action which may be unsuitable in numerous situations.[28]

In the majority studies, a suitable timing of tracheal intubation has been resolute by 3 ways-

1. Clinical Judgement.
2. Neuromuscular monitoring either by Twitch suppression or TOF ratio.
3. Predetermined time after the administration of neuromuscular blocking Agent eg. 60 secs, 90 secs, 120 secs etc.

Method utilizing judgment alone is relatively insensitive. Onset time varies with diverse nerve stimulation rates utilized. Cooper *et al.*[24] establish onset time for rocuronium 0.6 mg/kg as 90 seconds by 0.1 Hz stimulation and 58 seconds using TOF stimulation. On the other hand, a fixed time for tracheal intubation can be utilized. In current study we have utilized all the 3 parameters.[29-30]

Clinical criteria like jaw relaxation, vocal cord movement were evaluated according to Copenhagen consensus conference rating scale. Onset time and duration of action were measured using neuromuscular monitoring. Patients were intubated at predetermined intervals. At the time of intubation clinical conditions were noted. Land and Stovner[25] were most likely the primary to bring in a rating scale as a tool for the evaluation of intubating conditions in which the three main criteria: Jaw relaxation, vocal cords (position and motility) and reaction to intubation were rated by descriptive scores such as excellent, satisfactory and fair.

Findings of current research, concerning intubating conditions show excellent, good and poor conditions accomplished after the administration of rocuronium 0.9 mg/kg, or succinylcholine 1.5 mg/kg subsequent routine induction for voluntary operations. Present research data demonstrated that there is not an considerable dissimilarity in the intubating conditions after the administration of rocuronium 0.9 mg/kg, or succinylcholine 1.5 mg/kg. Parallel findings were establish in the studies done by, Cooper *et al.*[9], Fredrick *et al.*[14], Zhou *et al.*[13], Wierda *et al.*[15] and Weiss JH *et al.*

In a study carry out by Mc Court K C *et al.*[5] the intubating conditions after 0.9 mg/kg rocuronium come out to be nearly indistinguishable to those observed after 1.0 mg/kg succinylcholine i.e. 96% v/s 97% clinically acceptable intubating conditions. Sparr[19] and Crul[16] *et al.*, examined rocuronium's efficay in emergency intubating conditions utilizing it firmly as for the situation for rapid sequence induction in unintended but still optional cases. In those studies, the frequency distribution of 'excellent', 'good', or clinically acceptable intubating conditions, 60 seconds after 0.6 mg/kg or 0.9 mg/kg rocuronium were compared with those observed after 1.0 mg/kg succinylcholine. The findings specify that intubating conditions were more encouraging at 60 sec after administration of rocuronium in the dose of 0.9 mg/kg compared to dose of 0.6 mg/kg in unpremedicated patients. Analogous outcome were observed in further studies of Bhardwaj N. *et al.*[22] In a study by cooper *et al.*[9], they found the onset time of 88.90 seconds and 60.40 seconds for rocuronium 0.6 mg/kg and succinylcholine 1.0 mg/kg respectively. The time to accomplish utmost block of 72 seconds with rocuronium 0.9 mg/kg was significantly longer than a time of about 47 seconds with succinylcholine 1.5 mg/kg in the current study and is in agreement with the result of other studies.[31-32]

There were no significant changes in HR and MAP after the administration of muscle relaxant in each of group in this study. The tiny rise in HR and diminish in MAP after induction and muscle relaxant may be owing to cardiovascular effects of induction dose of thiopentone.

Conclusion

We conclude that rocuronium, a newer nondepolarizing muscle relaxant with a concise onset of action and transitional duration, but devoid of the unfavorable reactions connected with succinylcholine may be a appropriate substitute to succinylcholine for tracheal intubation. Rocuronium in a dose of 0.9 mg/kg may be precious option to succinylcholine for quick tracheal intubation in emergency situations.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1373-1376
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.44

Comparison of Bilateral Superficial Cervical Plexus Block and Incision Line Infiltration for Postoperative Analgesia for Thyroid Surgeries Under General Anesthesia

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Abstract

Introduction: Thyroid surgeries are usually performed under general anesthesia as it involves manipulation of the trachea.Studies comparing bilateral superficial cervical plexus block and incision line infiltration for postoperative analgesia in thyroid surgeries are sparse. Hence, we decided to evaluate the effect of BSCPB and incision line infiltration of local anaesthetic on post-operative VAS and analgesic requirements. *Methods:* After obtaining ethical clearance from the institutional ethical committee, 70 patients were randomly assigned to 2 groups of 35 patients each. Patient's in group were administered BSCPB with 20 ml of 0.125% bupivacaine and 10 ml of normal saline along the line of incision. Patient's in group I were administered BSCPB with 20 ml of normal saline and 10 ml of 0.25% bupivacaine along the line of incision. Intra-operatively requirement for analgesics were recorded. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance was assessed at 5% level of significance. Student t test (two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. *Results:* Mean VAS scores obtained postoperatively to assess postoperative pain were slightly lower statistically significant in the 2nd, 12th and 24th hour. Requirement of inj paracetamol ande inj tramadol was not significantly different between the two groups. Vocal cord movement and the incidence of sore throat was comparable between the two groups. None of the patients in both the two groups had any episode of nausea or vomiting. *Conclusion:* We found that both BSCPB and incision line infiltration are effective methods for providing analgesia for thyroid surgeries. There is no difference between the requirement of analgesics or postoperative pain scores over a 24 hr period.

Keywords: Analgesia; Cervical plexus block; Infiltration; Thyroidectomy

How to cite this article:

Nagaraj AV, Pradeep A Dongare. Comparison of Bilateral Superficial Cervical Plexus Block and Incision Line Infiltration for Postoperative Analgesia for Thyroid Surgeries Under General Anesthesia. Indian J Anesth Analg. 2019;6(4):1373-1376.

Introduction

Thyroid surgeries are usually performed under general anesthesia as it involves manipulation of the trachea. Local anesthesia and regional anesthesia alone for thyroidectomy have been used previously[1,2]. Postoperative analgesia for thyroid surgeries has conventionally been intravenous opioids and acetaminophen. Opioids like fentanyl, morphine provide very good intra-operative and

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Received on 19.04.2019, **Accepted on** 22.05.2019

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postoperative analgesia, but are associated with side effects such as respiratory depression, pruritus, constipation, urinary retention & nausea vomiting[3].

Acetaminophen provides good analgesia, but Sormer JM *et al.*[4] have found that 70% of the patients had an VAS score of more than 40 mm when it was used as sole analgesic. Gozal *et al.* in a study found that the mean pain scores post thyroidectomy was 69 mm and 90% of the patients required opioids postoperatively[5].

Bilateral superficial cervical plexus block has been used for regional anesthesia & analgesia. Andrieu *et al.* conducted a study to assess the analgesic efficacy of bilateral superficial cervical plexus block (BSCPB) under general anesthesia & found that BSCPB improved intraoperative analgesia & reduced analgesic requirements[3] Wound infiltration after thyroid surgeries have also been found to provide adequate analgesia[1-4]. Bagul A *et al.* conducted a study on pre incision infiltration of local anaesthetic on post-op pain & concluded that it provided easy & better analgesic control[6]. Studies comparing bilateral superficial cervical plexus block and incision line infiltration for postoperative analgesia in thyroid surgeries are sparse. Hence, we decided to evaluate the effect of BSCPB and incision line infiltration of local anaesthetic on postoperative VAS and analgesic requirements.

Materials and Methods

After obtaining ethical clearance from the institutional ethical committee, 70 patients were randomly assigned to 2 groups of 35 patients each. It was a prospective randomized double blinded study. The sample size of 35 patients in each group was calculated from a study conducted by Aysenur *et al.*[8], comparing BSCPB and Wound infiltration. In their study they found that the total requirement of postoperative morphine to be 14.3 ± 4.32. Based on this we calculated a sample size of 31 considering a reduction of 20% in the requirement of morphine. We included 35 patients in our study to allow for dropouts. ASA 1 & 2 patients, undergoing thyroid surgeries were included in the study. Patients with known allergy, sensitivity or contraindication to opioids, local anaesthetics or any NSAID, renal or liver failure, history of asthma, history of clotting disorder, retrosternal goiter and previous history of difficult intubations were excluded from the study. After obtaining an informed consent, they were premedicated with tablet ranitidine 150 mg and tablet alprazolam 0.5 mg the previous night & were asked not to consume solid food after 12.00 AM on the day of surgery. Patients were shifted into the operation theatre and a large bore intravenous cannula (18G) were secured.Pulse oximeter, non invasive blood pressure, ECG, end tidal carbon-dioxide, bispectral index monitors were connected. Patients were pre-oxygenated with 100% O_2 for 3 mins. Inj. glycopyrrolate 0.2 mg IV, inj. midazolam 1 mg IV & inj. fentanyl 2 mcg/kg body weight were administered. Patient'swere induced with Inj. Propofol 2 mg/kg body weight and the airway secured with Inj. vecuronium 0.1 mg/kg body weight. Patient's in group were administered BSCPB with 20 ml of 0.125% bupivacaine and 10ml of normal saline along the line of incision. Patient's in group I were administered BSCPB using the landmark technique with 20 ml of normal saline and 10 ml of 0.25% bupivacaine along the line of incision. Intra-operatively requirement for analgesics were recorded. SpO_2, blood pressure, ECG, $EtCO_2$, BIS was recorded every 5 mins. Intra-operatively patients were maintained with oxygen, nitrous oxide, sevoflurane & titrated vecuronium 1 mg intermittent boluses to the BIS of 40-60. After completion of surgery neuromuscular blockade were reversed with Inj. neostigmine 2.5 mg and Inj. glycopyrrolate 0.4 mg IV.

After adequate clinical parameters are achieved, patient'swere extubated.

Postoperatively, patient'swere monitored for 1hr in the recovery & then shifted to the ward. If the patient complained of pain inj. tramadol 50 mg IV bolus were given slowly. SpO_2, NIBP, VAS scores were assessed hourly for the 1st 2 hours & subsequently every 5 hours for the next 10 hours & 6th hourly for the next 12 hours. The time to demand of 1st analgesic (Inj. tramadol 50 mg) were noted. Total dose of tramadol administered during the 1st 24 hours were noted. Adverse effects such asbradycardia, hypotension/hypertension, sedation, nausea/vomiting, desaturation, interscalene block, stellate ganglion block were noted down. The results of the above observations were subjected to statistical analysis. Descriptive and inferential statistical analysis was carried out. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance was assessed at 5% level of significance. Student t test (two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance. Chi-square/

Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher Exact test used when cell samples are very small.

Results

All 70 patients completed the study. There were no dropouts or loss to failure of technique. Demographic parameters, age, height, weight, type of surgery, gender distribution and duration of surgery were comparable between the two groups (Table 1). Intraoperative and postoperative heart rate, systolic blood pressure was comparable between the two groups. The data showed a statistically significant difference in the diastolic blood pressure between the 2 groups at the 75th minute intraoperatively but clinically it was not significant. Postoperative diastolic blood pressure was comparable between the two groups. The mean arterial pressure was also clinically comparable between the two groups eventhough the statistically significant difference was found in the 75th minute. The intraoperative and postoperative saturation was comparable between the two groups. 15 patients in group W received 1000 mg of inj paracetamol in the 24 hr period whereras 20 patients did not receive any paracetamol. In group I, 20 patients received 1000 mg of inj paracetamol in the 24 hr period and 15 patients did not receive any inj paracetamol (p=0.339) (Table 2). Tramadol was the other rescue analgesic used. In group W, 8 patients did not receive any tramadol, 25 patients received 50 mg and 2 patients received 100 mg, whereas in group I, 5 patients did not receive tramadol, 25 patients received 50 mg and 5 patients received 100 mg of tramadol in the first 24 hrs postoperatively (p=0.448) (Table 2). Mean VAS scores obtained postoperatively to assess postoperative pain were slightly lower statistically significant in the 2nd, 12th and 24th hour (Table 3). Duration of postoperative analgesia was comparable between the two groups (Fig. 1). Vocal cord movement and the incidence of sore throat was comparable between the two groups. None of the patients in both the two groups had any episode of nausea or vomiting.

Table 1: Demographic Parameters

Variables	Group W	Group I	p value
Height (cm)	155.66 ± 7.34	157.6 ± 5.73	0.221
Weight (kg)	57.06 ± 6.99	56.89 ± 6.37	0.915
Age (yrs)	38.63 ± 10.51	38.37 ± 9.20	0.941
Female	34 (97.1%)	30 (85.7%)	0.198
Male	1 (2.9%)	5 (14.3%)	
Duration of surgery	90.29 ± 26.84	88.43 ± 24.79	0.765

Table 2: Total dose of PCT/Total dose of tramadol in two groups of patients studied

	Group W (n=35)	Group I (n=35)	p value
Tot dose of PCT			
• 0	18 (51.4%)	13 (37.1%)	0.218
• 1000	15 (42.9%)	20 (57.1%)	
Total dose of tramadol			
• 0	3 (8.6%)	3 (8.6%)	
• 50	22 (62.9%)	17 (48.6%)	0.448
• 100	10 (28.6%)	15 (42.9%)	

Table 3: VAS Score-A Comparison in two groups of patients studied in different time points

VAS Score	Group W	Group I	p value
30 minutes Extubation	2.54 ± 1.20	2.57 ± 1.20	0.921
2 hr	2.14 ± 1.03	2.77 ± 1.17	0.020
4 hr	3.37 ± 1.24	3.63 ± 1.21	0.384
8 hr	3.63 ± 1.46	4.23 ± 1.59	0.105
12 hr	3.23 ± 1.00	3.97 ± 1.54	0.020
24 hr	4.00 ± 1.31	4.91 ± 1.84	0.019

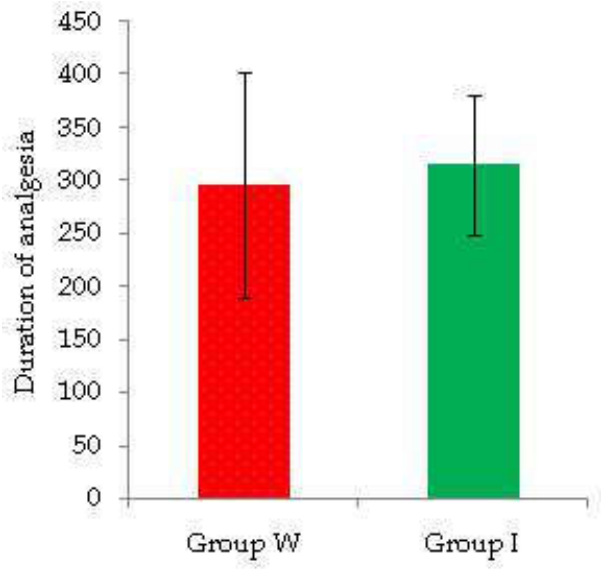

Fig. 1: Showing the duration of Analgesia between the two groups.

Discussion

Bilateral superficial cervical plexus block has been used as an effective analgesic option for patients undergoing thyroidectomies. The technique is simple and has the least amount of complications, without palsy of the phrenic nerve

in comparison to deep cervical plexus block. There have been various studies which have compared the use of BSCPB and other analgesics and have found the reduced requirement of opioids. The post-thyroidectomy pain seems to last for a period of 24 hours after which duration most patients are able to tolerate the pain. In a study conducted by Gozal *et al*.[5] the mean pain score was 6.9 and there was requirement of morphine in the first 24 hrs. Traditionally post-thyroidectomy pain has been treated with opioids or non steroidal anti inflammatory drugs. Supplementation with wound infiltration or BSCPB has been found to reduce the requirement of opioids substantially. It has been hypothesised that this is mainly because of the large superficial component of the surgery. In our study we have tried to compare the effectiveness of incision line infiltration and BSCPB as analgesic modalities. Since both these techniques involve superficial infiltration of the local anaesthetic we have assumed that there is not much of a technical bias. Also, we have used the same cumulative dose of local anaesthetic in our study. Shih *et al.* in their study found that the median time to first analgesic requirement was 360.8 minutes, but they had used 0.5% bupivacaine for administration of the block. Their study was under powered to detect any difference 3 in the incidence of PONV and did not show any increase in intraoperative anaesthetic requirements. In our study we have administered only a single dose of opioid analgesic at the time of induction of anesthesia.

Conclusion

A study conducted by Aysenur *et al*.[8] showed that the duration of analgesia was longer in the wound infiltration group in comparison to the group which received BSCPB but we found no such difference. They even found a statistically significant difference in the requirement of morphine unlike our study. They added adrenaline 1:2,00,000 in order to prolong the duration of action of 0.25% bupivacaine whereas we administered only 0.25% bupivacaine.

Eti *et al*.[9] have found that there is no significant difference in the duration of analgesia or opioid requirement with the two techniques.

In conclusion, we found that both BSCPB and incision line infiltration are effective methods for providing analgesia for thyroid surgeries. There is no difference between the requirement of analgesics or postoperative pain scores over a 24 hr period.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1377-1382
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.45

Crystalloid Preload Versus Crystalloid Co-load During Elective Caesarean Section Under Spinal Anesthesia

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Abstract

Background and Aim: Spinal anesthesia is a preferred technique of anesthesia for pregnant women undergoing caesarean section. The major disadvantage with this technique is maternal hypotension which carries the greatest risk to mother and foetus. This study was designed to analyse various advantages and disadvantages associated with crystalloid preloading and co-loading during spinal anesthesia. *Methods:* Hundred parturients aged 20 to 40 years of physical status ASA I and II undergoing elective caesarean section under SAB were divided into two groups with 50 patients in each group. In Crystalloid Preload group, 15 ml/kg of Ringer lactate (RL) was preloaded 20 minutes before spinal anesthesia. In Co-load group, 15 ml/kg of RL was co-loaded 20 minutes just after lumbar puncture. Vital parameters were noted before and after giving spinal anesthesia. *Results*: The occurence of hypotension (SBP < 100 mmHg) in Group P is 30% and 20% in Group C which is statistically insignificant (p = 0.35). The incidence of nausea is 8% & 6% in group P & group C respectively (p = 0.69). The incidence of vomiting is 2% in group P & 4% in group C (p = 0.55). Mephentermine was used in 19 patients in Group P & 13 patients in Group C which is statistically insignificant. *Conclusion:* Both preloading and co-loading with RL have similar effect on occurence of hypotension in pregnant women receiving spinal anesthesia. Precious time need not be wasted in preloading. Periodic measurement of BP in parturients for early detection of hypotension and administration of vasopressors for maintaining BP close to baseline can ensure better outcome.

Keywords: Subarachnoid block; Hypotension; Crystalloid preloading; Crystalloid co-loading.

How to cite this article:

Naveed Abrar, Ahmedi Fathima, Waseem Anjum. Crystalloid Preload Versus Crystalloid Co-load During Elective Caesarean Section Under Spinal Anesthesia. Indian J Anesth Analg. 2019;6(4):1377-82.

Introduction

Spinal anesthesia has been extensively used for caesarean section because of greater maternal safety and fetal benefits.[1] But the major disadvantage with this technique is hypotension which is more common and profound in pregnant women due to various causes. This hypotension can cause nausea, vomiting, cardiovascular collapse in the mother, along with fetal hypoxia and acidosis due

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Received on 23.04.2019, **Accepted on** 08.06.2019

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to placental hypoperfusion[2]. Therefore, Prevention of hypotension is necessary for better outcome of both mother and the foetus.

Fluid loading before spinal anesthesia which is referred to as preload is followed for prevention of hypotension. It is a common conventional practice in anesthesia. But, preloading of crystalloid is rapidly redistributed, and may induce atrial natriuretic peptide secretion, resulting in peripheral vasodilatation followed by an increased rate of excretion of the preloaded fluid.[2]

Routinely used methods to prevent or treat maternal hypotension include preloading with fluids (colloid or crystalloid), wedge placement to prevent aortocaval compression and administration of vasopressor drugs.

A more logical approach might be to administer fluid at the time that the local anaesthetic block starts to act. This might increase intravascular volume expansion during vasodilatation from the sympathetic blockade and decrease fluid redistribution and excretion.[2]

Fluid administered before induction of spinal anesthesia is referred to as "preloading" and fluid infused at the time of induction is referred to as "co-loading". Various studies suggest fluid infusion to be more effective if delayed until induction of spinal anesthesia and rapidly administered subsequently. Three possible fluid combinations have been compared in various studies: crystalloid versus colloid preloading, crystalloid preloading versus crystalloid co-loading, and colloid preloading versus colloid co-loading.

The present study was planned to analyse various advantages and disadvantages associated with crystalloid preloading and co-loading during spinal anesthesia and the possible relative benefits of each of these methods.

Objective of the study

1. To assess and compare the safety and efficacy of crystalloid preload and crystalloid co-load for prevention of maternal hypotension in parturients undergoing elective caesarean section under spinal anesthesia.
2. To assess various haemodynamic parameters like heart rate, systolic BP, diastolic BP & mean arterial pressure.
3. To assess side-effects like nausea and vomiting in patients with crystalloid preload and co-load.

Materials and Methods

Study Participants and Recruitment

We conducted a prospective double blinded randomized controlled study over a 2 year period between December 2014 to December 2016. Hundred patients aged 20-40 years belonging to ASA I and II undergoing elective caesarean section were randomly distributed for the study into two groups.

Allocation of groups

Based on the study done by Manu Bose *et al*.[5] considering significant Hypotension in Group 1 and Group 2 with odds ratio of 3.25, alpha error 5% and power of 80% the sample size was calculated using OpenEpi software version 2.3.1 which came to be 49 in each group which is rounded to 50 per group.

Group P (preload group) - 15 ml/kg of Ringer lactate was preloaded 20 minutes before commencement of spinal anesthesia.

Group C (co-load group) - 15 ml/kg of Ringer lactate was co-loaded in 20 minutes just after lumbar puncture.

The following patients were excluded from the study

1. Emergency surgeries.
2. ASA grade III and IV.
3. Severe anaemia, coagulation abnormalities and bleeding disorders.
4. Morbid obese patients.
5. Patients with multiple pregnancies.
6. Patients with other co-morbid conditions.
7. Patients with raised ICP.
8. Patients with previous history of surgeries on the spine.
9. Patients with spinal deformities and with history of backache.
10. Patients with active skin lesions over lumbosacral region.

After a detailed pre-anaesthetic examination and obtaining informed consent, all the patients were cannulated with 18G IV cannula and premedicated with Inj Ranitidine 50 mg & Inj. Metoclopramide 10 mg IV one hour before surgery. In operation theatre, Patient was made to lie on operating table with left lateral tilt. Monitors like pulse oximetry, non-invasive blood pressure & electrocardiography were connected. Base line heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure values were recorded.

Under strict aseptic precautions, lumbar puncture was performed in left lateral position by midline approach by using disposable Quincke spinal needle (25 G) at L3-L4 intervertebral space. Patients were monitored continuously using pulse oximeter, non invasive blood pressure, and electrocardiogram. After spinal anesthesia, Oxygen was delivered by facemask.

Parameters observed and recorded

Heart Rate, Systolic BP, Diastolic BP, Mean Arterial Pressure, Respiratory Rate and SpO_2 levels were recorded at 0, 2, 4, 6, 8, 10, 15, 20, 25, 30, 35, 40, 45 minutes till the end of surgery.

Bradycardia was considered when heart rate was less than 50/min (treated with Inj. Atropine).

Hypotension was defined as systolic BP less than 100 mmHg or a 20% fall in BP from the baseline (treated with Inj. Mephentermine).

Ethical Considerations

The study was initiated only after obtaining Institutional Ethical Committee (IEC) approval. Informed written consent was taken from the patient or the patient's next of kin prior to the study.

Statistical analysis

All recorded data were entered using MS Excel software and analysed using SPSS 20 version software for determining the statistical significance.

Results were expressed as mean ± standard deviation. Proportions were compared using Chi-square test.

The student 't' test was used to determine whether there was a statistically significant difference between the study groups.

"*p* " value of >0.05 was considered not to be statistically significant, <0.05 was considered to be statistically significant, a value of <0.01 was considered highly statistically significant & a "*p*" value of <0.001 was considered as extremely statistically significant.

Results

The patient characteristics like age, weight, height, ASA status, and average total fluid administered were comparable among the two groups as shown in Figure 1. There was no statistically significant difference in heart rate & SBP among the groups. The incidence of hypotension (SBP<100) in Group P is 30%, whereas in Group C it is 20% as shown in Figure 2. This difference is statistically insignificant (*p* = 0.35). DBP & MAP are slightly lower in Group P, but without any statistically significant difference. The incidence of nausea is 8% & 6% in preload group & Co-load group respectively (p 0.69) (Table 1). The incidence of vomiting is 2% in preload group & 4% in co-load group (*p* = 0.55) (Table 1). Mephentermine was used in 19 patients in Group P & 13 patients in Group C which is statistically insignificant (Fig. 3).

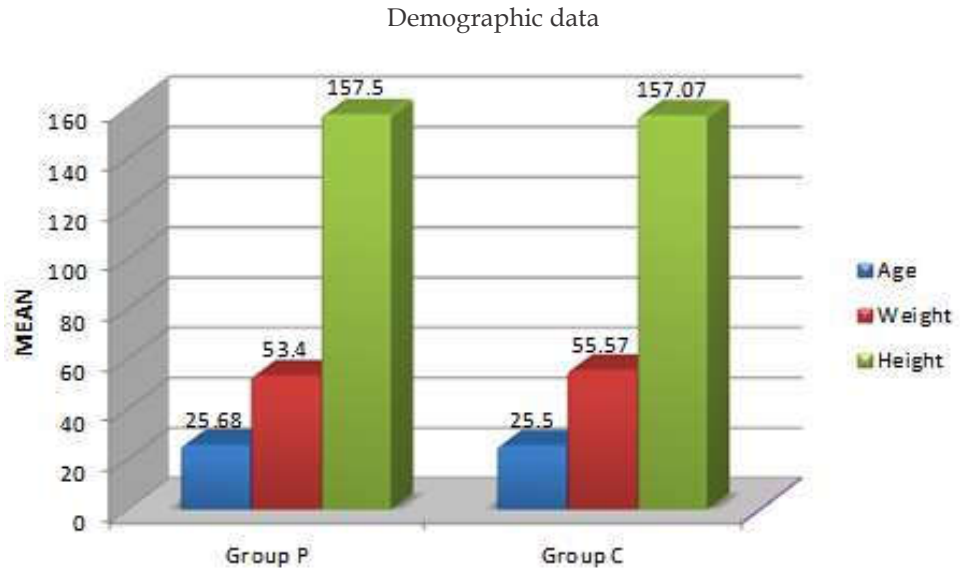

Fig. 1: Comparison of demographic data between the groups.

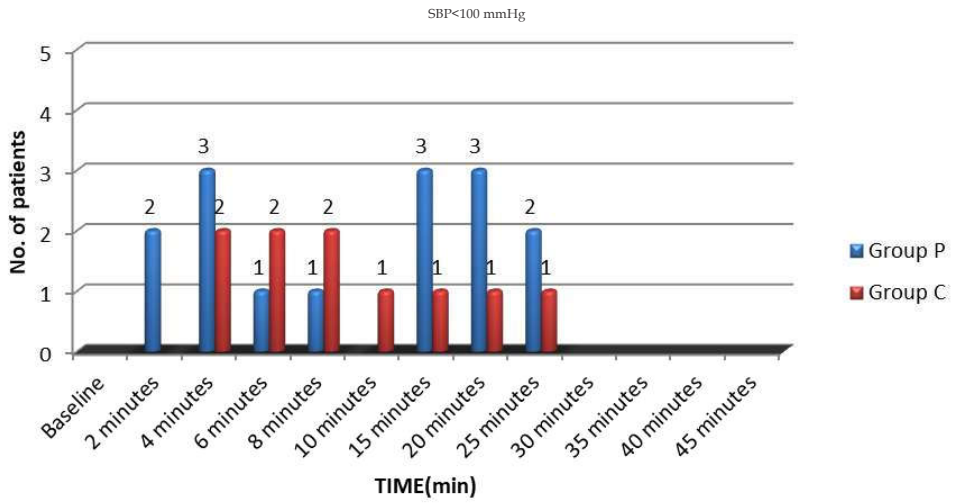

Fig. 2: Number of patients with SBP<100 mmHg in the groups.

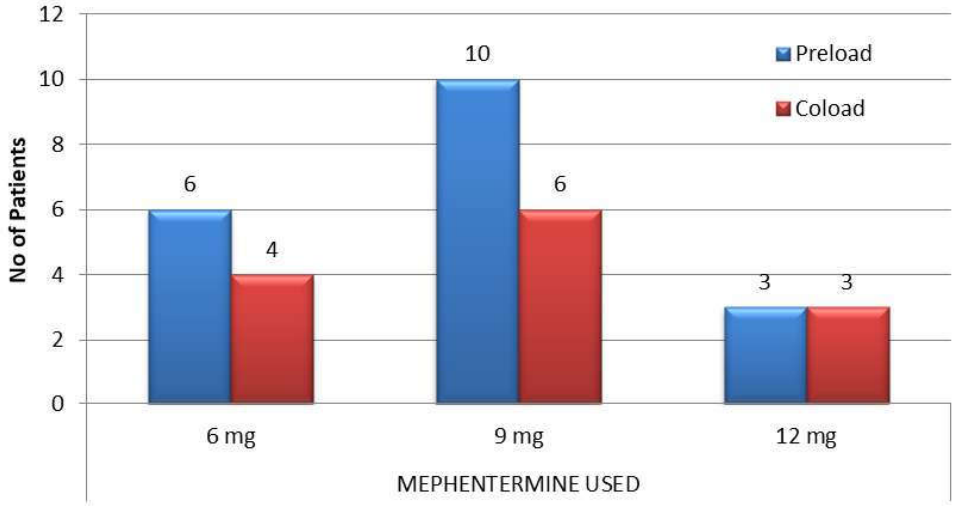

Fig. 3: Comparison of usage of Mephentermine in both the groups.

Table 1: Incidence of Nausea and Vomiting.

Group	NAUSEA		Vomitting		Total
	Yes	No	Yes	No	
Preload	4 (8%)	46 (92%)	01 (2%)	49 (98%)	50
Coload	03 (6%)	47 (93%)	02 (4%)	48 (96%)	50
Total	7	93	03	97	100

Discussion

Spinal anesthesia is a standard technique for pregnant women undergoing elective caesarean section but hypotension remains the main complication with this technique. This hypotension has harmful effects on both mother and foetus, leading to maternal nausea, vomiting and fetal hypoxia.

Hence various measures have been utilized to decrease the incidence of hypotension following spinal anesthesia. One such measure is fluid preloading, but it is associated with several drawbacks. An alternate measure is co-loading during spinal anesthesia. Although, experience with this approach is limited.

Studies done by Parmar *et al.* found that Co-loading with 20 ml/kg of ringer lactate is as

effective as preloading with same volume over 20 minutes in lower limb surgeries and believes that it is not required to spend time to deliver preload and delay surgery for the prevention of SA induced hypotension.[1]

Dyer *et al.* conducted a study and concluded that an equivalent volume of crystalloid administered rapidly, immediately after the performance of spinal anesthesia for elective caesarean section, is associated with a lower pre-delivery requirement for the vasopressor ephedrine than a traditional preload[2].

Khan *et al.* conducted a study and concluded that there is significantly lower incidence of post-spinal hypotension found in co-load group than preload group and parturient in the co-load group required significantly less vasopressor doses than the pre-load group.[3]

Aparna Williams *et al.* conducted a study and concluded that both preloading and co-loading with 15ml/kg of RL solution are ineffective in prevention of spinal induced maternal hypotension.[4]

Bose *et al.* conducted a study concluding that co-loading with 15 ml/kg of Ringer lactate solution is as effective as preloading with same volume over 20 minutes before subarachnoid block to prevent hypotension and bradycardia.[5]

Singh *et al.* conducted a study where he found that fluid preloading had no effect on the incidence of hypotension and bradycardia following spinal anesthesia.[6]

In a study conducted by Tamilselvan *et al.* he found that despite increase in cardiac output following fluid preload, particularly with HES 1.0 L, hypotension still occurred. His data suggested that increase in CO after fluid preload cannot compensate for reductions in arterial blood pressure following spinal anesthesia.[7]

Rout *et al.* conducted a study and found that hypotension associated with spinal anesthesia for caesarean section cannot be eliminated by fluid preloading in the supine wedged patient.[8]

Gunusen *et al.* conducted a study where he found that the frequency of moderate or severe hypotension was lower in the ephedrine group than in the crystalloid or colloid preload group. The incidence of nausea was significantly different between the crystalloid preload and ephedrine group. Umbilical blood gas analysis and Apgar scores were similar in all groups. The combination of an ephedrine infusion at 1.25 mg/min with a crystalloid co-load was more effective than fluid preloading with crystalloid or colloid in the prevention of moderate and severe hypotension.[9]

NganKee *et al.* conducted a study where he found that the combination of high dose phenylephrine infusion and rapid crystalloid co-loading is effective for preventing hypotension during spinal anesthesia for caesarean delivery.[10]

From our study it can be concluded that preloading & co-loading have similar effects on the incidence of hypotension following spinal anesthesia in caesarean section. Therefore, it is preferable to avoid the time delay which occurs in preloading the parturient. Co-loading or Preloading may not be very effective in preventing hypotension, it is sensible to use vasopressors alongside to prevent hypotension & its adverse effects.

Conclusion

From our study it can be inferred that:

1. Both preloading and co-loading with 15 ml/kg of RL solution, have similar effect on the occurence of hypotension in the obstetric population receiving spinal anesthesia.
2. Time delay due to preloading can be avoided as preloading alone is not very effective for the prevention of maternal hypotension.
3. Periodic measurement of the blood pressure in the patients (at 1 min intervals) for early detection of hypotension and administration of vasopressors for maintaining the maternal blood pressure close to the baseline can ensure better outcome.

Conflict of Interest: None

Financial Support and Sponsorship: Nil

Acknowledgement: Nil

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1383-1386
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.46

Intraarticular Ozone Therapy for Knee Osteoarthritis: A Single Centre Experience

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Abstract

Introduction: Osteoarthritis of the knee joint is a widely prevalent problem and leads to decrease in physical function through pain and reduced range of motion. Since there is no cure for the disease, the main aim of treatment if to reduce pain and preserve function. While early osteoarthritis is treated with exercise and lifestyle modifications only, measures like intra-articular ozone administration and platelet rich plasma therapy reduce pain, restore function and enable patients to exercise more effectively. We studied the effectiveness of ozone administration in patients with knee osteoarthritis. *Materials and Methods:* Thirty patients with Kellgren-Lawrence grade 2-3 osteoarthritis of both knees were recruited and administered intra-articular ozone. Pain and patient global assessment scores were recorded on the visual analogue scale at baseline and at 6 months. *Results:* All patients experienced improvement with an improvement of mean pain VAS from 6.9 at baseline to 2.9 at 6 months. Patient global assessment also improved from 5.1 to 1.3. *Conclusion:* Intra-articular ozone administration is effective in reducing pain in patients with osteoarthritis of the knees.

Keywords: Knee; Osteoarthritis; Ozone; Pain.

How to cite this article:

Neha Goyal. Intraarticular Ozone Therapy for Knee Osteoarthritis: A Single Centre Experience. Indian J Anesth Analg. 2019;6(4):1383-1386.

Introduction

Osteoarthritis (OA) of the knee is a commonly prevalent condition that causes both pain and functional limitation. Long known to be caused by mechanical stress only, chemical factors like oxidative stress have come to be recognised as contributing factors in the causation of OA. Female gender, advancing age and obesity are the frequently encountered associates of OA of knees.[1] The diagnosis of OA remains largely clinical.[2,3] The common complaints by the patients are pain, stiffness, swelling and difficulty in using stairs and getting up from sitting position. Tenderness and joint crepitus may be appreciated on clinical examination. Significant swelling may be seen in wet OA where there is effusion of the joint and limb deformity may be seen in advanced cases. A thorough history and clinical examination are usually sufficient to ascertain the diagnosis. A further roentgenogram helps to stage the OA of

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Received on 06.05.2019, **Accepted on** 22.05.2019

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knees and help decide the further course of action. In absence of a cure, the main aim of management of the condition is to alleviate pain and restore function. While exercise and lifestyle modification remain the mainstay, other modalities like pain relieving medications, interventional procedures like ozone administration, platelet rich plasma therapy, radiofrequency ablation and surgeries like proximal fibular osteotomy and total knee replacement have been used.[4,5]

Ozone has for long been used in dentistry and cosmetology because of its anti-inflammatory and anti-oxidant properties. US-FDA approved the use of intra-articular ozone therapy (a mixture of oxygen and ozone) for the treatment of knee osteoarthritis in 1997.[6] Besides, ozone discectomy has been used for herniated discs and ozone has also been used in tears of the meniscus and inflammation of the plantar fascia.

The exact mechanism of the anti-inflammatory properties of ozone has not been elucidated but it has been observed that ozone administration results in reduced tumour necrosis factor (TNF) concentrations.[4,5,7] The safety profile of ozone has been a major reason of its popularity.[4,8]

Here we study the effect of administration of intra-genicular ozone in 30 patients with osteoarthritis of the knee.

Materials and Methods

OA of knees was staged by Kellgren-Lawrence radiologic scoring (KLS) (score from grade 0 to 4).[9] Thirty consecutive patients having bilateral knee OA grade 2-3 and who underwent intra-articular ozone administration in both knees were included in the study. Patients above the age of 70 years and those with other physical comorbidities which could interfere with assessment of function (e.g. hip OA, inflammatory polyarthritis, spondyloarthritis, paraplegia/paresis etc.) were excluded. Patients with history of trauma, surgery, lower limb deformities, and abnormal haematologic and coagulation parameters were also excluded.

Using medical grade ozone generator machine, 20 cc of 30 mcg/mL ozone-oxygen mixture was injected in both the knee joints. Administration of this mixture was preceded by injection of 2 mL of 2% lignocaine solution. Taking all sterile precautions, patient was made to lie in supine position and knee was flexed to 90 degrees. A 22-gauge needle was inserted through the antero-medial approach and lignocaine was injected. The needle was secured by a stop cock in the meantime. 10 ml of 30 mcg/mL ozone was then inserted after removing the stop cock. The procedure was performed by a qualified anaesthesiologist wit special training in pain medicine. Patient was advised relative rest for 72 hours after ozone administration. All the patients were taught and advised to undertake regular home based quadriceps strengthening exercise after 72 hours of ozone administration.

Patients were evaluated at baseline and after 6 months of the procedure. Pain was assessed on a visual analogue scale (VAS) (scored from 0 to 10, with 0 being no pain and 10 being the worst pain ever).[10] Patient's global assessment was also recorded from 0 to 10 on the visual analogue scale. The data was put through student t test.

Results

Thirty patients with mean age 64.3 ± 3.4 (age range 58 to 69) years, KLS grade 2-3 osteoarthritis of the knee on the roentgenograms were included in the study. None of patients has any serious intra-procedure or post-procedure adverse events. Three patients had stiffness in the joint on the morning after the procedure which lasted 12-36 hours.

The mean pain VAS score at baseline was 6.9 ± 1.13 (range 5 to 9) and the mean patient global assessment on VAS was 5.1 ± 1.92 (range 2 to 8).

The mean pain score reduced from 6.9 at baseline to 2.9 at 6 months after the procedure. All the 30 patients had a minimum of 3-point improvement in pain on the VAS. The mean patient global assessment score improved from 5.1 at baseline to 1.3 at 6 months after administration of ozone. All the 30 patients had a minimum of 4-point improvement on the VAS.

The comparison of pain and global assessment scores at baseline and at 6 months is given in table 1.

Table 1: Comparison of VAS scores at baseline and at 6 months

	VAS score at baseline	VAS score at 6 months	
Pain	6.9 ± 1.13	2.9 ± 1.64	p<0.01
Patient Global Assessment	5.1 ± 1.92	1.3 ± 1.27	p<0.01

Discussion

Osteoarthritis of the knee can be a crippling disease. In absence of a cure for the disease, the main aim of treatment is to reduce pain and preserve joint

function. Ozone injection into the joint has been used for the treatment of knee OA. Ozone leads to production of reactive oxygen species and lipid oxidation products.[8,11] It thus reduces inflammation and improves function through repair and vascularization. There is downregulation of proteolytic enzymes and proinflammatory. Articular cartilage and matrix may be formed through secondary proliferation of fibroblasts and chondrocytes.[4]

The primary objective of this study was to assess the efficacy of intra-articular ozone administration in alleviating pain in patients with osteoarthritis of the knee. Multiple studies have documented the beneficial effects of intra-articular ozone administration in patients with osteoarthritis of the knees over a short term.[12] This study assesses the effect of this procedure on knee pain over an intermediate period. While most of the studies included administration of ozone unilaterally, we have included patients who underwent bilateral intra-articular ozone administration.

The intermediate to longer term benefits of ozone administration may be derived from post ozone administration downregulation of cytokines which are responsible for sustained inflammation and progression of structural damage as noted in certain studies.[4]

One study demonstrated intra-articular ozone to be significantly superior to intra-articular methylprednisolone in patients with knee OA.[11] Jesus *et al.* and Hashemi *et al.* compared intra-articular ozone with sterile air and found ozone to be effective at 4 months.[13,14] Ozone was also found to be effective in post-arthroscopic surgery patients of knee OA.[15]

In our study, patients had significant improvement at 6 months after intra-articular ozone administration. Regular quadriceps strengthening exercise is a contributory factor for maintaining function and is likely to have accounted for better patient global assessment scores at 6 months.

Conclusion

Intra-articular ozone administration is an effective tool for reducing pain and improving function in patients with knee osteoarthritis. Regular quadriceps strengthening exercise after the procedure can prolong the effect of ozone.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1387-1397
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.47

Comparison Between Intravenous Fentanyl and Dexmedetomidine to Decrease Sevoflurane – Induced Agitation in Paediatric Patients Undergoing Lower Abdominal Surgery: A Prospective Randomized Observational Study

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Abstract

Introduction: Sevoflurane is widely used in paediatric anesthesia. It has a rapid induction and rapid recovery profile. It is pleasant, non-pungent and non irritant to the respiratory airways. Emergence agitation (EA) in children early after sevoflurane anesthesia is a common postoperative problem, with incidence up to 80%. Fentanyl and α_2-agonists like Dexmedetomidine have been shown to be effective measures in decreasing the incidence of EA. *Aims and Objectives:* To compare the incidence of intravenous dexmedetomidine and fentanyl to decrease the post operative agitation after sevoflurane anesthesia in paediatric patients undergoing lower abdominal surgery. *Material and methods:* Sixty ASA physical status I and II children aged 2–9 years were included in this study. After inhalation induction with sevoflurane, patients were randomly assigned to receive either Saline (group N, n=20), fentanyl 1 mic/kg IV (group F, n=20) or dexmedetomidine 0.3 mic/kg IV (group D, n=20) 10 minutes before discontinuation of anesthesia. *Results:* The incidence of agitation was significantly higher in group N compared with other two groups, the incidence of agitation was 60% in Group N, 45% in Group F and 20% in Group D. There was no significant difference ($p > 0.05$) between the three groups in modified Aldrete recovery scores, but emergence time was more in dexmedetomidine when compared with other groups which was statistically significant. *Conclusion:* Fentanyl 1 mic/kg iv or dexmedetomidine 0.3 mic/kg iv that is administered 10 minutes before the termination of anesthesia reduces the postoperative agitation in children.

Keywords: Agitation; Dexmedetomidine; Fentanyl; Sevoflurane.

How to cite this article:

Puneeth J, Mahantesh S Mudakanagoudar. Comparison Between Intravenous Fentanyl and Dexmedetomidine to Decrease Sevoflurane – Induced Agitation in Paediatric Patients Undergoing Lower Abdominal Surgery: A Prospective Randomized Observational Study. Indian J Anesth Analg. 2019;6(4):1387-1397.

Introduction

Sevoflurane is an inhalational agent of choice in paediatric anesthesia practice since many years. The relative lack of airway irritation, non-pungency, low blood gas partition coefficient with rapid induction and rapid recovery as well as limited cardio-respiratory depression made it a suitable inhalational agent in children.

Emergence agitation (EA) following general anesthesia in children is an evolving problem since sevoflurane has become a popular anesthetic for pediatric anesthesia.[1] Although EA is self-limited and occurs within the first 30-minutes of recovery

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Received on 24.05.2019, **Accepted on** 11.07.2019

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in Post Anesthesia Care Unit (PACU), but it can last up to 2 days and end up in causing physical injuries to the child and mental trauma to parents.[2]

Apart from sevoflurane several other factors can lead to EA such as rapid awakening in an unfamiliar environment, painful events like surgical wounds, agitation on induction, airway obstructions, environmental disturbances, the duration of anesthesia, hyperthermia, hypothermia, type and site of operation, premedication.[2] Among these postoperative pain and inhalation induced agitation are commonly seen in our practice. Various medications and procedures like caudal block will combat postoperative pain induced agitation.

However, the exact etiology of agitation after Sevoflurane anesthesia is still not known. There being a possibility that it exerts an irritant effect on the central nervous system.[3]

Various medications, including opioids, sedatives and alpha-2 agonists have been tried with various success.

Fentanyl is a potent opioid receptor agonist with sedative and analgesic effects. It is routinely used in the practice of pediatric perioperative medicine. Some clinical trials have shown that fentanyl can prevent EA under sevoflurane anesthesia in children.[4]

Dexmedetomidine is the latest addition to the Group of α_2-adrenergic receptor agonist approved by FDA in 1999 for use in humans for analgesia and sedation. It is a highly selective adrenergic receptor agonist, exhibits sympatholytic, sedative, and analgesic effects.

Dexmedetomidine has several advantages over traditional medications such as narcotics and benzodiazepines. Owing to its sedative and analgesic action, no respiratory depression, better haemodynamic stability, minimal or no significant adverse effect profile has lead to its use in paediatric anesthesia. It can be used as premedication, sedative for invasive procedures, anti-shivering agent and reduction of emergence agitation.

We decided to undertake this study to compare the effect of the selective α_2-adrenergic receptor agonist Dexmedetomidine with Fentanyl to reduce emergence agitation and also observe the recovery characteristics after Sevoflurane anesthesia in children aged 3-10 years undergoing lower abdominal surgeries

Materials and Methods

Clearance for this prospective randomized double blind study was obtained from the institutional ethical committee. After thorough preoperative evaluation, written and informed consent from the patient's parent/guardian was taken. Nil by mouth status of the child was confirmed and Midazolam 0.5 mg/kg orally as a premedication was given half an hour before surgery.

The patients were randomly allocated into either of the three groups:-

1. Group N: to receive normal saline 10 ml i.v. 10 minutes before the end of anesthesia, (n=20)
2. Group F: to receive Fentanyl 1 mcg/kg diluted to 10 ml of normal saline i.v. 10 minutes before the end of anesthesia, (n=20)
3. Group D: to receive Dexmedetomidine 0.3 mcg/kg diluted to 10 ml of normal saline i.v. 10 minutes before the end of anesthesia, (n=20) by using envelope method.

In the operation theatre, standard monitoring with electrocardiogram, noninvasive oscillometric blood pressure (NIBP) and pulse oximetry was initiated and baseline values were recorded and continuous monitoring was done during the whole study. Patients were induced with inhalation induction via transparent face mask after saturating the breathing system (Jackson-Rees modification of Ayer's t-piece) with a mixture of sevoflurane 8% with N_2O 60% in O_2. After loss of consciousness, intravenous line was inserted and when adequate depth of anesthesia was reached, a Proseal laryngeal mask airway (PLMA) of appropriate size for the age and weight of the child was placed and patient was allowed to breath spontaneously. Ventilation was assisted if the patient becomes apneic or if the end-tidal carbon dioxide increased to ≥55 mmHg.

After PLMA insertion and before the start of surgery, Caudal block with 1.0 ml/kg of 0.25% bupivacaine was performed in all patients. Failure of caudal block was defined as increase in heart rate and or mean arterial blood pressure (MAP) > 10% than pre-incisional value at the start of surgery. Sevoflurane was reduced to 2% with 60% N_20 in O_2. The anesthetic agents were delivered in a concentration that maintained a stable heart rate, blood pressure and respiratory rate (base line ± 20%).

Ten minutes before the end of anesthesia, Group N: received Normal saline 10 ml i.v., Group F: received Fentanyl 1 mcg/kg diluted in 10 ml of normal saline i.v., Group D: received Dexmedetomidine 0.3 mcg/kg diluted in 10 ml of normal saline i.v., slowly over ten minutes.

At the end of the procedure anesthetic gases were discontinued and maintained on O_2 100% > 5L/min. PLMA was removed when patient showed adequate recovery from anesthesia. Then the patient was transferred to the post anesthesia care unit (PACU) for monitoring of vital signs and scoring of various scales used in our study at regular intervals.

The following parameters were recorded: duration of anesthesia (time from the start of induction till discontinuation of anesthetics) in min., duration of surgery (from skin incision to final skin sutures) in min., time of emergence (time from the discontinuation of anesthesia till first response/eye opening to command/stimuli) in min., Emergence scoring was done using watcha scale scoring (Table 1). Paediatric Anesthesia Emergence Delirium Score (PAEDS) and Objective pain scale (Table 2 & 3) was used to differentiate delirium from pain behavior and vital parameters like heart rate, mean arterial pressure, respiratory rate, end tidal carbon dioxide, oxygen saturation and MAC of sevoflurane were monitored.

In PACU parents/gaurdian were allowed to be at the child's bed side immediately upon admission along with one trained nurse and the junior resident, to stay with the patient until discharge to the ward and recorded each score of different scales at regular intervals.

Patients were kept in PACU until they attained an Aldrete score of 9 (Table 4) or more and free from vomiting. The time to meet these criteria was also recorded as recovery time in minutes. Patients who had vomiting were given ondansetron 0.1 mg/kg i.v. Patients who had pain were given morphine 0.1 mg/kg. i.v.

Statistical Analysis

All the data obtained were presented in mean ± SD form and analysis of their significance was done by using the p values obtained through Student t- test. The ANOVA test (analysis of variance) was used for continuous variables and chi-square test for discrete variables. The software used for statistics is SPSS 20.00. $p < 0.05$ was considered to be statistically significant.

Results

Demographic data (gender, age, weight) and type of surgery were comparable in all the groups Tables 5-7. Duration of Anesthesia and duration of surgery were also comparable in all the three groups Table 8. The duration of emergence was more in Dexmedetomidine group when compared with other two groups Figure 1. There was no significant difference in heart rate and mean arterial pressure in between each groups. But there was a decrease in heart rate and mean arterial pressure in Dexmedetomidine group when compared with other two groups after administration of the study drug but was not significant statistically Figures 2 and 3.

Table 1: The Watcha scale scoring.

Behaviour	Score
Asleep	0
Calm	1
Crying, but can be consoled	2
Crying, but cannot be consoled	3
Agitated and thrashing around	4

Scores of zero, one and two were considered as absence of EA, and scores of three and four as presence of EA.

Table 2: The Paediatric Anesthesia Emergence Delirium (PAED) Scale scoring.

Behaviour	Not at all	Just a little	Quite a bit	Very much	Extremely
Makes eye contact with caregiver	4	3	2	1	0
Actions are purposeful	4	3	2	1	0
Aware of surroundings	4	3	2	1	0
Restless	0	1	2	3	4
Inconsolable	0	1	2	3	4

The scores are summed and the total correlates positively with the degree of ED.

Figure 4 shows the number and percentage of patients in whom agitation was present according to Watcha Scale. The incidence of agitation was 60% in Group N, 45% in Group F and 20% in Group D on arrival to PACU which was significant.The number of patients who had agitation was comparable by the end of 20 minutes in all the three groups.

According to the PAED scale scoring, the scores were higher in Group N when compared with Group F, and group F scores was higher when compared with Group D on arrival and gradually decreased over time Table 9. Hence in our study we found that the degree of agitation was less in Group D when compared with other two groups and that in Group F was less when compared with Group N.

According to the Objective Pain Scale scoring Table 10, the scores were higher in Group N when compared with Group F, and Group F scores was higher when compared with Group D on arrival and gradually decreased over time. This showed that the groups which were having higher degree of agitation also had a higher Objective Pain Scale score.The difference in duration of recovery time in three groups was not significant Table 11.

Table 3: Objective Pain scale scoring.

Parameter	Finding	Points
Systolic blood pressure	Increase < 20% of preoperative blood pressure	0
	Increase 20-30% of preoperative blood pressure	1
	Increase > 30% of preoperative blood pressure	2
Crying	Not crying	0
	Responds to age appropriate nurturing (tender loving care)	1
	Does not respond to nurturing	2
Movements	No movements relaxed	0
	Restless moving about in bed constantly	1
	Thrashing (moving wildly) or rigid (stiff)	2
Agitation	Asleep or calm	0
	Can be comforted to lessent the agitation (mild)	1
	Cannot be comforted (hysterical)	2
Complains of pain	Asleep or states no pain	0
	Cannot localize pain	1
	Localizes pain	2

Total score = SUM (points for all scorable parameters)

Interpretation

- Minimum Score: 0
- Maximum Score: 10
- Maximum Score if too young to complain of pain 8.
- The higher the score the greater the degree of pain.

Table 4: Aldrete Recovery Scoring.

Criteria	Points
Color	
Pink	2
Pale or dusky	1
Cyanotic	0
Respiration	
Can breathe deeply and cough	2
Shallow but adequate exchange	1
Apnea or obstruction	0

Circulation	
BP +/- 20% of normal	2
BP +/- 20-50% of normal	1
BP > 50% of normal	0
Consciousness	
Awake, alert and oriented	2
Arousable but readily drifts back to sleep	1
No response	0
Activity	
Moves all extremities	2
Moves two extremities	1
No movement	0

Patients were kept in PACU until they attained an Aldrete score of ≥ 9.

Table 5: Distribution of male and female in three study groups (Dexmedetomidine, Fentanyl and Normal saline).

Sex	Dexmedetomidine	%	Fentanyl	%	Normal saline	%	Total
Male	19	95.00	19	95.00	18	90.00	56
Female	1	5.00	1	5.00	2	10.00	4
Total	20	100.00	20	100.00	20	100.00	60

The difference in distribution of male and female samples in three groups was not significant (Chi-square=0.5357) ((*p* value=0.765017).

Table 6: Comparison of three study groups (Dexmedetomidine, Fentanyl and Normal saline) with respect to mean age and weight by one way ANOVA.

Groups	Age		Weight		Gender
	Mean	SD	Mean	SD	
Dexmedetomidine	4.10	2.59	13.35	6.49	
Fentanyl	3.95	2.33	13.40	5.54	
Normal saline	4.00	2.18	13.75	5.10	
F-value	0.0207		0.0288		
P-value	0.9795		0.9716		

The difference in distribution of samples by age and weight in three groups was not significant (P value=0.9795 and 0.9716 respectively).

Table 7: Comparison of three study groups (Dexmedetomidine, Fentanyl and Normal saline) with respect to type of surgery.

Types of surgery	Dexmedetomidine	%	Fentanyl	%	Normal saline	%	Total
Circumcision	10	50.00	12	60.00	11	55.00	33
Herniotomy	8	40.00	6	30.00	8	40.00	22
Orchidopexy	2	10.00	2	10.00	1	5.00	5
Total	20	100.00	20	100.00	20	100.00	60
Chi-square=0.4820, p=0.9740							

The difference in distribution of samples by types of surgery in three groups was not significant (Chi-square=0.4820) (*p* value=0.9740).

Table 8: Comparison of three study groups (Dexmedetomidine, Fentanyl and Normal saline) with respect to mean Anesthesia and Surgery duration by one way ANOVA.

Groups	Anesthesia duration		Surgery duration	
	Mean	SD	Mean	SD
Dexmedetomidine	56.90	8.87	31.25	8.72
Fentanyl	54.90	8.73	30.50	8.72
Normal saline	54.55	9.20	31.00	8.97
F-value	0.4027		0.0376	
P-value	0.6704		0.9631	

The difference in duration of anesthesia and surgery in three groups was not significant (p value=0.6704 and 0.9631 respectively).

*p<0.05 indicates significant at 5% level.

Table 9: Comparison of three study groups (Dexmedetomidine, Fentanyl and Normal saline) with PAED scale scores at different intervals by one way ANOVA test.

Time points	Summary	Dexmedetomidine	Fentanyl	Normal saline	Total	F-value	p-value
On arrival	Mean	9.60	12.35	13.80*	11.92	4.4245	0.0164*
	SD	3.98	4.86*	4.72	4.79		
15 min	Mean	8.00	9.70	10.40	9.37	4.2668	0.0188*
	SD	2.45	2.81	2.74	2.82		
30 min	Mean	3.90	4.15	4.35	4.13	0.9839	0.3801
	SD	0.79	1.09	1.14	1.02		
45 min	Mean	3.00	3.00	3.00	3.00	0.0000	1.0000
	SD	0.00	0.00	0.00	0.00		
60 min	Mean	2.20	2.45	2.60	2.42	3.5946	0.0339*
	SD	0.41	0.51	0.50	0.50		

*(p < 0.05 indicates significant at 5% level.

Table 10: Comparison of three study groups (Dexmedetomidine, Fentanyl and Normal saline) with OP scale scores at different intervals by one way ANOVA test.

Time points	Summary	Dexmedetomidine	Fentanyl	Normal saline	Total	F-value	p-value
On arrival	Mean	2.75*	4.00	4.50	3.75	5.9091	0.0047*
	SD	1.86	1.69*	1.40	1.79		
15 min	Mean	2.65*	3.75	4.15	3.52	5.5090	0.0065*
	SD	1.73	1.48	1.18	1.59		
30 min	Mean	0.15	0.35	0.45	0.32	2.2075	0.1193
	SD	0.37	0.49	0.51	0.47		
45 min	Mean	0.00	0.00	0.00	0.00	0.0000	1.0000
	SD	0.00	0.00	0.00	0.00		
60 min	Mean	0.00	0.00	0.00	0.00	0.0000	1.0000
	SD	0.00	0.00	0.00	0.00		

*p < 0.05 indicates significant at 5% level.

Table 11: Comparison of three study groups (Dexmedetomidine, Fentanyl and Normal saline) with mean recovery time

Groups	Mean	SD
Dexmedetomidine	57.0	10.8
Fentanyl	61.0	11.7
Normal saline	66.3	14.1
F-value	1.8561	
p-value	0.1681	

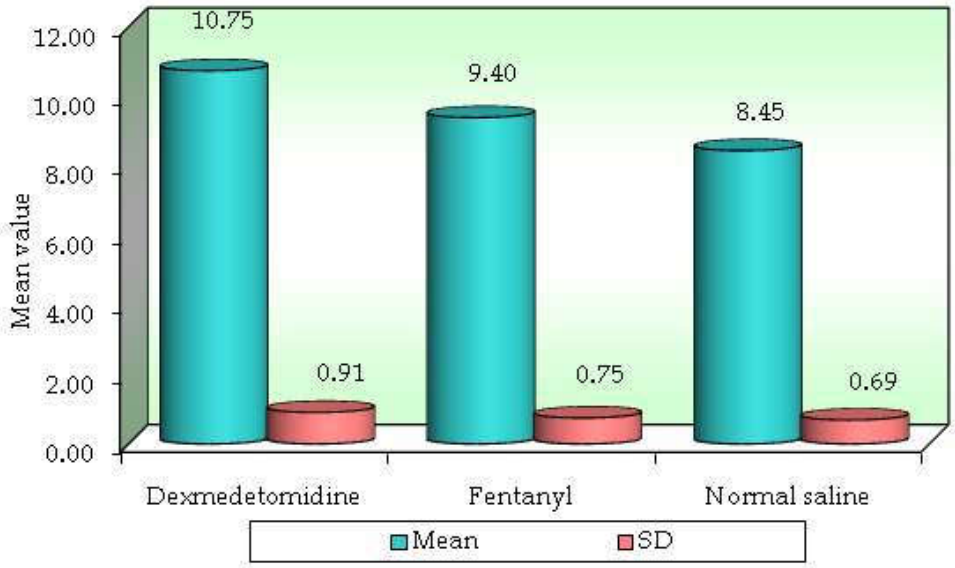

Fig. 1: Comparison of three study groups (Dexmedetomidine, Fentanyl and Normal saline) with respect to mean emergency time.

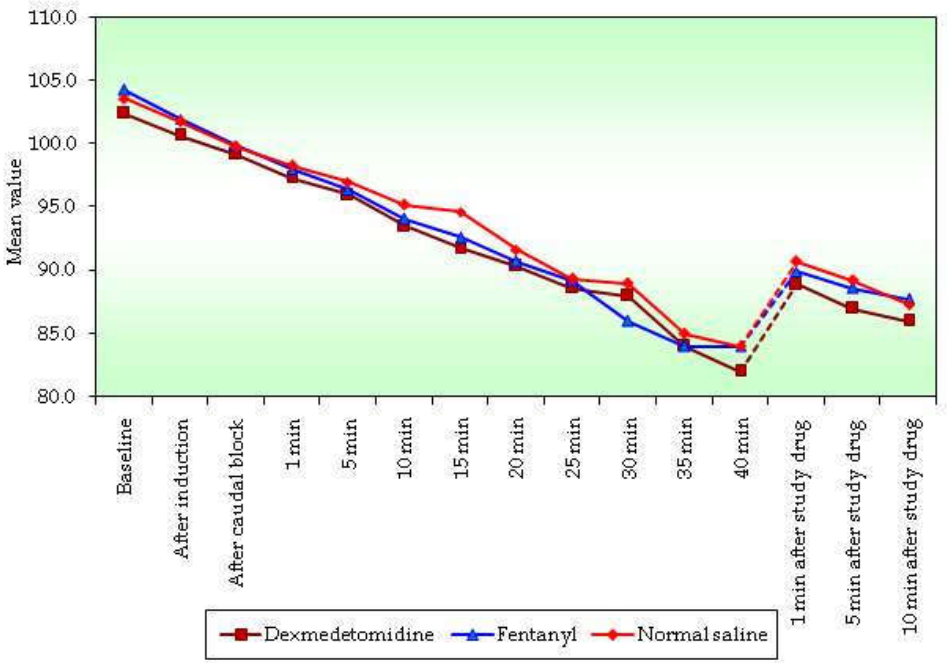

Fig. 2: Comparison of three study groups (Dexmedetomidine, Fentanyl and Normal saline) with respect to heart rate at different intervals.

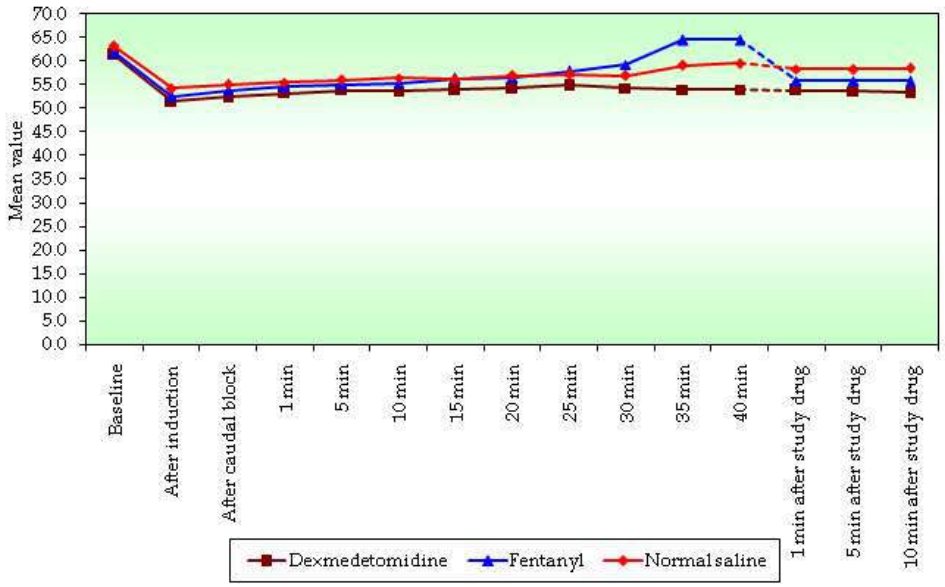

Fig. 3: Comparison of three study groups (Dexmedetomidine, Fentanyl and Normal saline) with respect to mean arterial pressure at different intervals.

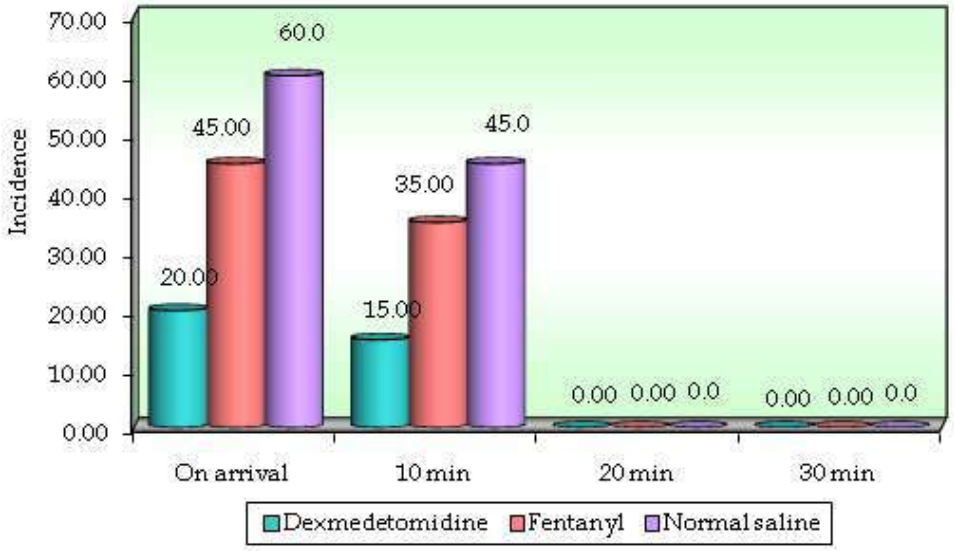

Fig. 4: Comparison of three study groups (Dexmedetomidine, Fentanyl and Normal saline) with Watcha scale at different intervals for presence of agitation.

Discussion

Emergence Agitation is identified as one of the significant problems in children recovering from anesthesia. It usually occurs in the first 30 minutes post operatively but may last upto two days.[2]

EA can be dangerous to patients, particularly to young children. Patients suffering from emergence agitation may harm themselves and dislodge the drains, catheters or intravenous cannulae which affect the result of surgery. They may inflict a bodily injury on the nursing staff or cause a paranoiac accident, which makes the management and monitoring of patients at the post anesthesia care unit difficult. This may lead to an increased length of stay in the post anesthesia care unit, resulting in patient discomfort and increased perioperative costs.

In our study, we chose Sevoflurane as the inhalational anaesthetic agent to observe the incidence of EA. Kulka *et al.*[1] stated that Sevoflurane is associated with higher incidence of emergence

agitation in upto 80% in children. Singh *et al.*[5] found a higher incidence of emergence agitation associated with Sevoflurane (40%) than with Desflurane (26%) and Isoflurane (18%) in children. Two unique intrinsic characteristics of Sevoflurane were speculated by Holzki *et al.*[5] that might account for the development of emergence agitation.

First, this anaesthetic agent exerts an irritating side effect on the central nervous system. Second, epileptiform activity has been reported during the use of Sevoflurane anesthesia. Agitation may be related to the similar CNS effects of these anesthetics, which may affect brain activity by interfering with the balance between neuronal synaptic inhibition and excitation in the CNS.

Davis *et al.*[6] suggested that inadequate pain relief may be the cause of agitation, particularly after short surgical procedures for which peak effects of analgesics may be delayed until the child is completely awake. Postoperative pain has been the next probable factor when assessing a child's behaviour upon emergence because of the overlapping clinical picture with emergence agitation. The children in all the three groups in our study were given Caudal block with 1.0 ml/kg of 0.25% bupivacaine after PLMA insertion and before the start of surgery to exclude pain as the confounding factor.

Intense preoperative anxiety, both in children and their parents has also been associated with an increased likelihood of restless recovery and agitation from anesthesia. The children in all the three groups in our study were premedicated with midazolam 0.5 mg/kg orally half an hour before surgery. Kain *et al.*[7] determined the relationship between preoperative anxiety, ED, and postoperative maladaptive behaviours. He found a higher incidence in children who were not premeditated and underwent surgery and general anesthesia using Sevoflurane.

However, the aetiology of Sevoflurane induced EA is still unknown and a clear-cut strategy for its prevention has not been developed.

The decision of whether to treat emergence agitation with additional pharmacological medication depends upon the severity and duration of symptoms.

Various pharmacological agents are used to combat sevoflurane induced agitation in Paediatric age group. Use of opioids like Fentanyl, which serve as sedatives and analgesics have been tried and used widely for control of agitation.[8,9,10] Use of analgesics like Ketorolac, paracetamol have been used to decrease emergence agitation.[11] Use of alpha 2 adrenoreceptor agonists like Clonidine and Dexmedetomidine have been recommended to elimininate pain as a potential source of agitation.[12,13] Use of benzodiazepines like Midazolam, owing to their sedative property have been suggested to calm the post operative agitation.[14]

Among them opioids like Fentanyl and alpha 2 adrenoreceptor agonist like Dexmedetomidine have sedative and analgesic effects and both are known to reduce emergence agitation. Thus we selected these two drugs in our study.

Matin *et al.*[15] suggested that Fentanyl premedicated children experienced less anxiety and strain during surgery and had better recovery. Manaa *et al.*[9] and Cravero *et al.*[8] in their studies observed a significant reduction in emergence agitation in children receiving Fentanyl. In our study, we chose Inj. Fentanyl in the dose of 1 mic/kg i.v. which was in consensus with the dose chosen by Manaa *et al.*[9], Cravero *et al.*[8].

Because of its sedative and analgesic effects, α_2 adrenoreceptor agonists like Clonidine and Dexmedetomidine have been used safely and effectively for the management of Sevoflurane agitation in paediatric patients. Cravero *et al.*[8] and Kulka *et al.*[1] found a reduction of agitation with Clonidine 2 mcg/kg i.v. in children undergoing surgery under Sevoflurane anesthesia. Dexmedetomidine a recent addition to the α_2 adrenoreceptor agonist group has also been studied extensively in the reduction of emergence agitation.

Dexmedetomidine owing to its sedative and analgesic action, no respiratory depression, better haemodynamic stability, minimal or no significant adverse effect profile has lead to its use in paediatric anesthesia. It can be used as a premedication, sedative for invasive procedures, shivering and reduction of emergence agitation.

Isik *et al.*[16] and Guler *et al.*[17] observed that Dexmedetomidine 0.5 mic/kg or 1 mic/kg reduced post Sevoflurane agitation significantly but it also prolonged to early phase of post anesthesia recovery.

Backache *et al.*[13] used Dexmedetomidine i.v. after induction of anesthesia in the dose of 0.15 mic/kg and 0.3 mic/kg. He observed that incidence of postoperative agitation was 37% in the control group, 17% in children receiving 0.15 mic/kg and 10% in children receiving 0.3 mic/kg. In our study, we used Inj. Dexmedetomidine 0.3 mic/kg i.v.; this was in accordance with the dose chosen by Manaa *et al.*[9], Masami *et al.*[12].

We have given the study drug 10 minutes before the end of anesthesia, our study was in consensus with the study conducted by Manaa *et al.*[9].

Thus, we decided to conduct our study with Dexmedetomidine 0.3 mcg/kg and comparing it with Fentanyl 1 mcg/kg on reduction of emergence agitation after Sevoflurane anesthesia in children aged 2-9 years of ASA physical status I or II undergoing elective lower abdominal surgery.

Post operative scales used for agitation scoring and pain scoring were the Watcha scale[18,19] and The Paediatric Anesthesia Emergence Delirium (PAED) Scale[20]. The PAED scale is validated but is difficult to use in the routine clinical practice.It is better to use a simple scale like watcha scale to detect delirium and then use the PAED scale to measure its degree[21].

Agitation due to pain is a significant confounding factor for the evaluation of the presence or measurement of the degree of ED.

The patient can be agitated even if they have pain, hence we used objective pain scale, so that we can differentiate if the patient was agitated due to pain or due to general anesthesia with sevoflurane. The total score in objective pain scale is 10, But since the patient in our study was in the age group of 2 to 9 years, not all the patient were able to complaint of pain. Hence, that parameter was removed from the objective pain scale for all the patients and then the maximum score had become 8. Among other parameters like systolic blood pressure, crying, movements and agitation except for systolic blood pressure other parameters were overlapping to an extent with the parameters used in the PAED scale. Hence in our study we observed that the groups which were having higher degree of agitation according to PAED scale also had a higher objective pain scale score.

In our study we observed that the patients in the Group N showed higher scores of agitation in comparison to Group F, and Group F showed higher scores of agitation in comparison to Group D.

The difference between Group D and Group F was significant, suggesting that Dexmedetomidine is more effective in reduction of the emergence agitation after Sevoflurane anesthesia compared to Fentanyl.

We also observed that the agitation scores were higher in the first ten minutes post operatively and by the end of 30 minutes, patients in all the three groups were comparable with regard to agitation scorings. This was in consensus with the observation made by Vlajkovic *et al.*[14].

Erdil *et al.*[10] observed that Dexmedetomidine proved to be better than Fentanyl in reducing the agitation; however the difference was not significant.

In contrast to Manaa *et al.*[9] who proved that Fentanyl was slightly better than Dexmedetomidine. In our study 60% of the children in Group N showed presence of agitation as against 45% in Group F and 20% in Group D on arrival in post anesthesia care unit.

Aldrete Recovery Score was used to assess recovery of patient in PACU and those patients who attained an aldrete recovery score of ≥ 9 were dischared from the PACU to the ward and the time taken to achieve this score was noted[22].

None of the patients showed any adverse effects or intraoperative event of significance or post operative complications like nausea/vomiting, hypotension, bradycardia, hypoxemia, hypoventilation, apnoea, and respiratory depression.

Conclusion

The dose of fontanel 1 mcg/kg i.v. or dexmedetomidine 0.3 mcg/kg i.v. that is administered 10 minutes before the discontinuation of anesthesia reduced the postoperative agitation in children.

Dexmedetomidine was more effective when compared with fentanyl in attenuation of sevoflurane-induced agitation in paediatric patients undergoing lower abdominal surgery.

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Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1399-1411
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.48

A Comparison Between Airtraq Optical Laryngoscope and Conventional Macintosh Laryngoscope for Intubation in Adult Surgical Patients: A Prospective Randomized Controlled Study

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Abstract

Tracheal intubation using a laryngoscope is considered as a gold standard [1] of airway management during administration of general anesthesia and also in critical care settings because of its several advantages including [2,3] - Isolation of respiratory tract from Gastro intestinal system and hence minimal risk of aspiration. Allows delivery of oxygen and anaesthetic gases via positive pressure ventilation without inflation of stomach. Access to tracheobronchial tree for pulmonary lavage and drug administration (e.g. inhaled bronchodilators). Improved access to head and neck surgeries. Airway management is important for anesthesia because adverse respiratory events are responsible for 75% of ASA closed claims. Of these failed ventilation is the main culprit (38%), followed by faulty placement of endotracheal tube in esophagus (17%) and difficult intubation (18%). Approximately 600 patients die each year in the developed world from complications due to airway management and also in the underdeveloped world is much grimmer.[4,5,6] *Context:* We compared tracheal intubation using airtraq optical laryngoscope with macintosh laryngoscope in adult patients undergoing elective procedures under general anesthesia *Aims*: This study is to compare the intubating conditions in adult surgical patients using airtraq optical laryngoscope with macintosh laryngoscope with respect to ease of intubation, time taken for intubation, airway trauma and hemodynamic response to laryngoscopy. *Settings and Design:* Prospective randomised interventional study. *Materials and Methods:* This study was done in Sree Balaji Medical College and Hospital, Chennai at Department of Anaesthesiology and Critical Care from August 2016 to February 2018. It was a Single centre, prospective, randomized, parallel group, open label, interventional controlled study. After obtaining institutional ethical committee approval. 60 patients (sample size) who were posted for elective surgery requiring general anesthesia (Recruitment) with satisfying inclusion criteria were enrolled in the study after obtaining informed consent from the patients and relatives. 2 groups by random number allotted by computer based randomization *Statistical Analysis*: Descriptive and inferential statistical methods were used. *Results*: Mean duration of intubation with the Airtraq group was 15.93 secs whereas in the Macintosh group it was found to be 38.70 secs. It was computed using Levene's T test and was found to be statistically significant. In the Macintosh group, 4 patients had an Total IDS of 5 or greater, indicating moderate to severe intubation difficulty, whereas no patient in the Airtraq group had an Total IDS of more than 3 and was found to be statistically significant. *Conclusion*: Our study concludes that endotracheal intubation is easier with Airtraq compared to Macintosh laryngoscope as it provides good glottis view. In addition to that Airtraq have less intubation duration, less hemodynamic response for intubation and less Airway trauma compared to Macintosh.

Keywords: Macintosh; Airtraq; Laryngoscope; Intubation; Airway.

How to cite this article:

S Selvamani, P Anand. A Comparison Between Airtraq Optical Laryngoscope and Conventional Macintosh Laryngoscope for Intubation in Adult Surgical Patients: A Prospective Randomized Controlled Study. Indian J Anesth Analg. 2019;6(4):1399-1411.

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Received on 24.01.2019, **Accepted on** 11.07.2019

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Introduction[7]

Airway management has been the domain of dominance for anesthesiologists over ages.

Laryngoscopy and intubation are the fundamental skills that every clinician aspires to learn and practice. The most frequent end point for almost all the studies was the ease of intubation along with ability to minimize the sympathetic response to tracheal instrumentation. Airtraq is a recently developed laryngoscope which facilitates easy visualisation of glottis through matrix of sequentially arranged lenses and mirror.

Materials and Methods

This study was done in Sree Balaji Medical College & Hospital, Chennai at Department of Anaesthesiolgy and Critical Care from August 2016 to February 2018.

It was a Single centre, prospective, randomized, parallel group, open label, interventional controlled study.

After obtaining institutional ethical committee approval. 60 patients (sample size) are posted for elective surgery requiring general anesthesia (Recruitment) with satisfying inclusion criteria were enrolled in the study after obtaining informed consent from the patients and relatives.

Randomization: 2 groups by random number allotted by computer based randomization.

Allocation and intervention: 2 groups

Group A: 30 Patients –airtraq optical laryngoscope

Group B: 30 Patients –conventional macintosh laryngoscope

Inclusion Criteria

- ASA 1 & 2 patients
- Age 18-65 years, both sexes
- Elective surgical cases requiring GA
- MPC 1, 2, & 3 patients

Exclusion Criteria

- Severe CVS, RS, hepatic, renal disease patients
- Any valvular, conduction abnormality, IHD, Hypertensive patients
- Patients on antihypertensive drugs or beta blockers
- Anticipated difficult airway patients
- BMI more than 40
- Patient refusal

Material

- Airtraq optical laryngoscope adult size
- Macintosh laryngoscope 3 & 4 size blade

Airway Assessment [3,8,9,10]

Previous surgery and anesthesia records, H/O snoring, H/O voice change, H/O previous surgery, Burns, Trauma, Tumour in and around the oral cavity, neck or cervical spine were asked in the history. H/O systemic illness like Hypertension, Diabetes, Ankylosing spondylitis, Rheumatoid arthritis were asked and recorded. General examination included examination for facial anomalies, Anomalies of the mouth, Temperomandibular joint pathology, and tongue, pathology of palate and pathology of nose. Weight in kilograms and Height in centimeters were recorded and Body Mass Index was calculated. Individual airway indices were measured.

Samson and Young modification of Mallampatti grading:[9]

The patient kept in sitting position with maximal mouth opening with protruding tongue, without phonation and the observer's eye in level with patient's mouth and the degree to which the faucial pillars, uvula, soft palate, and hard palate were visible were recorded and classified as follows:

Grade I: Faucial pillars, uvula, soft palate and hard palate visible

Grade II: Uvula, soft palate and hard palate visible

Grade III: Base of uvula or none, soft palate and hard palate visible

Grade IV: Only hard palate visible.

Thyromental distance

Distance between the thyroid notch and mental symphysis when the neck is fully extended and mouth closed (>6.5 cm or < 6.5 cm)

Other ways of airway assessment

A-O joint movement: Patient asked to look at the ceiling without raising the eyebrow and the range of movements were measured

Neck flexion: Patient was asked to touch the manubrium sternum with chin and the range of movements measured.

TMJ function: The patient was asked to open the mouth wide open and the inter incisor distance measured. Examiner's index finger was placed in front of the tragus and thumb over the mastoid process and the patient was asked to open the mouth and sliding movement of the mandibular condyle was assessed.

Upper lip bite test: The patient was asked to bite the upper lip with the lower incisor and graded as follows:

Class 1: Lower incisor can bite the upper lip above the vermilion line

Class 2: Lower incisor can bite the upper lip below the vermilion line

Class 3: Lower incisor cannot bite the upper lip

Sterno mental distance: Distance between the sternal notch and mental symphysis when the neck was fully extended and mouth closed.

Neck circumference: Measured in cm at the level of thyroid notch.

Examination of dentition: Abnormalities like cracking, buck tooth, loose, artificial and absence of incisors were examined and recorded.

Procedure

After assessment patient shifted to operating room. i.v line started and SpO_2, ECG, NIBP and $ETCO_2$ (After intubation) moniters connected.

Premedication: 0.2 mg glycopyrrolate, 2 mcg/kg fentanyl iv route 10 mins before Induction.

Preoxygenation: with 100% 02 for 3mins at tidal volume respiration

Base line: SpO_2 HR, Systolic BP, Diastolic BP, MAP was noted

Induction: 2.5 mg /kg propofol

Relaxant for intubation: 0.5 mg/kg induction dose of atracurium 0.1 mg/kg maintenance dose of atracurium

Intubation: airtraq/macintosh laryngoscopy according to the group

Monitoring: SPO2, HR, Systolic BP, Diastolic BP, MAP at 3rd, 5th, 10th minute.

Outcome Measures

Primary measures

- Ease of intubation assessed by IDS score

Secondary measures

- Haemodynamic response
- Airway trauma
- Intubation time

Intubation Difficulty Score:[3, 11,12]

Intubation difficulty score was used to evaluate intubating performance of laryngoscopy. IDS scoring was developed by adnet *et al.* in 1997. IDS score is a blend of objective and subjective criteria that permit a quantitative and qualitative approach to the progressive nature of the difficulty in intubation. It appears to be the best indicator till date.

7 variables are used.

N1 - No of supplementary attempts. An attempt is defined as one advancement of tracheal tube in the direction of the glottis during direct laryngoscopy. (for Attempt 1/2/3/4, N1 Score is 0/1/2/3)

N2 - No of supplementary operators directly operating (not assisting) (for operators 1/2/3/4, N2 Score is 0/1/2/3)

N3 - No: of alternative techniques used. (each additional techniques like oral intubation to blind nasotracheal intubation, curved blade to straight blade etc N3 Score is 1 or more)

N4 - Cormack Lehane grade minus one. (for CLG 1/2/3/4, N5 Score is 0/1/2/3)

N5 - Subjectively increased lifting force required during laryngoscopy. (for normal N 5=0, for increased N 5=1)

N6 - Need for external laryngeal manipulation (for not required N6=0, for required N6=1)

N7 - Position of vocal cords.(N7 Score 0 for abduction, 1 for adduction)

Total IDS Score = sum of scores (N1 to N7)

IDS Score Degree of difficulty

0 - Ease

1 to 5 - Slight difficulty

> 5 - Moderate to major difficulty

Infinitive - Impossible intubation

In this scoring the value of IDS is '0' in full visual view of glottic opening with vocal cords are seen to be nicely abducted. Every variation from this defined 'ideal 'intubation increases the scoring that indicate increasing difficulty of intubation. The total IDS score being the sum of all variation from the definition.

Cormack and Lehane Grading System:[9,13]

Entire vocal cord visualized - Grade I

Posterior part of vocal cords seen - Grade IIa

Arytenoids only seen - Grade IIb

Epiglottis only seen (liftable) - Grade IIIa

Tip of epiglottis only seen (adherent) - Grade IIIb

No glottis structure seen - Grade IV

Apart from Cormack-Lehane and Intubation Difficulty Score, the following factors were also noted.

• *Intubation time:* It measured from entry of the device into the oral cavity until confirmation of proper placement of tracheal tube.

• *Heart rate, systolic BP, diastolic BP, mean arterial pressure and* SPO_2 were measured at 3rd, 5th & 10th minute from pre induction.

• *Airway trauma:* All complications will be recorded, with special attention to common complications such as upper airway, dental trauma and blood soiling of airtraq or macintosh blade after intubation. If intubation with Airtraq failed and saturation maintained, Macintosh blade was used for intubation and if the saturation decreased, mask ventilation with 100% oxygen followed by intubation with Macintosh laryngoscope.

Results

All data were collected and tabulated.

Table 1: Age

Age (in years)	Group A	%	Group B	%	*p*-value
< 20	2	07	1	03	0.092
21–30	8	27	9	30	
31–40	7	23	8	27	
41–50	5	17	4	13	
51–65	8	27	8	27	
Total	30	100	30	100	

Table 2: Gender

Gender	Group A	%	Group B	%	*p*-value
Male	18	60	16	53	0.524
Female	12	40	14	47	
Total	30	100	30	100	

Table 3: BMI Distribution

BMI	Group A		Group B		*p*- Value
	No	%	No	%	
< 18.5	4	13	3	10	0.001
18.5 – 24.9	10	33	11	37	
25 – 29.9	12	40	11	37	
> 30	4	13	5	17	
Total	30	100	30	100	

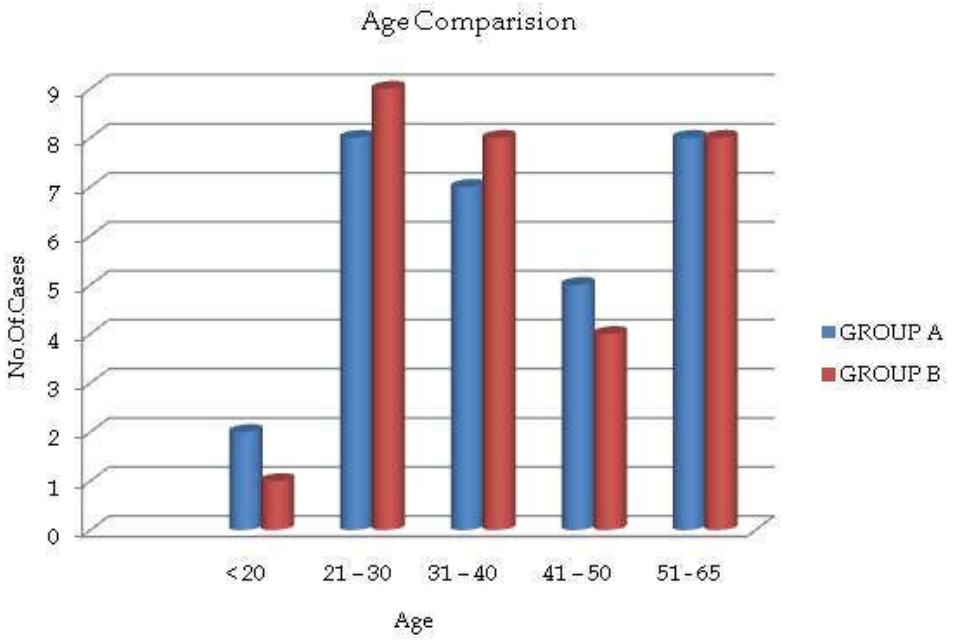

Fig. 1: Comparison of age in both groups

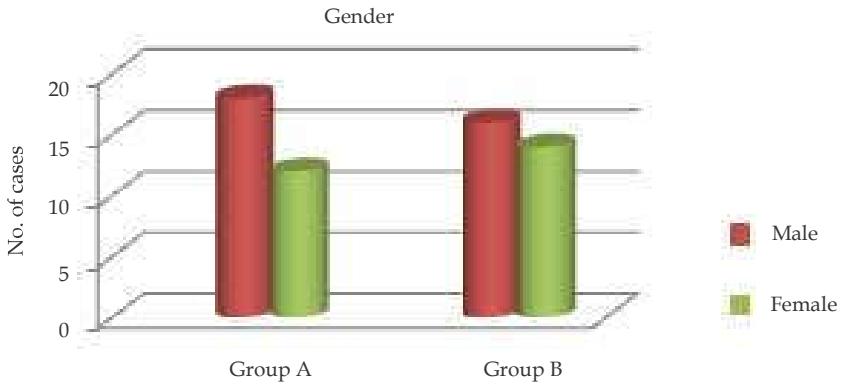

Fig. 2: Comparison of sex distribution in both groups

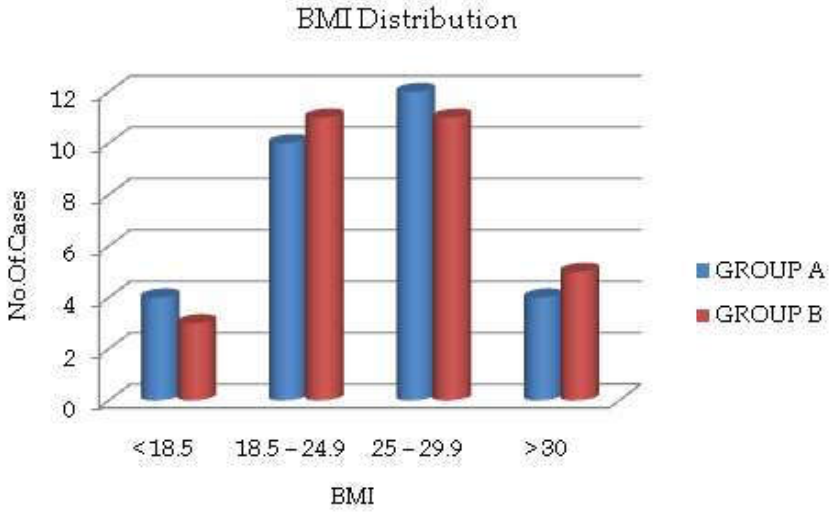

Fig. 3: Comparison of BMI distribution in both groups

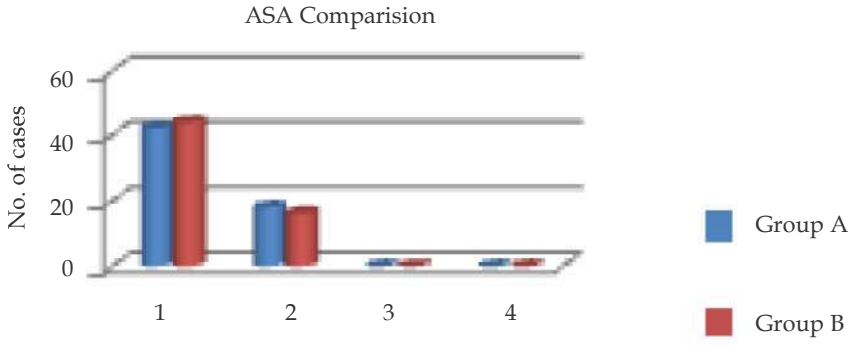

Fig. 4: Comparison of ASA distribution in both groups

Table 4: ASA

ASA Grade	Group A		Group B		P Value
	No	%	No	%	
1	21	70	22	73	0.0648
2	9	30	8	27	
3	0	00	0	00	
4	0	00	0	00	
Total	30	100	30	100	

Table 5: Comparision of Thyromental Distance

Parameter Assessed	Group A		Group B		P Value
	No	%	No	%	
>6.5 cm	26	87	19	63	0.524
<6.5 cm	4	13	11	37	
Total	30	100	30	100	

Table 6: Comparision of MPC

MPC Grade	Group A		Group B		P Value
	No	%	No	%	
1	17	57	15	50	0.534
2	7	23	9	30	
3	6	20	6	20	
4	0	00	0	00	
Total	30	100	30	100	

Among the total cases, In Group A, 57% belong to the MPC Grade 1, 23% belong to the MPC Grade 2, 20% belong to the MPC (Table 6)

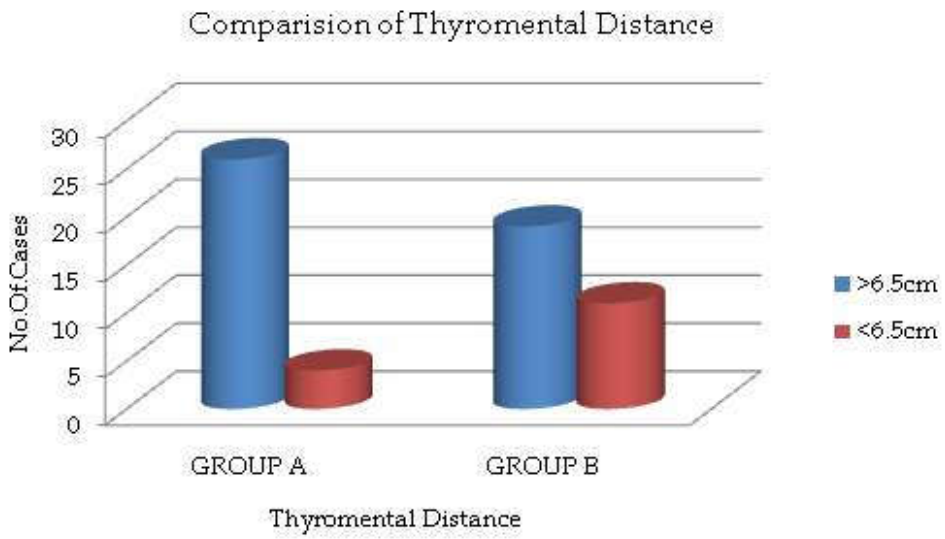

Fig. 5: Comparison of thyromental distance in both groups

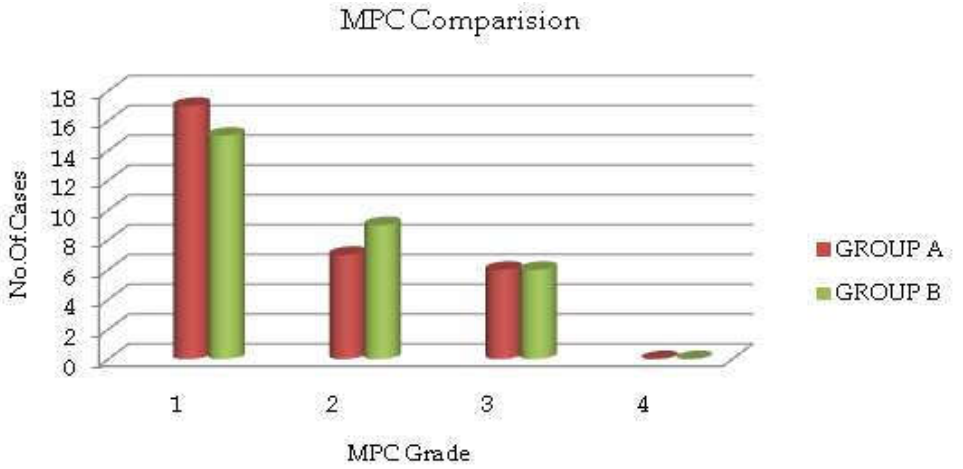

Fig. 6: Comparison of MPC grading in both groups

Table 7: Comparision of IDS

Total Intubation Difficulty Score	Group A		Group B		P Value
	No	%	No	%	
0	25	83.3	20	66.8	
1	0	0	0	0	
2	3	10.0	4	13.3	
3	2	6.7	4	13.3	
4	0	0	0	0	0.000
5	0	0	1	3.3	
6	0	0	0	0	
7	0	0	0	0	
8	0	0	1	3.3	
Total	30	100	30	100	

Among the cases, the following IDS parameters where observed.

All the patients in airtraq group intubated in single attempt, in macintosh group 3 patients out of 30 intubated in 2nd attempt**. (N1)**

All the patients in both groups intubated by single operaters. No need supplementary operaters. **(N2)**

All patients in airtraq group intubated without using additional techniques. But in macintosh group 4 patients out of 30 required additional techniques like changing blade, using stylet and using gum elastic bougie. **(N3)**

Cormack and Lehane grade 1/2/3/4 found in airtaq group 17/3/0/0 patients, in macintosh 10/6/2/2 patients. **(N4)**

Lifting force required in 5 0ut 30 patients in macintosh group, only one patient out of 30 in airtraq group**. (N5)**

Laryngeal pressure applied in 10 out of 30 patients in macintosh group, 3 out of 20 patients in airtraq group. **(N6)**

In all patients of both groups vocal cord mobility were in abduction. **(N7)**

3 patients in the Airtraq group had an Total IDS of more than 1, whereas 10 patients in the Macintosh group had an Total IDS of 1 or greater. In the Macintosh group, 4 patients had an Total IDS of 5 or greater, indicating moderate to severe intubation difficulty, whereas no patient in the Airtraq group had an Total IDS of more than 3. This was computed based on Levene's T test for equality of variances and the result was found to be statistically significant with a *p* value of 0.0011 (Table 7).

CORMACK and LEHANE grading:

Cormack and Lehane grade of both the group of patients were compared to grade the glottic view.

85% of patients in the Airtraq group had a CL grade of 1, compared to 50% of patients in the Macintosh group.

In the Airtraq group 15% of patients had a CL grade of 2 compared to 30% of patients in the Macintosh group.

No patient in the Airtraq group had a CL grade of 3 or 4, whereas in the Macintosh group 10% patients had a CL grade of 3 and 10% patients had a CL grade of 4 (Table 8).

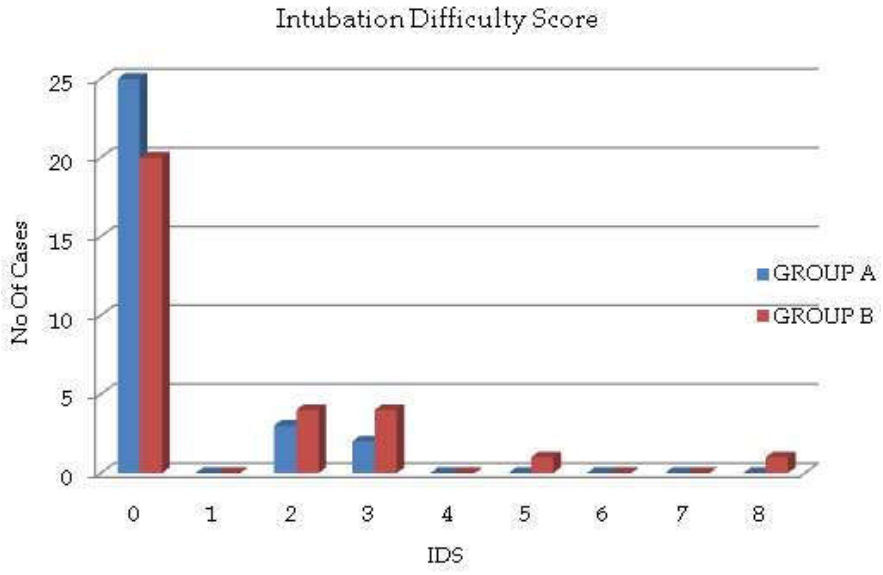

Fig. 7: Comparison of total IDS score in both groups

Table 8: Comparison of Cormack and lehane grading in both groups

Group	Airtraq		Macintosh		P Value
CL 1	27	90	16	53	0.0024
CL 2	3	10	9	30	
CL 3	0	00	3	10	
CL 4	0	00	2	07	
Total	30	100	30	100	

Table 9: Duration of Intubation

Parameter assessed	Group	N	Mean	S.D	P value
Intubation time	Airtraq	30	15.93	2.55	0.000
	Macintosh	30	38.70	15.81	

Mean duration of intubation with the Airtraq group was 15.93 secs whereas in the Macintosh group it was found to be 38.70 secs. It was computed using Levene's T test and was found to be statistically significant (Table 9).

Table 10: Comparison of Airway Trauma

Parameter assessed	Group	Lips	Gums	Teeth	Tongue
Airway Trauma	Airtraq	2	1	3	2
	Macintosh	5	4	8	5

No trauma in laryngeal structures were found in both the groups (Table 10).

Hemodynamic Changes

The heart rate, blood pressure and SpO_2 of the patients were measured baseline, aft intubation, after 3 minutes and 5 minutes and after 10 minutes post intubation and the values were computed by Chi – square test and it was found that the tracheal intubation with Macintosh laryngoscope resulted in a significant increase in heart rate, systolic, diastolic and MAP, compared with preintubation values, in contrast to the Airtraq (Table 11).

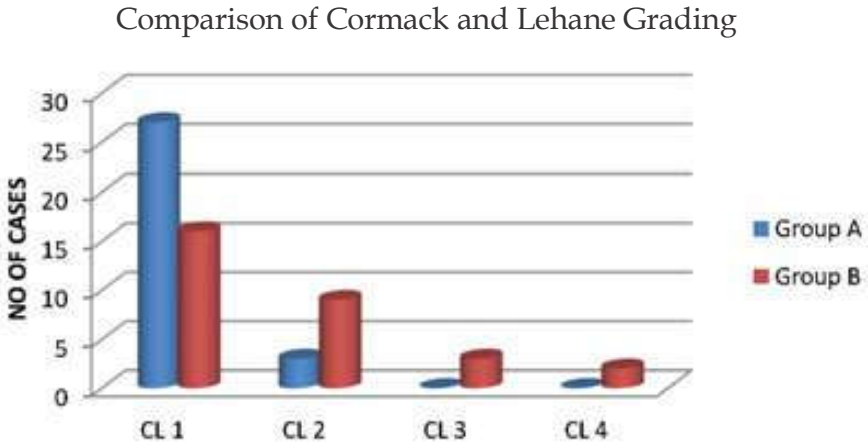

Fig. 8: Comparison of cormack and lehane grading in both groups

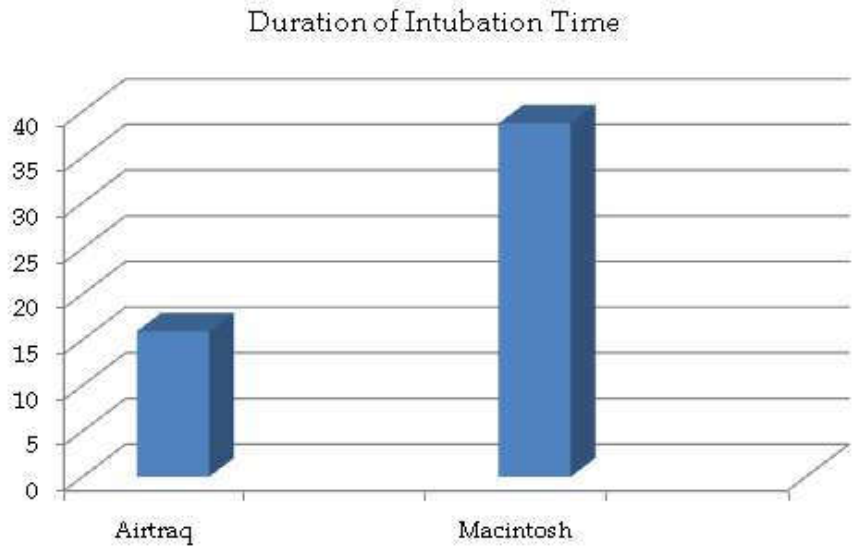

Fig. 9: Comparison of intubation duration in both groups

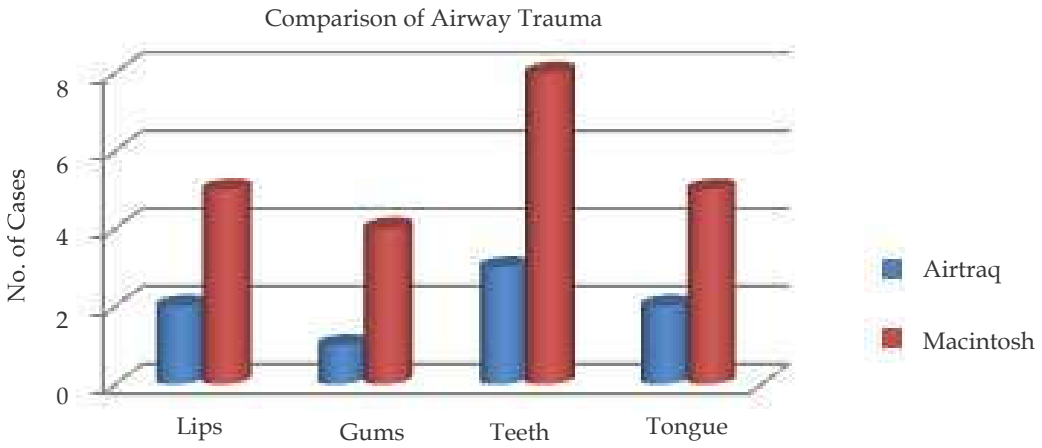

Fig. 10: Comparison of airway trauma in both groups

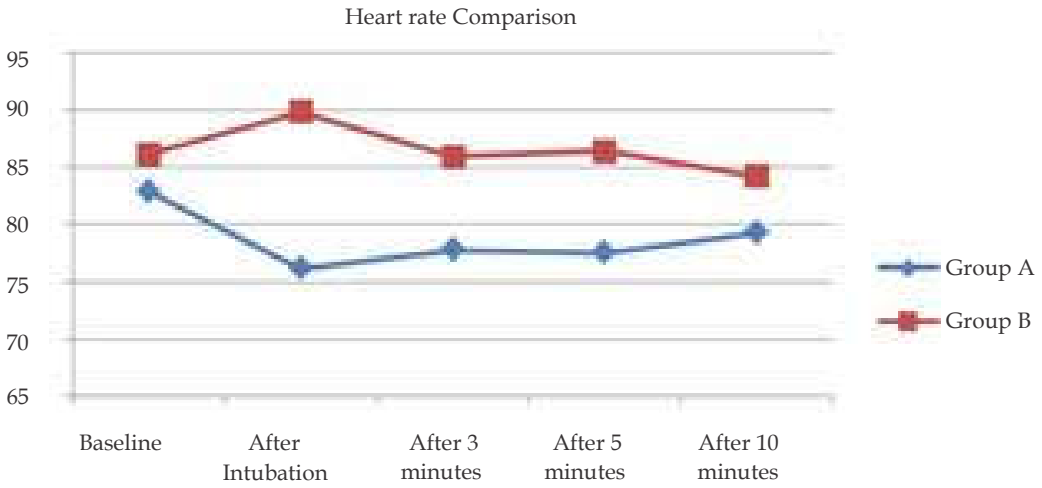

Fig. 11: Comparison of heart rate in both groups

Table 11: Heart Rate Comparison

Variables	Group A		Group B		*p* – value
	Range	Mean ± SD	Range	Mean ± SD	
Baseline	60 – 112	82.9 ± 12.23	63 – 110	86.20 ± 12.70	0.541
After intubation	54 – 104	76.17 ± 10.27	70 – 118	89.87 ± 3.31	0.000
After 3 minutes	55 – 105	77.80 ± 11.40	60 – 124	85.97 ± 12.25	0.002
After 5 minutes	55 – 110	77.50 ± 11.90	65 – 127	86.43 ± 12.41	0.004
After 10 minutes	60 – 95	79.27 ± 8.87	62 – 106	84.27 ± 10.02	0.217
Grand Mean					
p-value			0.001		

Table 12: Systolic Blood Pressure

Variables	Group A		Group B		*p* – value
	Range	Mean ± SD	Range	Mean ± SD	
Baseline	104 – 160	127.07 ± 14.52	101 – 148	123.43 ± 10.62	0.512
After intubation	90 – 169	125.37 ± 17.95	100 – 180	139.87 ± 18.33	0.025
After 3 minutes	83 – 160	114.33 ± 15.11	102 – 174	126.21 ± 18.55	0.004
After 5 minutes	87 – 162	115.57 ± 15.71	102 – 176	127.23 ± 18.52	0.023
After 10 minutes	92 – 164	124.73 ± 15.61	104 – 179	127.20 ± 13.52	0.287
Grand Mean					
p-value			0.014		

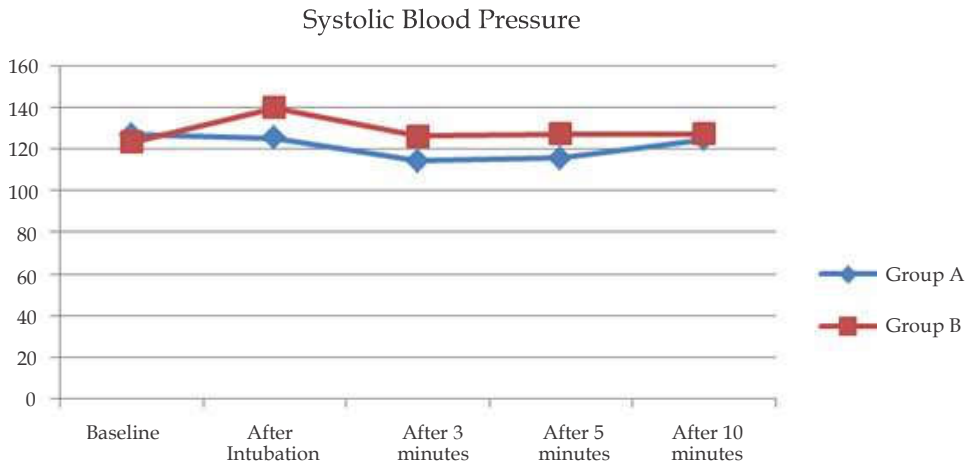

Fig. 12: Comparison of systolic blood pressure in both groups

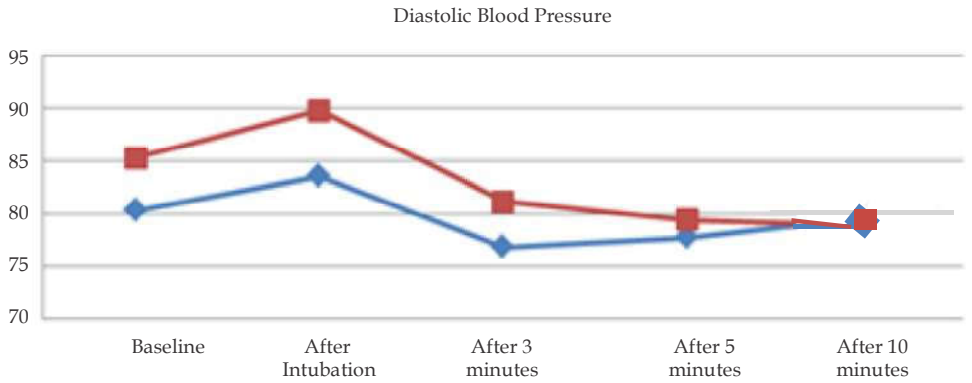

Fig. 13: Comparison of diastolic blood pressure in both groups

Table 13: Diastolic Blood Pressure

Variables	Group B		Group N		*p* – value
	Range	Mean ± SD	Range	Mean ± SD	
Baseline	62 – 100	80.3 ±9.24	53 – 107	85.27 ± 12.16	0.254
After intubation	57 – 109	83.53 ± 12.35	60 – 116	89.73 ± 12.51	0.021
After 3 minutes	60 – 100	76.88 ± 9.44	57 – 100	81.14 ± 12.55	0.001
After 5 minutes	58 – 105	77.76 ± 11.84	56 – 98	79.44 ± 12.41	0.019
After 10 minutes	51 – 100	79.70 ± 11.65	60 – 97	78.87 ± 10.92	0.341
Grand Mean					
p-value		0.000			

Table 14: Mean Arterial Pressure Comparison

Variables	Group A		Group B		*p* – value
	Range	Mean ± SD	Range	Mean ± SD	
Baseline	62 – 100	80.3 ±9.24	53 – 107	85.27 ± 12.16	0.254
After intubation	57 – 109	83.53 ± 12.35	60 – 116	89.73 ± 12.51	0.021
After 3 minutes	60 – 100	76.88 ± 9.44	57 – 100	81.14 ± 12.55	0.001
After 5 minutes	58 – 105	77.76 ± 11.84	56 – 98	79.44 ± 12.41	0.019
After 10 minutes	51 – 100	79.70 ± 11.65	60 – 97	78.87 ± 10.92	0.341
Grand Mean					
p-value		0.014			

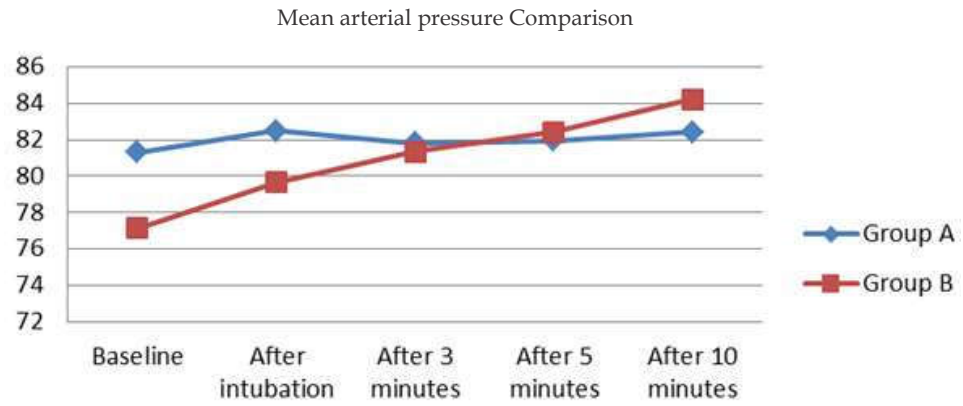

Fig. 14: Comparison of mean arterial pressure in both groups

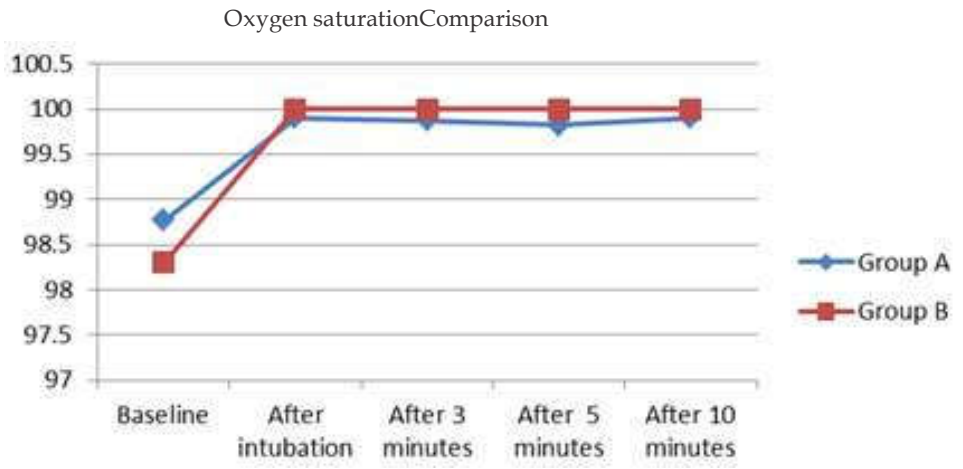

Fig. 15: Comparison of oxygen saturation in both groups

Table 15: Oxygen Saturation Comparison

Variables	Group A		Group B		*p* – value
	Range	Mean ± SD	Range	Mean ± SD	
Baseline	97 – 100	98.77 ± 0.94	81 – 100	98.3 ± 3.38	0.458
After intubation	98 – 100	99.90 ± 0.55	100 – 100	100 ± 0	0.524
After 3 minutes	97 – 100	99.87 ± 0.55	100 – 100	100 ± 0	0.264
After 5 minutes	97 – 100	99.82 ± 0.55	100 – 100	100 ± 0	0.365
After 10 minutes	97 – 100	99.90 ± 0.41	100 – 100	100 ± 0	0.527
p-value			0.0681		

However, SpO_2 changes in the pre and post intubation periods in both the groups was not statistically significant.

Discussion

Expert airway management is an essential skill for anesthesiologist. Difficult endotracheal intubation is mostly caused by difficult direct laryngoscopy with impaired view of vocal cords. Despite all the information currently available, no single factor reliably predict these difficulties. Unfortunately many difficult intubations are not be recognized until after induction of anesthesia. Unexpected difficult intubation lead to critical situation, especially who are difficult to ventilate by mask, who are at risk for gastric regurgitation and patients with limited cardiopulmonary reserves.

When a person in supine position and head in the neutral position, the laryngeal axis is almost horizontal. The pharyngeal axis is 30-45^0 from the horizontal axis and the oral axis almost perpendicular to the laryngeal axis. For a successful direct laryngoscopy for the exposure of the glottis

opening, the oral, pharyngeal and laryngeal axes alignment is required. Elevation of the head about 10cm with pads below the occiput aligns the laryngaeal and pharyngeal axes[14]

Conventional macintosh laryngoscopy fails to get desired laryngeal view in patients with difficult airway like short neck, anteriorly placed larynx, small jaw, MPC 3 & MPC 4 patients, cervical spine immobilization needed patients etc. But reports said that airtraq have shown improvement in laryngeal view and ease of intubation in normal and difficult airway patients[15]

The advantages of airtraq optical laryngoscope from the available literatures are[15]

1. Airtraq does not need alignment of the axes to improve intubating condition because the axis of airtraq is curved and the image is transmitted through lenses and mirrors.
2. Airtaq is useful in patients with altered airway and magill's position contraindicated patients.
3. The displayed anatomy is magnified in proximal viewfinder.
4. The anatomical structure and anomalies are easily viewed with help of airtraq.
5. Airtraq associated with less hemodynamic changes due to less manipulation of the airway and only clockwise or anticlockwise movement and upwards or downwards movement was required, not the lifting movement as in macintosh laryngoscope.
6. Airtraq significantly reduces the duration of intubation.
7. A clip on wireless video system is also available in airtraq which allows viewing on an external screen. It is also useful for teaching purposes.
8. Shortens the endotracheal intubation learning curve in novice personnel.
9. Channel loading type of video laryngoscope example Airtraq optimal laryngoscope provides perfect visualization of larynx yet may result in failure of endotracheal intubation[17].
10. When insufficient visualization occurs the airtraq may be used to open an airway path. Insert Fibreoptic bronchoscope with an endotracheal tube either in channel or ext to the device and direct it towards the epiglottis.
11. We too have employed this combined technique in both adult and paediatric patients in difficult airway.[16,17]
12. Many compared the degree of cervical spine movement in laryngoscope performed using airtraq and conventional macintosh laryngoscope. Although significant movement of cervical spine from baseline was noted during all procedure (p<0.05), cervical spine extension with airtraq was 29% less than measured during macintosh laryngoscopy between occiput and c4 and 44% less at the c3/c4 motion segment. Anterior deviation of the vertebral bodies from baseline were 32%, 35%, 38% and 40% less at the atlass, c2, c3 and c4 vertebrae respectively during airtraq laryngoscopy (p<0.01).
13. Some study also demonstrated that laryngoscopy using the airtraq laryngoscope involves less movement of cervical spine compared to conventional procedure using macintosh laryngoscope.[18]
14. Videolaryngoscope are new intubating device which provide an indirect view of the upper airway in difficult airway management, they improves Cormack-lehane grade and achieve the same or a higher intubation success rate in less time compared with direct laryngoscope.[18]

It was generally easy to insert the airtraq in to the oral cavity, to obtain a full view of the laryngeal aperture and to intubate the endotracheal tube into the trachea without major complication. In airtraq the endotracheal tube can be attached to the side of the blade and the tip of the ET tube is visible on the proximal viewfinder. Once laryngeal aperture was positioned in the centre of the proximal viewfinder, it was easy to introduce the ET tube into the trachea.

Eventhough we have a good view of glottis there was difficulty in negotiating the ET tube into the trachea, that result in prolonged intubation. The back and up maneuver or clockwise or anticlockwise movement of airtraq was needed to introduce the ET tube into the trachea.

Summary

In our study Airtraq laryngoscopy had less intubation difficulty score than macintosh laryngoscopy. Airtraq had less Cormack and Lehane grading, less intubation duration, less airway trauma and less hemodynamic response for intubation than Macintosh.

Conclusion

Our study concludes that endotracheal intubation is easier with Airtraq compared to Macintosh laryngoscope as it provide good glottis view. In addition to that Airtraq have less intubation duration, less hemodynamic response for intubation and less Airway trauma compared to Macintosh. Airtraq laryngoscope significantly improve the view of glottic opening and facilitates fast, easy and reliable intubation. Airtraq reduce the need of more sophisticated and complex airway instrument like flexible fibreoptic bronchoscope to a particular extent. It can also be useful in routine anesthesia management, in critical care, anticipated, unanticipated airway situations. Due to less hemodynamic response for laryngoscopy for airtraq may have advantage in clinical situation like coronary artery disease or cardiac arrhythmias and neuro surgery patients.

Conflict of Interest: None

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1413-1421
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.49

Comparison of Oral Pregabalin Versus Bolus Dose of Intravenous Dexmedetomidine in Attenuating the Hemodynamic responses During Laparoscopic Cholecystectomy: A Prospective Randomized double Blind Study

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Abstract

Background and Aims: Laparoscopic cholecystectomy is being preferred surgery for gall bladder diseases under general anesthesia in the present era. This study was designed to compare oral pregabalin versus intravenous dexmedetomidine as premedication in attenuating the hemodynamic responses in laparoscopic cholecystectomy. *Material and Method:* This prospective randomized double blind study was conducted in 90 patients (ASA) grade I or II, divided into two groups of 45 each. Group P- received oral pregabalin 150 mg 1 hr prior to surgery and intravenous normal saline (0.9%). Group D- received oral placebo tab 1 hr prior to surgery and IV dexmedetomidine 1 μg/kg with normal saline. Demographic data and haemodynamic parameter like heart rate, systolic, diastolic and mean blood pressure along with oxygen saturation and end tidal CO_2 were noted. Assessment of pain by visual analogue pain score (VAS) and sedation by Ramsay Sedation Scale (RSS) was done. The time to first rescue analgesic and total dose of analgesics in 24 hrs were noted. Statistical analysis was done using SPSS software (version 17, SPSS, Chicago, IL). *Result:* In group P significant haemodynamic response was observed at laryngoscopy, after intubation and during pneumoperitonium while in group D it was significantly attenuated (p<0.05). In group D VAS score was lower and RSS score was more as compare to group P which was statistically significant (p< 0.05). The time for first resque analgesic was earlier in group P (37.5 ± 9.30) than group D (58.06 ± 11.62) (p<0.001). *Conclusion:* Dexmedetomidine was found to be more effective than pregabalin in maintaining hemodynamic responses along with better postoperative analgesia and more sedation than pregabalin group.

Keywords: Pregabalin; Dexedetomidine; Laproscopic cholicystectomy; Pneumoperitoneum.

How to cite this article:

Seema Partani, Lalita Jeenger, Karishma Johari *et al.* Comparison of Oral Pregabalin Versus Bolus Dose of Intravenous Dexmedetomidine in Attenuating the Hemodynamic responses During Laparoscopic Cholecystectomy: A Prospective Randomized double Blind Study. Indian J Anesth Analg. 2019;6(4): 1413-1421.

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Received on 23.05.2019, **Accepted on** 11.07.2019

Introduction

Laparoscopic abdominal surgery is being preferred in present era as it has many advantages over open surgery like less postoperative pain, shorter hospitalstay, early mobilization, faster recovery and bettercosmetic results[1]. Laryngoscopy, intubation and pneumoperitoneum during general anesthesia are severe noxious stimuli that can produce an intense sympathetic stimulation leading to increased level of serum catecholamines and vasopressin which further leads to adverse hemodynamic response like tachycardia, hypertension, arrthymias etc[2]. Inaddition toincreased intraabdominal pressure with

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raised diaphragmas well as reverse trendelenburg position required for surgery may result in adverse cardiopulmonary changes like diminished venous return, decreased cardiac output, elevated arterial pressure and increased systemic and pulmonary vascular resistance. These adverse hemodynamic changes may predispose to myocardial ischemia which may be life threatening in vulnerable patients[2,3]. Various studies[4,5,6] have been done to attenuate these sympathoadrenal response to pneumoperitoneum and intubation which include deepening the plane of anesthesia with inhalational or intravenous anaesthetic agents. Various drugs like lidocaine, sedatives, sodium nitroprusside, calcium channel blockers, beta blokers, alpha-2agonists (clonidine, dexmedetomidine), magnesium sulphate and GABA analogueslike gabapentin, pregabalin etc. have also been used but the drug of choice is still notproven. This study aims to evaluate and compare the efficacy of oral pregabalin versus intravenous bolus dose of dexmedetomidine as premedication for attenuating the haemodynamic pressor response during intubation, pneumoperitoneum and extubation as well as perioperative stability and requirement of postoperative analgesics.

Materials and Methods

This prospective randomized doubleblind study was conducted at tertiary care centre from January 2017 to July 2018 after obtaining approval from Institutional Research Ethical Board [IREB] and written informed patient consent A total of 90 patients of American Society of Anaesthesiologists (ASA) grade I or II between the age group of 18-60 years posted for elective laparoscopic Cholecystectomy under general anesthesia were included in this study. Patients with preexisting cardiac disease, uncontrolled hypertension, diabetes and asthma, severe renal & hepatic dysfunction, severe chronic obstructive pulmonary disease, chronic pain syndrome, history of regular use of opiates/ painmedication, antidepressants and anti-epileptic therapy, pregnant or lactating females, patients with anticipated difficult intubation and those with known allergy to study drugs were excluded from the study. Those casesin which procedure was converted to open cholecystectomy were withdrawn from the study. Sample size of 90 patients were included with 45 patients in each group. We took 100 patients considering dropouts from the study. Randomization was performed using computer generated random number table. Patients were randomly assigned to one of the two groups. Group assignments was sealed within opaque envelopes. The envelope was opened by the principle administrator just before the administration of study drug. Anaesthesiologist (who was not one of the observer of the study) prepared the study drug according to randomization group. The anaesthesiologist (who monitored and recorded the hemodynamic parameters), nurses, surgeon, research assistant and the patient were blinded to the randomization. Patients in both the groups received study drug as per the protocol: Group P- received oral pregabalin 150 mg with a sip of water 1 hr prior to surgery and intravenous normal saline (0.9%) 10 ml over 10 mins (10 mins prior toinduction). Groupd- received oral placebo tablet[vitamin c, (celin)] with a sip of water 1 hr prior to surgery and IV dexmedetomidine 1 μg/kg diluted with normal saline to make a volume of 10 ml over 10 mins (10 mins prior to induction). All patients were subjected to thorough preanaesthetic evaluation and educated about visual analogue pain score (VAS) of 0-10 prior to surgery (0-3=no pain, 4-7=discomfort, 8-10=severe pain). Tab alprazolam 0.25 mg at night before surgery and tab ranitidine 150 mg orally at night before and on morning of surgery was given to every patient.

Patients were kept nil orally 8 hrs prior to surgery. An 18 gauge cannula was inserted and intravenous infusion of crystalloid at 6-8 ml/kg was started. Standard monitoring including pulse oximetry, noninvasive blood pressure, end-tidal CO_2 and three-lead electrocardiography was done. Baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure(MAP),oxygen saturation (SpO_2) and $EtCO_2$ were recorded. Oral tab of study drug/placebo was given 1 hr prior to surgery with a sip of water. Anaesthetic and surgical technique was standardized and residual neuromuscular block was reversed with appropriate doses of IV neostigmine 0.05 mg/kg and IV glycopyrrolate 0.01 mg/kg. Patients were extubated when the respiration was spontaneous with adequate efforts and good muscle power and transferred to post anesthesia care unit for further monitoring. Vital parameters like HR, SBP, DBP, MAP, SpO_2 and $EtCO_2$ were noted before premedication and induction (baseline) at the end of induction and at laryngoscopy andat intubation (I_0) and then at 1, 3, 5, 10 mins after intubation as well as at start of pneumoperitoneum (P_0) and then after every 10 mins interval till the deflation of CO_2 and also at the time of extubation and 10 mins thereafter. Assessment of pain by VAS score and Sedation by Ramsay Sedation Scale (RSS) were recorded

at 30 min interval for 2 hrs postoperatively and subsequently at 1 hr intervals for 6 hrs and then at 12 hrs and at 24 hrs postoperatively. If VAS score was more than 3 (at rest), the patient was given inj. Tramadol 100 mg IV as rescue analgesic. The time to first rescue analgesic and total dose of analgesics in 24 hrs were noted. Patients with sedation scale of ≥3 were considered as sedated. Any episodes of nausea and vomiting, headache, dizziness and shoulder pain were recorded. Rescue anti-emetic inj. ondansetron 4 mg IV was given for nausea and vomiting.

Sample size

Sample size was calculated by assuming alpha error 5% and power of study 80%. Assumption of exposed group taken to be 95% with 10% margin of error, so total 90 patients were taken for study.

Statistical Analysis

Statistical analysis was done using SPSS software (version 17, SPSS, Chicago, IL). Data was presented as mean, standard deviation, median (range) or percentage. Quantitative data was analyzed using paired and unpaired t-test while categorical variables were analyzed by Chi-square test. *p* values less than 0.05 were considered significant.

Results

In our study Group P and group D were comparable regarding mean value of age, sex, weight of patients, duration of surgery and anesthesia (p>0.05) (Table 1). When comparing hemodynamic parameters during laryngoscopy and intubation (I_0), HR remain stable (84.77 ± 15.67) from baseline (84.90 ± 12.38) in group D while there was statistically significant increasein HR (95.5 ± 15.92) in group P (p=0.002) from baseline (86.20 ± 17.49). A significant decrease in the mean heart rate was observed in group D at 3 min after intubation (I_3)(79 ± 14) and at 5 min after intubation(I_5) (80.5 ± 18.1) when compared to baseline (84.90 ± 12.38) (p<0.05)) while in group P, a significant increase in the mean HR at (I_3) (89.59 ± 15.60 and at (I_5) (88.66 ± 16.12) from baseline (86.20 ± 17.49) was observed (Fig 1). No significant change was observed in HR from

Table 1: Comparison of demographic data between two groups

Demographic data	Group D (n=45)	Group P (n=45)	p value
Age (yrs)	42.7 ± 11.47	42.27 ± 11.29	0.846(NS)
Weight (kg)	61.38 ± 7.33	62.87 ± 5.50	0.651(NS)
Sex (M/F)	7/38	10/35	-
Duration of Surgery	59.77 ± 18.92	65.95 ± 13.21	0.06(NS)
Duration of Anesthesia	81.47 ± 20.84	79.13 ± 15.59	0.54(NS)
ASA Grade I/II	27/18	33/12	-

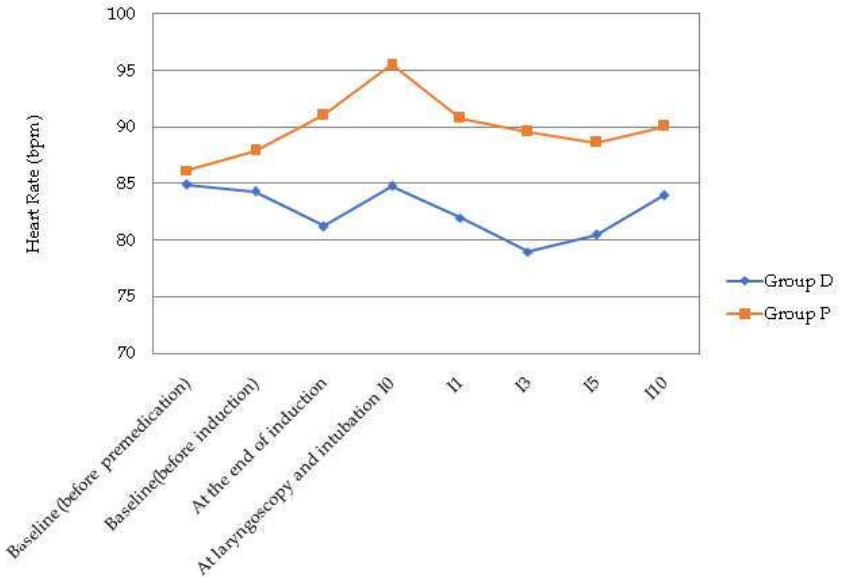

Fig. 1: Comparison of Heart Rate (HR) between two groups duringlaryngoscopy and intubation

baseline (P_0) at various time intervals following pneumoperitonium in both the group, however decrease in HR was more in group D as compared to group P at various time intervals. (Fig. 2). Asignificant decrease in MAP from baseline (101.00 ± 14.75) was observed in group D at 1,3,5,10 minute intervals following intubation (p<0.0001)) which was least at 3 min (87.45 +± 17.23) and in group P a significant rise in the mean MAP from baseline (100.93 ± 14.37) was observed at laryngoscopy and intubation(Io) (107.82 ± 18.20) (p<0.05) after that it remained stable at all other time intervals (Fig. 3). During pneumoperitoneum a significant increase in MAP was observed from baseline (start of pneumoperitoneum (P_0) (94.64 ± 16.19) till 30 min in group P which was maximum at 20 min (109.25 ± 15.05) (p<0.001) while in group D no significant rise in MAP was observed from baseline (Po)(89.23 ± 17.88) till deflation of CO_2(89.93 ± 10.91) (Fig 4). Mean values of VAS score postoperatively till 1 hr was less than 3 (2.48) in group D while it was (3.11) in group P, though

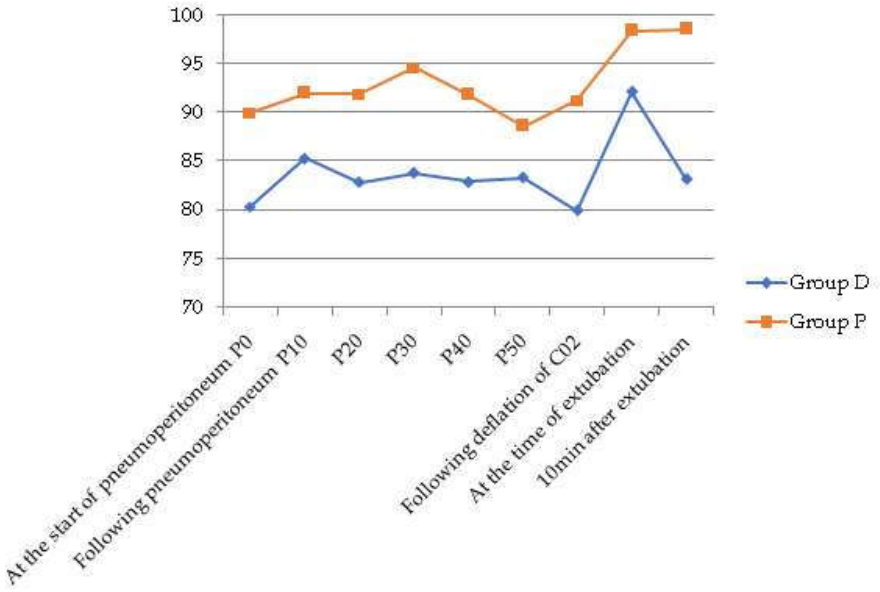

Fig. 2: Comparison of Heart Rate (HR) between two groups during pneumoperitoneum till 10 minutes after extubation in two groups

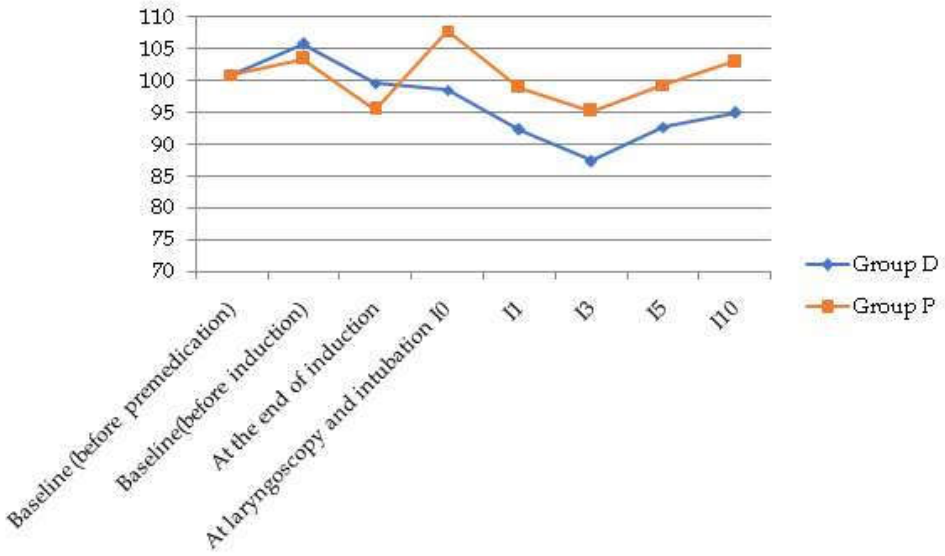

Fig. 3: Comparison of Mean Arterial Pressure (MAP) between two groups during laryngoscopy and intubation

after 1 hr VAS score was <3 in both group till 24 hrs. When comparing two group it was lower in group D at all time intervals (p<0.05). Mean values of RSS was lower in group P (1.00 ± 0.00) as compared to group D (1.14 ± 0.35) till 4 hours postoperatively after that it remained stable in both groups upto 24 hrs (Table 2). The time to request for first rescue analgesic was earlier in group P (37.5 ± 9.30) when compared to group D (58.06 ± 11.62), which was highly significant (p<0.001). Total requirement of rescue analgesic in 24 hrs period postoperatively was comparable in both the groups (Table 3) The incidence of intraoperative adverse effects and postoperative complications like hypotension, hypertension, tachycardia, bradycardia intraoperative and postoperative complication nausea, vomiting, dizziness, headache and shoulder pain were comparable between two groups (Table 4).

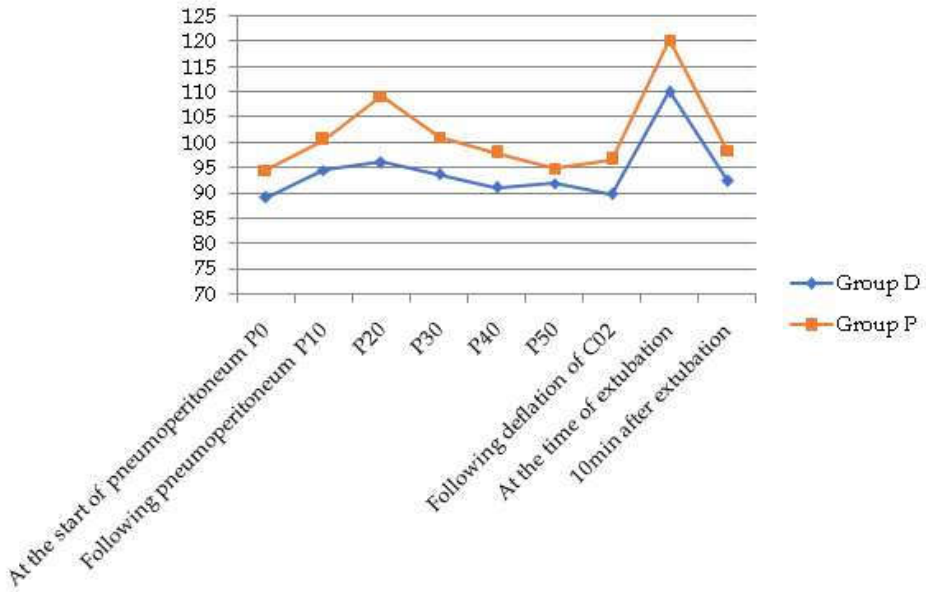

Fig. 4: Comparison of Mean Arterial Pressure (MAP) between two groups during pneumoperitoneum till 10 minutes after extubation in two groups

Table 2: Comparison of Visual Analogue Scale (VAS) Score and Ramsay Sedation Score (RSS) in between two groups

Time (min)	Visual Analogue Scale (VAS)			Ramsay Sedation Score(RSS)		
	Group D (Mean±SD)	Group P (Mean±SD)	P value	Group D (Mean±SD)	Group P (Mean±SD)	*p* value
30 min	3.05 ± 0.53	3.68 ± 0.56	0.000	3.57 ± 0.73	2.45 ± 0.50**	0.000
60 min	2.48 ± 0.59**	3.11 ± 0.49**	0.000	3.02 ± 0.66**	2.09 ± 0.29**	0.000
90 min	1.86 ± 0.55**	2.61 ± 0.49**	0.000	2.39 ± 0.72**	1.75 ± 0.44**	0.000
2 hr	1.50 ± 0.55**	2.16 ± 0.37**	0.000	1.95 ± 0.61**	1.23 ± 0.42**	0.000
3 hr	1.02 ± 0.66**	1.91 ± 0.29**	0.000	1.50 ± 0.51**	1.02 ± 0.15**	0.000
4 hr	0.66 ± 0.53**	1.57 ± 0.50**	0.000	1.14 ± 0.35**	1.00 ± 0.00**	0.011
6 hr	0.52 ± 0.51**	1.11 ± 0.32**	0.000	1.00 ± 0.00**	1.00 ± 00**	0.00
12 hr	0.09 ± 0.29**	0.98 ± 0.26**	0.000	1.00 ± 0.00**	1.00 ± 0.00**	0.00
24 hr	0.00 ± 0.00**	0.77 ± 0.42**	0.000	1.00 ± 0.00**	1.00 ± 0.00**	0.00

Data are mean ± SD, NS= Nonsignificant

D-Dexmedetomidine P- Pregabalin

**- Statistically significant (p<0.001).

Table 3: Data of patients requiring rescue analgesics in both groups

	Group D (n=45) (mean ± SD)			Group P (n=45) (mean ± SD)			*p* value
Time of 1st rescue Analgesic	58.06 ± 11.62			37.5 ± 9.30			0.0001
Total no of patients requiring rescue analgesics	1st dose	2nd Dose	3rd dose	1st dose	2nd Dose	3rd dose	–
	28	13	1	23	15	3	
Total dose of analgesic in 24 hrs	134.09 ± 52.57			147.72 ± 62.83			0.26

Data are mean±SD, NS= Nonsignificant
D-Dexmedetomidine P- Pregabalin
**- Statistically significant (p<0.001)

Table 4: Comparison of intraoperative adverse effect and postoperative complications between two groups

Variable	Group D (n=45)		Group P (n=45)		*p* value
Hypotension	3	6.66%	8	17.77%	0.10
Hypertension	2	4.44%	5	11.11%	0.23
Tachycardia	3	6.66%	9	20%	0.06
Bradycardia	5	11.11%	1	2.22%	0.09
Nausea	1	2.22%	3	6.66%	0.29
Vomiting	1	2.22%	2	4.44%	0.55
Dizziness	2	4.44%	6	13.33%	0.13
Headache	1	2.22%	4	8.88%	0.16
Shoulder pain	1	2.22%	2	4.44%	0.55

Data are mean±SD, NS= Nonsignificant
D-Dexmedetomidine P- Pregabalin
**- Statistically significant (p<0.001).

Discussion

Laparoscopic cholecystectomy is considered gold standard and one of the preferred surgery for gall bladder diseases under general anesthesia in the present era due to its well known advantages. However, like any other surgery it is also associated with sympathoadrenal response occurring due to direct laryngoscopy, tracheal intubation, extubation and pneumoperitoneum which evokes hemodynamic instabilities. Various methods have been used to attenuate stress response. This study was designed to compare oral pregabalin versus bolus dose of intravenous dexmedetomidine as premedication in attenuating the hemodynamic responses to laryngoscopy, intubation and also during pneumoperitoneum in laparoscopic cholecystectomy. The incidence of bradycardia was 11.11% in group D while 2.22% in group P, this difference may be due to highly selective α2 agonist action of dexmedetomidine resulting in sympatholysis. The incidence of tachycardia was 6.66% in group D while it was 20% in group P which reflects better hemodynamic stability of dexmedetomidine than pregabalin. A significant reduction in HR following loading dose of Dexmedetomidine (6 mcg/kg) after intubation and after 20 min of pneumoperitoneum as compared to saline group was observed in a study done by Vora K.S *et al*.[13]. Rastogi B *et al*.[10] studied the effect of two different doses of oral pregabalin (75 mg and 150 mg) as premedication and observed an increase in HR in group P_{150} from baseline (80.65 ± 3.84) after 1min of laryngoscopy (107 ± 2.41) which was similar to our study. Gupta K *et al*.[9] reported that after premedication with oral pregabalin (150 mg) and placebo, there was a significant increase in HR in both groups but the increase was less in pregabalin group. We recorded a decrease in MAP (98.61 ± 19.21) from baseline (101 ± 14.75) in group D at the time of laryngoscopy and intubation, while in group P there was a significant increase in MAP (107.82 ± 18.20) from baseline (100.93 ± 14.37). Maximum decrease in MAP was found in group D, at 3 min after intubation (87.45 ± 17.23) although there was no significant change in MAP from baseline was found in group P following intubation. When comparing both the groups, fall in MAP was significantly more in group D than in group P (p<0.05). This may be attributed to sympatholytic action of dexmedetomidine on α2A receptors located in brainstem vasomotor centre and difference in the route of administration of study drugs. Similar to our study Rastogi B *et al*.[10]

in compared the effect of two different doses of oral pregabalin (75 mg and 150 mg) and observed a decrease in MAP (87.06 ± 3.90) from baseline (93.15 ± 2.59) after induction in patients receiving pregabalin (150 mg). Meena R *et al.*[14] in 2016 studied the effect of oral diazepam [10 mg (HS) + 5 mg (1 hr before surgery)] with two different doses of oral pregabalin [75 mg (HS) + 150 mg, 300 mg (1 hr before surgery)] and reported significant increase in MAP (106.44 ± 6.24) from baseline (91.14 ± 4.16) with diazepam while increase in MAP was less in pregabalin group P_{150} (98.43 ± 7.78) from baseline (91.22 ± 6.90) which was similar to our study.

CO_2 insufflation along with trendelenburg position required in laparoscopic surgeries causes significant release of catecholamines, cortisol, renin and vasopressin leading to increase in systemic vascular resistance and pulmonary vascular resistance and tachycardia[7]. In our study an increase in MAP from baseline during pneumoperitoneum in bothgroups were observed, however this increase was more in pregabalin group when compared to dexmedetomidine groupthat shows dexmedetomidine is better than pregabalinin attenuating the stress response during pneumoperitionium, Vora KS *et al.*[13] also reported that dexmedetomidine is better than pregabalin in attenuating the stress response during pneumoperitonium. Manne GR *et al.*[15] reported significant decrease in MAP after starting the infusion (dexmedetomidine 1 µg/kg) and there was no significant rise in MAP during pneumoperitonium till release of CO_2 (p<0.001). Gupta K *et al.*[9] studied the effect of clonidine (200 µg) and pregabalin (150 mg) as oral premedication during laparoscopic cholecystectomy and observed that haemodynamic responses were attenuated by both drugs and were maintained throughout intraoperative period, however clonidine was superior to pregabalin for attenuation of haemodynamic responses to laryngoscopy and laparoscopy. Analgesic efficacy of dexmedetomidine and pregabalin in different doses has been studied in various studies with different results. Dexmedetomidine had a moderate analgesic effect with sedation due to its action on postsynaptic alpha-2 adrenergic receptor, located in locus coeruleus and receptors in the dorsal horn of spinal cord[20,21] The analgesic effect of pregabalin is due to binding of pregabalin at α-2-delta site with consequent reduction in release of excitatory neurotransmitter like norepinephrine, glutamate, substance P.[8,22-24] In our study, group P patients experienced more postoperative pain as compared to group D (p<0.05). The time to first request for rescue analgesic was earlier (37.5 ± 9.30) in group P than group D (58.06 ± 11.62)(p<0.001). The total dose of analgesic in 24 hrs was higher in group P (147.72 ± 52.57) as compared to group D (134.09 ± 62.83). Though this difference was statistically insignificant (p=0.26) but we observed that patients in group D were pain free in immediate postoperative period and more comfortable in 24 hrs. Pathak AS *et al.*[7] compared the two different doses of dexmedetomidine (1 mcg/kg and 0.7 mcg/kg) given preoperatively as bolus in patients undergoing laparoscopic surgery and found better postoperative analgesia with lower VAS scores and delayed time for first rescue analgesia in patients receiving dexmedetomidine 1 µg/kg. Esmat IM *et al.*[12] observed a significant reduction in VAS Score in patients receiving two different doses of pregabalin (150 mg, 300 mg) 1 hr prior to surgery. Pain scores were lower in pregabalin 300 mg. Sundar AS *et al.*[25] found no difference in VAS Score and total fentanyl requirement postoperatively among group P (PG_{150mg}) and group C (NS) at 6, 12 or 24 hrs after coronary artery bypass grafting (CABG) surgery. Dexmedetomidine and pregabalin also have anxiolytic and sedative properties. Dexmedetomidine provides sedation by stimulation of α2A and α2C receptors which are located in locus ceruleus in the spinal cord.Theanxiolytic property of pregabalin is by decreasing the synthesis of neurotransmitter glutamate to act on central nervous system. In our study the sedation score was higher in group D than group P at all time intervals (p < 0.05) but none of the patients in bothgroups had sedation score more than ≥4. Dexmedetomidine in a dose of 1 mcg/kg has been shown to cause increased sedation levels and need for oxygen supplementation by few authors[26,27]. Sebastian B *et al.*[17] found higher sedation scores in Dexmedetomidine groups (dex 0.5, 0.75 µg/kg) than normal saline (p < 0.05), Similarly Manne. GR *et al.*[15] also observed increased sedation levels in patients receiving low dose dexmedetomidine infusion (0.2 µg/kg/h, 0.4 µg/kg/h). In contrast to our study Parveen S *et al.*[19] found higher sedation score in pregabalin group (2.73 ± 0.55) as compared to oral clonidine (2.20 ± 0.41), this can be attributed to difference in the route of administration as we administered alpha-2 agonist dexmedetomidine IV. Anand LK *et al.*[18] showed that sedation score measured by somnolence sedation scale wascomparable between the control and pregabalin group (150 mg) (p > 0.05). No patient had sedation score of 3 and all patients were free of sedation at 6 hrs which is similar to our study. The adverse effects were found to be statistically insignificant in our study (p > 0.05).

In our study, the incidence of postoperative nausea and vomiting (PONV) was found higher in Pregabalin group (6.66%) than the dexmedetomidine group (2.22%), 2 patients from group D (4.44%) while 6 patients from group P (13.33%) experienced postoperative dizziness, 1 patient from group D while 4 patients in group P experienced headache and shoulder pain. All these complications were statistically insignificant in our study ($p > 0.05$). Esmat IM *et al.*[12] observed that postoperative vomiting was statistically significant in patients receiving pregabalin 300 mg ($p < 0.01$). Gupta P *et al.*[16] in 2017 and Meena R *et al.*[14] observed that only one patient in group P (150 mg) and 2 patients in group P (300 mg) suffered dizziness but it was statistically insignificant ($p > 0.05$).

Limitation of our study was that we could not measure stress mediators such as endogenous catecholamines or cortisol and dial concentration of sevoflurane. We did not use BIS monitoring and invasive blood pressure monitoring. A control group was not included in the study for comparison.

Conclusion

This studyconcluded that both dexmedetomidine (1 µg/kg IV bolus) and pregabalin (150 mg orally) is effective in attenuating haemodynamic stress response during laryngoscopy, intubation and pneumoperitoneum when given as premedication for laparoscopic cholecystectomy. Dexmedetomidine was found to be superior in ameliorating the haemodynamic responses to laryngoscopy and laparoscopy along with better postoperative analgesia without any significant adverse effects.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1422-1427
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.50

Study of the Effect of Different Temperatures on Quality of Subarachnoid Blockade using 0.5% Hyperbaric Bupivacaine for Infraumbilical Surgeries

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Abstract

Background: Factors affecting spread of local anaesthetic are baricity, position, volume injected, level of injection, concentration of local anesthetic, speed of injection, abdominal pressure (ascites, pregnancy) and other factors are density, viscosity and temperature of the local anaesthetics injected. Our study compares the effects on sensory and motor blockade when 0.5% hyperbaric bupivacaine is administered at various temperatures viz., 24°C, 37°C and 40°C intrathecally in patients coming for infraumbilical surgeries. *Methods:* In this study 90 patients, 30 in each group undergoing surgery below the umbilicus were randomly administered spinal anesthesia at 24°C (Group A), 37°C (Group B) and 40°C (Group C). Sensory blockade and two segment regression were assessed by pinprick and motor blockade with Bromage scale. *Results:* Study showed with increased temperature the cephalad spread of sensory dermatome was rapid and high. Drugs injected at room temperature (24°C) had slow onset of sensory and motor blockade (p<0.001). Two segment regression achieved from the maximum level also was rapid with increased temperature of the local anesthetic administered. *Conclusion:* The sensory and motor blockade is influenced by the temperature of the local anaesthetic that is administered following subarachnoid injection.

Keywords: Baricity; Density; Intrathecal; Viscosity; Warm hyperbaric bupivacaine.

How to cite this article:

Shobha Dhayalan, Asha Narayan Gowda, Raghavendra Rao. Study of the Effect of Different Temperatures on Quality of Subarachnoid Blockade using 0.5% Hyperbaric Bupivacaine for Infraumbilical Surgeries. Indian J Anesth Analg. 2019;6(4): 1422-1427.

Introduction

Spinal anesthesia involves the use of small amounts of local anaesthetic (LA) injected into subarachnoid space to produce reversible loss of sensation and motor function producing excellent operating conditions for infraumbilical surgeries. Apart from the factors like baricity, position, volume injected, concentration of LA and few other factors are density and viscosity of the LA which influences the distribution of sensory and motor blockade[1-6] where further density and viscosity is influenced by the temperature[7-10] of the LA. The onset of blockade, extent and two segment regression with warming of bupivacaine from room temperature 24°C to 37°C and 40°C was assessed.

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Received on 04.05.2019, **Accepted on** 08.06.2019

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Methods

This was a prospective observational study conducted from Sep 2018 to Jan 2019 after obtaining approval from Institutional Ethical Committee and was registered under CTRI (CTRI/2018/09/015610). Inclusion criteria were ASA physical status I and II, age group of 18-60 years of either sex, posted for elective infraumbilical surgeries and were willing to participate in the study. Exclusion criteria were any contraindications for neuraxial blockade, allergic to LA, any coagulation disorder and localised infection over injection point. Randomization was performed with computer generated codes maintained in sequentially numbered, opaque envelopes into 3 equal groups. All patients were examined a day before surgery and were kept fasting overnight. Once the patients were shifted to the operating table standard ASA monitors were attached. Non-invasive parameters 5 lead electrocardiogram, systolic, diastolic and mean arterial pressure and pulse oximetry were documented. Intravenous access was secured and Ringer Lactate solution 10 ml/kg/hr was started when spinal anesthesia block was performed. With strict aseptic and universal precautions subarachnoid block was performed using 25/26 G Quincke Babcock spinal needle in L_3-L_4 space with patient in lateral position. The safety of the study drug with warming as per the study[11] was taken into consideration. Group A received 3ml of 0.5% hyperbaric bupivacaine at room temperature 24°C, Group B received the same volume at 37°C and Group C received 3 ml at 40°C where the ampules were kept in water bath at a particular temperature for particular time to raise the temperature of the solution inside the ampule. The investigator not involved in the study prepared the drug. The study drug was drawn in the syringe, with in 20 sec of retrieval drug was injected over 10-15 sec once free flow of CSF was obtained after dural puncture. This time was considered as zero time of the study and all measurements were recorded from this point, following which patients were made to lie supine. Sensory anesthesia was assessed by pinprick method using 25-G short bevelled needle at 1 min interval for first 10 min, 5 min interval for next 60 min during surgery after spinal anesthesia and then every 10 min interval until regression to L_1. Time of onset of sensory block- L_1 dermatome, time to achieve T_{10} level, highest ascent achieved and two segment regression from the highest level achieved were recorded. Motor block was assessed every minute for first 15 min, then at every 5 min until the resolution of the motor block using Bromage scale (Appendix). Time of onset of motor block (Bromage scale 2) and time required for maximum level of motor block was recorded. Haemodynamic variables were monitored according to the institutional protocol. The patients were shifted to the post anesthesia care unit following surgery where haemodynamic variables was documented and discharged to the ward once recovered from sensory and motor blockade. Drop in systolic blood pressure of >30% Inj Mephentermine 6 mg IV and drop in heart rate below 50 beats/min Inj Atropine 0.6 mg IV was administered. The incidence of any adverse effects such as shivering, nausea and vomiting was recorded and treated accordingly.

Results

There was no significant differences between the Groups in terms of demographic data (Table 1).

Demographic data are presented as mean SD. Analysis of variance (ANOVA) has been used to find the significance of study parameters between the groups. Chi-square /Fisher Exact test has been used to find the significance of study parameters on categorical scale between the groups.

Speed of onset of sensory and motor block was faster in Group C (40°C) and Group B (37°C) with maximum sensory level achieved. There was moderate decrease in heart rate and blood pressure in Group C necessitating intervention but was not statistically significant. Time for two segment regression from the highest dermatome achieved was faster in Group C and Group B when compared to Group A (24°C) (Table 2 and Graph 1-5).

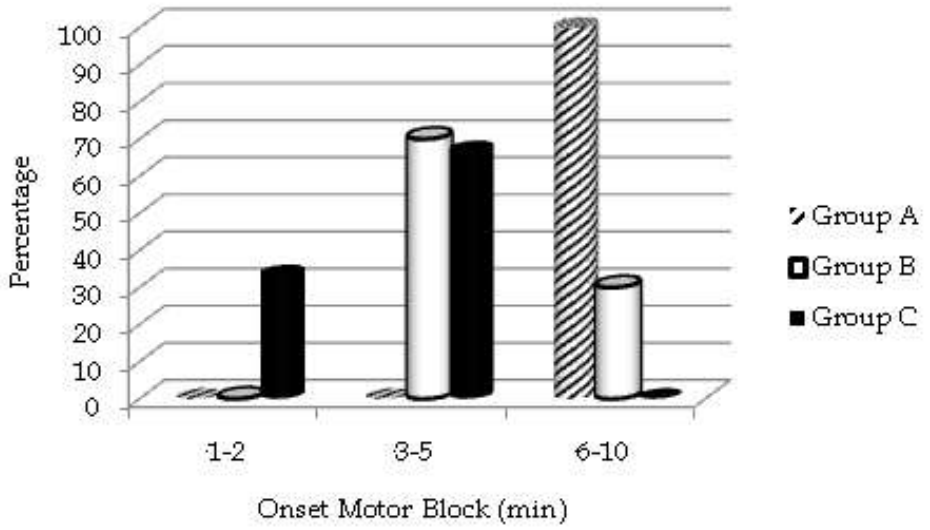
Table 1: Demographic characteristics

Characteristics	Group A (24°C)	Group B (37°C)	Group C (40°C)
No of patients	30	30	30
Age (yrs)	36	37	36
Sex (M:F)	20/10	18/12	17/13
Height (cm)	158	161	159
Weight (kg)	55	61	60

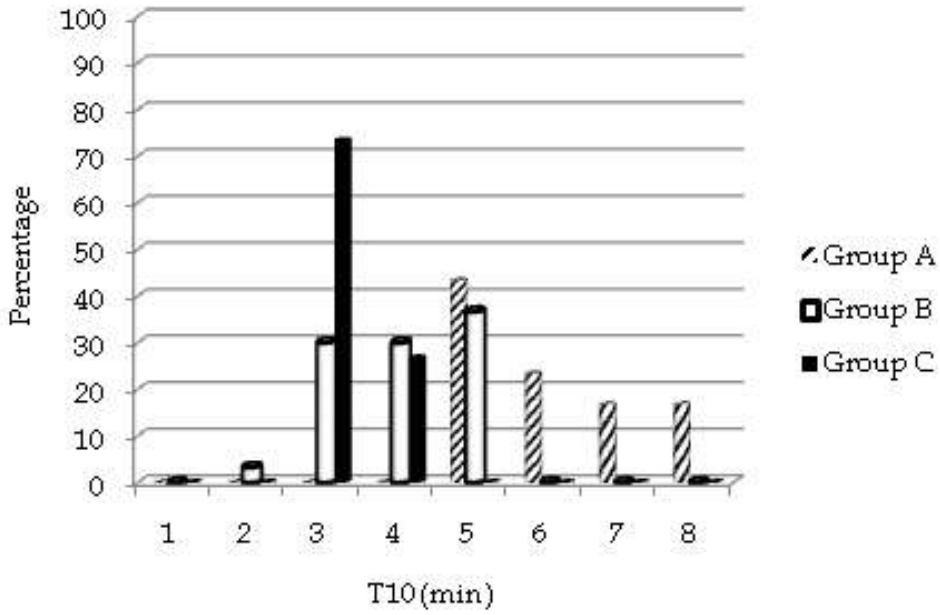
Data are Mean ± SD (Min-Max)

Table 2: Characteristics of Neural Block

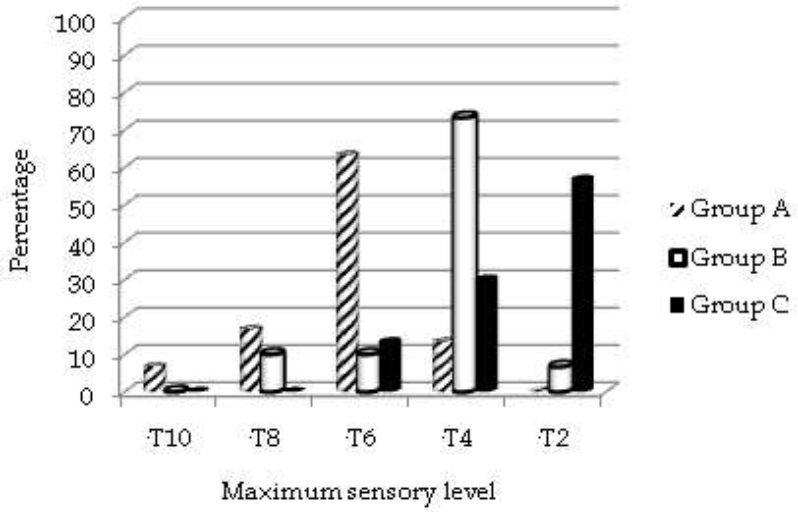
Minutes	Group A (24°C)	Group B (37°C)	Group C (40°C)	*p* value
Time for onset of sensory block (L1)	4.2 ± 0.8	2.6 ± 0.7	1.4 ± 0.5	<0.001
Time to reach T10 dermatome	6 ± 1	4 ± 0.9	3 ± 0.4	<0.001
Highest level of sensory block (MSL)	T6 (63%)	T4 (57%)	T2 (57%)	<0.001
Time for maximum level of sensory block (TMSL)	8 ± 1	6 ± 0.8	4 ± 0.8	<0.001
Time for onset of Motor block (B2)	7 ± 0.9	4 ± 0.8	3 ± 0.8	<0.001
Time for maximum level of motor block (TMMB)	8 ± 1	6 ± 0.8	4 ± 0.8	<0.001
Time for two segment regression (TSR)	103 ± 10	55 ± 8	51 ± 8	<0.001



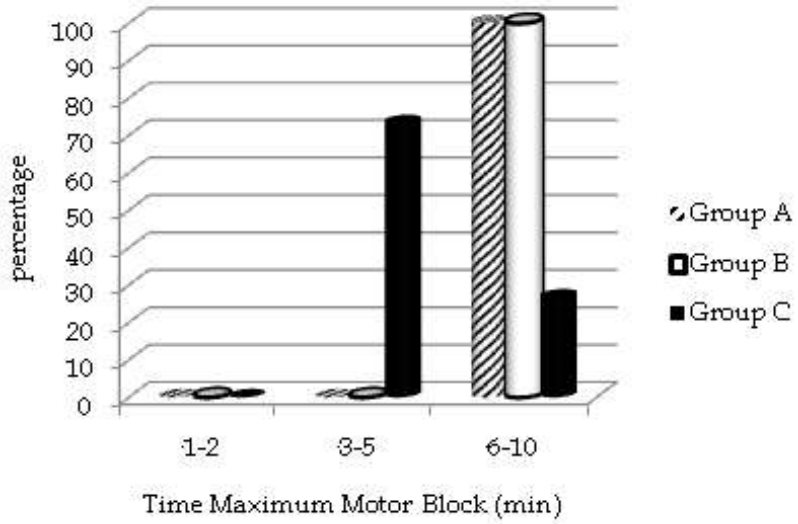
Graph 1: Onset of Motor Blockade (Bromage 2)



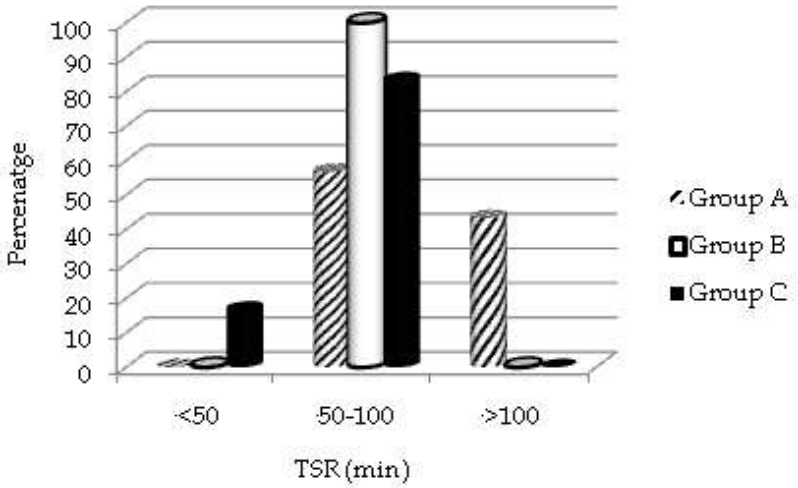
Graph 2: Time to reach T10 dermatome



Graph 3: Time to reach maximum sensory level



Graph 4: Time to reach maximum motor blockade



Graph 5: Time for two segment regression

Discussion

Large comparative studies and multiple prospective randomized control trials have reported with increase in temperature of bupivacaine there was faster onset of sensory blockade. In addition our study demonstrated when 0.5% hyperbaric bupivacaine was administered intrathecally at 24°C (room temperature) had slow onset of sensory blockade. At 37°C and 40°C when 0.5% hyperbaric bupivacaine was administered there was rapid onset of sensory and motor blockade. There was higher level of sensory block achieved. Regression of two segment from highest dermatome achieved also was faster with 37°C and 40°C compared to 24°C.

Miriam E Tucker[12] had failed spinal anesthesia in a group of 14 cases who underwent C-sections which was believed to be the result of exposure of the anaesthetic to lower temperatures. Due to which there will be significant clinical consequences like pain during surgery, repeat subarachanoid block or conversion to general anesthesia. The other contributing factors for failed neuraxial anesthesia like technical failure has to be identified and managed accordingly.

The density of LA is key determinant of LA distribution with in the subarachnoid space[13]. CSF density varies between 1.00028 to 1.00100 g/ml[14]. For every increase in temperature by 1°C between 23°C and 37°C the density of all plain solutions fall by 0.0003 mg/ml. Viscosity and density of the LA reduces with warming[15] and affects the distribution of spinal anesthesia. The time of onset of LA is related to the pka values which is between 7.8 and 9.1 when there will be a higher percentage of non-ionized free base which is close to the physiologic pH[16]. So a more rapid onset and higher level of sensory block is achieved[17,18].

Aria *et al.*[19] Showed increase in the fraction of unionized drug due to decrease in pka of LA solution when the temperature of the LA was increased which was demonstrated by increased uptake of LA by mammalian nerve with increased temperature.

Data from Higuchietal[20] proved strong relationship between CSF density and highest level of sensory block achieved.

Depending on thermodynamics, temperature serves to gauge the intensity of the thermal energy that is an actual energy of motion (kinetic energy) of the individual mobile particle matter. Higher level of sensory block achieved could be due to increased temperature with which molecular kinetic energy is increased and number of individual mobile particles increases.[21]

Limitations

Even though the waterbath was within the operating room the temperature of the ampule will drop once it is retrieved from the waterbath, so it was impossible to administer the drug exactly at 40°C or 37°C. The temperature of the injectate was not directly measured. In our research centre thermostatically controlled waterbath/incubator was not available. So precise temperature was not maintained. Waterbath which was used in our setup was relatively economical which can be used in low setup hospitals but precautions of contamination has to be taken.With precautions, prewarming of LA solutions is inherently safe. Using thermostatically controlled waterbath or intravenous solution warmer LA ampules may be warmed upto 43°C. Ensure that overheating is not allowed to occur[10]. Dry heating may prevent the risk of undetected contamination by water from heating in a water bath.

Conclusions

With increase in temperature of hyperbaric bupivacaine from 24°C to 37°C and 40°C for spinal anesthesia there is higher ascend of sensory block, rapid onset and faster regression of sensory and motor block. Warmed bupivacaine can be preferred in ambulatory surgery and in setups with high turnover rate of surgeries. With smaller dose we can achieve a high level of blockade so can reduce the dosage of the LA without much of change in haemodynamics which must be confirmed by further studies.

Source of support: Nil

Presentation at a meeting: Nil

Conflict of interest: None

Appendix: Bromage scale

Bromage 1- Free movement of legs and feet.

Bromage 2 - Just able to flex knee with free movement of the feet.

Bromage 3 - Unable to flex knees, but with free movement of the feet.

Bromage 4 - Unable to move the legs or feet.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1428-1433
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.51

Comparative Evaluation of the Role of 0.5% Hyperbaric Bupivacaine with and without Clonidine under Spinal Anesthesia

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Abstract

Background: Among the various modalities of regional anesthesia, spinal anesthesia is widely practiced. Clonidine is of interest because it preserves cardiovascular reflexes, provides sedation, greater intra operative haemodynamic stability and a reduction in anaesthetic and postoperative analgesics requirements and also has a marked opioid sparing effect. This study was carried out to compare the hemodynamic parameters between 0.5% hyperbaric Bupivacaine with and without Clonidine at various doses. *Methods:* This double blind randomized controlled trial was carried out in a total of 60 patients of age group 20 to 60 years of ASA grade I and II undergoing gynaecological and other lower abdominal surgery under spinal anesthesia. The control group consisted of 15 mg 0.5% hyperbaric bupivacaine while the experimental group was further classified into three groups based on the additional dosage of Clonidine. Presence of hypotension and bradycardia was documented. *Results:* Bradycardia was present in 73.3% of the participants in group IV while it was nil in Group I (controls). Hypotension was present in 73.3% of the participants in group IV while it was absent in group I participants. There was a statistically significant difference in the hypotension between group I & III, I & IV and II & IV ($p<0.05$). *Conclusion:* our study demonstrates that intrathecal clonidine at the usual dose of 1µg/kg is associated with bradycardia and relative hypotension. Therefore, 0.75 µg/Kg of clonidine is the preferred dose for addition to 0.5% hyperbaric bupivacaine in patients undergoing gynaecological and lower abdominal surgeries.

Keywords: Bradycardia; Clonidine; Hyperbaric bupivacaine; Hypotension; Spinal anesthesia.

How to cite this article:

Ashwini T, Subash S. Ananda Bhat. Comparative Evaluation of the Role of 0.5% Hyperbaric Bupivacaine with and without Clonidine under Spinal Anesthesia. Indian J Anesth Analg. 2019;6(4):1428-1433.

Introduction

Regional anesthesia has been advantageous to patients, surgeons and anaesthesiologists alike for many years now due to the simplicity of the method, preservation of consciousness, avoidance of airway instrumentation and rapid recovery with significant postoperative analgesia.[1] Among the various modalities of regional anesthesia, spinal anesthesia is widely practised because of its technical simplicity and a high success rate. It is a central neuraxial block in which drugs are injected into the subarachnoid space to produce sympathetic, sensory and motor block. It has the advantage of minimal systemic absorption of drugs

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Received on 15.05.2019, **Accepted on** 19.06.2019

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as compared to the drugs injected intravenously resulting in less physiological disturbances and negligible systemic side effects.

Although Lidocaine (Lignocaine), a synthetic local anaesthetic had been widely used due to its safety and popularity, recent studies have examined its effects on transient neurological symptoms following its use for subarachnoid block.[2] However, Bupivacaine has increased potency over lignocaine and is commonly used as local anaesthetic for spinal anesthesia although its duration of action is shorter.[2]

A number of drugs e.g. opioids, benzodiazepines, neostigmine and ketamine have been used intrathecally as an adjuvant to local anaesthetics.[3] The purpose of combining adjuvants with local anaesthetics is to lower dose of each agent, improve analgesic efficacy and reduce the severity of side effects. Most commonly used intrathecal adjuvants are opioids. They improve the quality of intraoperative analgesia and prolong the postoperative analgesia without significant motor or autonomic blockade. However, side effects such as pruritus, nausea and vomiting, urinary retention and delayed respiratory depression have prompted further research towards non-opioid analgesics with less serious side effects.

Clonidine is known to increase both sensory and motor blockade of local anaesthetics.[4] Intrathecal clonidine has been used as an adjuvant to local anaesthetics in various surgical procedures without any clinically significant side effects.[5] Clonidine is of interest because it preserves cardiovascular reflexes, provides sedation, greater intra operative haemodynamic stability and a reduction in anaesthetic and postoperative analgesics requirements and also has a marked opioid sparing effect. Moreover, intrathecal clonidine also prolongs the duration of hyperbaric bupivacaine spinal block.[6,7] Previous studies have described the use of clonidine in a wide range (15 µg–150 µg). However, the dose response relationship of using clonidine as an adjuvant is less explored. An insight into the role of Clonidine as adjuvant will help in achieving effective regional anesthesia with minimal adverse effects.

The present study is to assess the haemodynamic response and post operative analgesia provided by low dose (0.5, 0.75, 1.0 µg/kg body weight) intrathecal clonidine admixed with 0.5% hyperbaric bupivacaine as compared to 0.5% hyperbaric bupivacaine alone in patients undergoing gynaecological and other lower abdominal surgeries.

Objectives

This study was carried out to compare the hemodynamic parameters between 0.5% hyperbaric Bupivacaine with and without Clonidine at various doses.

Materials and Methods

Study setting and participants

This double blind randomized controlled trial was carried out in the Department of Anaesthesiology of a tertiary teaching institution for a period of four months. A total of 60 patients of age group 20 to 60 yrs of ASA grade I and II undergoing gynaecological and other lower abdominal surgery under spinal anesthesia were selected for the study.

Exclusion criteria

- Patients with spine abnormalities
- Presence of skin infection or local cellulitis.
- Presence of systemic disorders including cardiovascular, neurological, hematological and coagulation disorders.

Randomization

The participants were randomized into

Group I (control group) (15 mg of 0.5% hyperbaric bupivacaine)

Group II (Study Group): 15 mg of 0.5% hyperbaric bupivacaine + clonidine (0.5 µg/kg)

Group III (Study Group): 15 mg of 0.5% hyperbaric bupivacaine + Clonidine (0.75 µg/kg)

Group IV (Study Group): 15 mg of 0.5% hyperbaric bupivacaine + Clonidine (1 µg/kg)

Randomization was carried out using computer generated random numbers.

Sample size and sampling technique

All the patients who underwent elective surgical procedure under spinal anesthesia and were selected through the selection criteria participated in the study. A total of 60 patients were selected and were randomized into four treatment groups, with 15 participants in each group.

Ethical approval and Informed consent

Approval was obtained from the Institutional Ethics Committee prior to the commencement of

the study. Each participant was explained in detail about the study and informed consent was obtained prior to the data collection.

Data collection

Pre anaesthetic work up was carried out on all the participants. All the participants received T. Alprazolam 0.25 mg premedication on the day of surgery. In the operation theatre, the baseline pulse rate and blood pressure was recorded on all the participants. Before the subarachnoid block, preloading was done with 20 ml/kg of Ringer Lactate solution.

Procedure

On positioning the patients in lateral decubitus or sitting position, under complete aseptic precautions, lumbar puncture was performed with a 25 gauge Quincke's spinal needle. After ensuring free flow of CSF patients in control group were injected with 15 mg of 0.5% hyperbaric bupivacaine and patients in study group were injected with 15 mg of 0.5% hyperbaric bupivacaine with clonidine 0.5 µg/kg, 0.75 µg/kg and 1 µg/kg according to the groups. The total volume of solution to be injected intrathecaly was adjusted to 3.5 ml by adding normal saline. Immediately after injecting the drug the patients were turned supine and oxygen was administered. The following data was recorded during the course of anesthesia –

1. Intra operative monitoring of blood pressure every five minutes for 30 minutes followed by every 15 minutes till the completion of surgery.
2. Total dose of analgesia
3. Duration of surgery.

Operational definitions

Hypotension was defined as fall in systolic blood pressure more than 20% of baseline value or systolic blood pressure less than 90 mm of Hg in the first 20-30 minutes after giving the block. Bradycardia was defined as pulse rate less than 60 per minute. Hypotension was treated with rapid administration of intravenous fluids and use of vasopressors (injection mephentermine 3 mg iv) if needed. Supplemental oxygen was given to every patient through venti-mask during the surgery.

Data analysis

Data was entered and analyzed using SPSS ver. 20 software. Descriptive statistics were expressed in percentages. Mean scores of sedation and grades of motor blockade were compared with background characteristic using Independent sample t test and chi square test respectively. A p value <0.05 was considered statistically significant.

Results

This study was carried out a total of 60 participants, with 15 in each group. The mean age of the participants was similar in all the four groups with mean values ranging from 39.27 to 41.73 years. Similarly, the average weight of the participants was similar among the four groups, ranging from 53.33 to 57.33 kgs. (Table 1) Majority of the participants were females in all the four groups. (Fig. 1) The mean duration of surgery was highest among the controls (Group I), wherein the surgeries last for an average of 130 minutes (Fig. 2).

Heart rate was measured and evaluated throughout the course of surgery for all the four groups. Bradycardia was present in 73.3% of the participants in group IV while it was nil in Group I (controls). (Table 2) We observed a statistically significant correlation with respect to bradycardia between Group IV and all the other groups. The observed difference was statistically significant (p<0.005) (Table 3).

Systolic and diastolic blood pressure was recorded from the baseline throughout the surgery and hypotension was identified. Hypotension was present in 73.3% of the participants in group IV while it was absent in group I participants. (Table 4) There was a statistically significant difference in the hypotension between group I & III, I & IV and II & IV (p<0.05) (Table 5).

Table 1: Background characteristic of the study participants

S. No	Characteristic	No of patients	Mean ± S.D	Range
1	*Age*			
	I	15	41.73 ± 11.16	25-60
	II	15	40.73 ± 7.27	30-60
	III	15	39.27 ± 10.09	21-60
	IV	15	39.67 ± 11.39	16-56
2	*Weight*			
	I	15	55.67 ± 4.95	50-65
	II	15	57.33 ± 4.58	50-60
	II	15	53.33 ± 4.88	50-60
	IV	15	56.00 ± 5.07	50-60

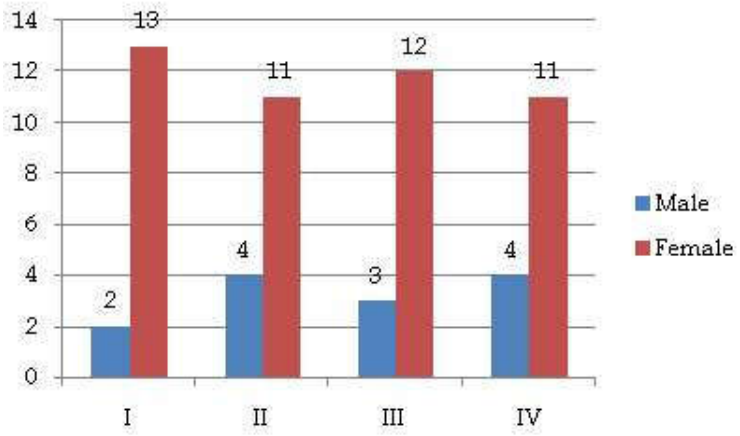

Fig. 1: Gender distribution among the participants:

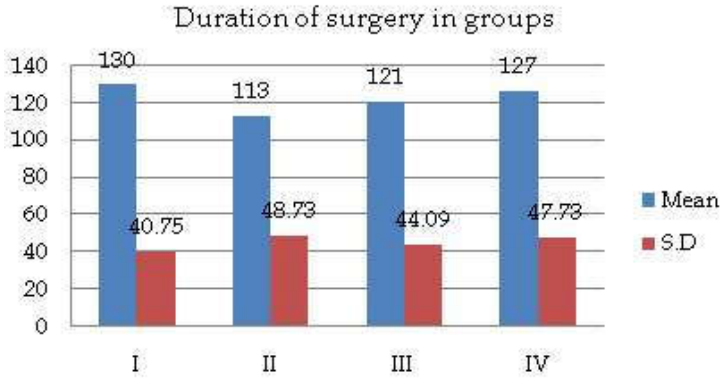

Fig. 2: Mean duration of surgery among all the groups

Table 2: Number of patients having bradycardia (HR <60 bpm)

S. No	Characteristic	Groups							
		I	(%)	II	(%)	III	(%)	IV	(%)
1	*Bradycardia*								
	Yes	0	0.0	2	13.3	4	(26.7)	11	(73.3)
	No	15	100.0	13	86.7	11	(73.3)	4	(26.7)

Table 3: Association between groups for Bradycardia and hypotension

S. No	Characteristic	Chi Sq	*p*
1	*Bradycardia Groups*		
	I vs IV	12.57	0.0001
	II vs IV	13.67	0.003
	III vs IV	7.52	0.027

Table 4: Number of patients having hypotension

S. No	Characteristic	Groups							
		I	(%)	II	(%)	III	(%)	IV	(%)
1	*Hypotension*								
	Yes	0	0	2	13.33	5	33.33	11	73.33
	No	15	100.0	13	86.67	10	66.67	14	26.67

Table 5: Association between groups for hypotension

S. No	Characteristic	Chi Sq	*p*
1	*Hypotension group*		
	I vs III	8.15	0.042
	I vs IV	12.37	0.0001
	II vs IV	16.17	0.003

Discussion

Spinal anesthesia is widely practised for surgeries of lower abdomen and lower limb of body because of its technical simplicity and a high success rate. Local anaesthetics are the most common agents used for this purpose but they are associated with short duration of action and thus requiring analgesic intervention in the early postoperative period. To enhance and prolong the effect of local anaesthetics and reduce their side effects many drugs have been used intrathecally in combination with local anaesthetics. These drugs are called as adjuvants.

Clonidine (a selective partial α_2 adrenergic agonist) has been used as an adjuvant to local anaesthetics intrathecally in various surgical procedures without any clinically significant side effects. Earlier studies have described the use of clonidine in a wide range (15-150 µg). However, the best regimen remains unknown.

In the present randomized, double blind study, there was a significant difference in the mean heart rate and blood pressure between control and experimental group, after 15 minutes of initiation of anesthesia. Similar statistical significance was observed with all the three experimental groups, from the 15th minute onwards in comparison with controls ($p < 0.05$). Our findings were in consonance with the study by P.S. Shetty *et al.* 2006.[3] Similar results were shown by Grandhe *et al.* 2008.[8] Clonidine is known to exert its hemodynamic effects by acting at several sites, either in the central nervous system or in the periphery. Clonidine decreases the heart rate by a presynaptic mediated inhibition of nor-epinephrine release and by direct suppression of atrioventricular node after systemic absorption. The potential for hypotension after spinal clonidine has been noted.

The hemodynamic effects of clonidine are complex and depend on factors such as plasma concentration, route of administration and presence and absence of anesthesia. It has been demonstrated that intrathecal clonidine has depressed effect on systemic blood pressuere, mediated by spinal α_2 adreno receptors. Similar results were shown by Kriton *et al.* 1992[9] It was also observed that the diastolic arterial pressure decreased significantly after intrathecal clonidine compared to control group from 15 to 120 min. Our observations were similar to several published studies.[10,3,8]

Conclusion

The number of participants who developed hypotension was increasingly higher in the experimental groups compared to the control groups and this was statistically significant. A higher dose of Clonidine attributed heavily to the development of hemodynamic changes. In conclusion our study demonstrates that intrathecal clonidine at the usual dose of 1 µg/kg is associated with bradycardia and relative hypotension. Therefore, 0.75 µg/Kg of clonidine is the preferred dose for addition to 0.5% hyperbaric bupivacaine in patients undergoing gynaecological and lower abdominal surgeries.

Conflict of interest: Nil

Funding: Nil

Ethical approval: Obtained

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1434-1437
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.52

Comparison of Levobupivacaine with or without Epinephrine for Lumbar Spine Surgery

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Abstract

Introduction: The aim was to establish if a decrease in the amount of epinephrine from 1:200,000 to 1:400,000 added to epidural levobupivacaine produces a comparable decrease in local anaesthetic assimilation from the epidural space while holding the similar clinical effectiveness and acceptability in patients undergoing elective lumbar spine surgery. *Materials and Methods:* A total of 120 patients with ASA physical status 1 to 3 and aged 18 – 85 years, who were schedule to undergo elective lumbar spine surgery, were enrolled for the study. Total dose of 75 mg was administered. The end of injection of study drug was termed "Time 0" for the purposes of subsequent patient assessment. Intraoperative sedation was offered with added IV midazolam and propofol as essential at the judgment of the anaesthesiologist. *Results:* Levobupivacaine 0.5% produces comparatively small motor blockade. In fact, in 53% of all patients studied, no motor block of the lower extremities could be demonstrated. even though the addition of either 1:200,000 or 1:400,00 epinephrine tended to increase the degree of motor blockade, it was not statistical significance. in addition, in those patients who did build up some degree of motor blockade, its period was not diverse among both the groups. *Conclusion:* Present Study reveals that 0.5% levobupivacaine, with or without epinephrine, is a appropriate anaesthetic for utilize in lumbar spine surgery. The addition of epinephrine be likely to increase the duration of blockade, diminish the ensuing local anaesthetic concentration, and advance intraoperative anaesthetic quality, even though statistical significance was not there for any T10 was achieved within 15 minutes of administering the epidural injection in all patient groups.

Keywords: Levobupivacaine; Epinephrine; Lumbar spine surgery.

How to cite this article:

Vijay Kumar, Anil Ratnawat. Comparison of Levobupivacaine with or without Epinephrine for Lumbar Spine Surgery. Indian J Anesth Analg. 2019;6(4): 1434-1437.

Introduction

Spinal anesthesia is the largely used technique for infraumbilical surgeries since its unmatchable dependability, cost effectiveness, effectual analgesia, muscle relaxation and long-lasting postoperative analgesia. Recent advances in anesthesia have authorized added surgeries to be carry out on day case basis.[1] The chattels of an anaesthetic agent used for day case surgeries in spinal anesthesia should have reduced incidence of anesthesia related difficulties, should offer sufficient postoperative analgesia and permit early patient discharge. Levobupivacaine, a pure S(−) enantiomer of bupivacaine is a long acting amide local anaesthetic

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Received on 22.05.2019, **Accepted on** 19.06.2019

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which creates disparity neuraxial block, which is, early onset and long-lasting duration of sensory block with shorter duration of motor block and lower cardiac toxicity.[2,3] Levobupivacaine has been extensively utilized in ambulatory surgeries after the growth of low dose spinal anesthesia technique. To advance the block characteristics of intrathecally administered low dose local anaesthetics, addition of adjuvant is necessity. Intrathecal opioids augment sensory block without prolonging motor and sympathetic block.[3,4]

Various central nervous system (CNS) and cardiovascular unfavourable reactions accounted in the literature following inadvertent intravascular injection or intravenous regional anesthesia have been linked to the R (+) isomer of bupivacaine.[5] The levorotatory isomers were exposed to have a secured pharmacological profile with fewer cardiac and neurotoxic unfavourable effects. The diminished toxicity of levobupivacaine is credited to its quicker protein binding rate. The pure S (−) enantiomers of bupivacaine, i.e., ropivacaine and levobupivacaine were therefore initiated into the clinical anesthesia practice.[6,7] Levobupivacaine has been newly introduced into Indian market and is being extensively utilized in a variety of health set-ups. Such an increased practice commands certification of evidence based literature with regards to jeopardy and security concerns as well as clinical issues allied to levobupivacaine.[8,9]

The aim of this study was to decide whether a reduction in the amount of epinephrine from 1:200,000 (5.0 g/mL) to 1:400,000 (2.5 g/mL) added to epidural levobupivacaine produces a alike decrease in local anaesthetic absorption from the epidural space while keeping the similar clinical effectiveness and acceptability in patients undergoing elective lumbar spine surgery.

Materials and Methods

A total of 120 patients with ASA physical status 1 to 3 and aged 18–85 years, who were schedule to undergo elective lumber spine surgery were enrolled for the study. All the participants were explained about the study and written inform consent was taken from all the patients. The exclusion criteria followed were: any allergy to local anesthesia, history of renal or hepatic, respiratory or cardiac diseases or neuromuscular or psychiatric condition. All the patients were premedicated with IV midazolam (1–5 mg) after the IV infusion of 500 ml of lactated Ringer's solution. At the L1-2 interface 1% Lidocaine was used to infiltrate the subcutaneous tissue. Epidural space was identified. After negative aspiration, the patients were randomized to receive one of the two study solutions: 0.5% levobupivicaine without epinephrine and 0.5% levobupivicaine with epinephrine incrementally over a period of 3 min period.

Total dose of 75 mg was administered. The end of injection of study drug was termed "Time 0" for the purposes of subsequent patient assessment. Intraoperative sedation was supplied with additional IV midazolam and propofol (25–100 g kg1 min1) as essential at the judgment of the anaesthesiologist. The chief usefulness measure was the duration of effective anesthesia, defined as the period of time from achieving bilateral T10 blockade to the time of bilateral regression to T10. Secondary efficacy measures incorporated peak block height, time to reach peak block, time to two-segment regression, time to regression to T10, and time to complete regression. Levobupivacaine levels were determined with liquid chromatography-mass spectrometry, with limits of determination of 10 ng/mL and coefficients of variation at these limits of approximately 0.8%.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA).

Descriptive statistics included computation of percentages, means and standard deviations. For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

A total of hundred and twenty patients were included into the study for the treatment. All the patients meet the criteria and were included in the study. All the patients were divided into two groups evenly. There was no dissimilarity in age, sex or body mass among the groups (Table 1). The mean time to onset of sensory block for surgery and effective duration were same in both the groups. (Table 2) Levobupivacaine 0.5% produces relatively little motor blockade. In 53% of all patients studied, no motor block of the lower extremities could be established (Table 3). even though the adding of either 1:200,000 or 1:400,00 epinephrine tended to augment the degree of motor blockade, this did not have statistical significance. in addition, in patients

who did build up a number of degree of motor blockade, its duration was not different among both the groups (Table 3).

In general quality of intraoperative epidural block was measured by the researcher as "excellent" or "good" in 85% of patients. There was fervent agreement between block quality ratings by the anesthesiologist and the surgeon ($p < 0.0001$). Even though patients in the Plain Levobupivacaine group had the leastt time before requesting analgesics, it was not also statistical significance. There were no differences between groups in time to first impulsive voiding after surgery ($p = 0.58$). Nausea (26%) and hypotension (18%) were the most common side effects attributed to study drug.

Table 1: Demographs of patients

Variable	Levobupivacaine plain solution	Levobupivacaine with 1:400,000 epinephrine
Age (yr)	60	56
Sex (M/F)	34/36	28/32
Height (cm)	165	170
Weight (kg)	80	82
Midazolam (mg)	3	4
Propofol	52	54
Time to first spontaneous void (min after t =0)	354	352

Table 2: Efficacy results – sensory block

Variable	Treatment group	Mean + SD
Onset to T10	LP	10 ± 9
	L400	11 ± 6
Time to two-segment regression (min)	LP	110 ± 50
	L400	112 ± 60
Duration min (T10-T10)	LP	187 ± 60
	L400	200 ± 60
Time to complete regression	LP	350 ± 110
	L400	378 ± 94

Table 3: Motor Blockade

Variable	Levobupivacaine plain solution	Levobupivacaine plain solution with 1:400,000 epinephrine
0	24	16
1	9	10
2	5	7
3	5	8
Motor block duration	204 ± 60	239 ± 90

Discussion

Traditionally, the levobupivacaine dose used for spinal anesthesia has been 15 mg. This dose supplies an adequate sensory and motor block for most surgical procedures lasting ~6.5 h. Levobupivacaine is lipid-soluble, highly protein-bound local anaesthetic with a dissociation constant (pKa) comparable to that of bupivacaine and ropivacaine, but superior than that of lidocaine. These pharmacological characteristics determine its relatively slow onset, high potency, and long duration of action. Analogous to other local anaesthetics, inhibition of impulse transmission in an variety of tissues leads to the development of adverse reactions.[10,11]

Levobupivacaine has a similar mechanism of action and pharmacodynamic properties as that of bupivacaine. It reversibly blocks the sodium channels at the nodes of Ranvier in myelinated nerves chief to quicker onset as match up to to unmyelinated nerves. Equally, nerves which are small in diameter are extra without exertion blocked than large nerves.[12]

This research described that 0.5% levobupivacaine, with or without epinephrine, is a appropriate anaesthetic for utilization in lumbar spine surgery. The adding up of epinephrine tends to augment the duration of blockade, lessen the ensuing local anaesthetic concentration, and get better intraoperative anaesthetic quality; though statistical significance was not there for any T10 was achieved within 15 minutes of administering the epidural injection in all patient groups. Few institutions regularly and productively use equally epidural and spinal anesthesia for lumbar spine surgery.

Projected compensation of neuraxial blockade comprise retaining the patient's capability to turn to the prone position; guarding against compressive injuries; vocal contact with the patient, agreed to precise localization of nerve root involvement; a reduce in intraoperative blood loss; and long-lasting postoperative analgesia. Anticipated difficulties of regional anesthesia for lumbar spine surgery include the incapability to instantly measure lower extremity motor function and a probable stoppage in bladder function. Nevertheless, in the present study, 53% of patients did not accomplish any degree of motor blockade.

Conclusion

Present study describes that 0.5% levobupivacaine, with or without epinephrine, is

a appropriate anaesthetic for utilization in lumbar spine surgery. The adding up of epinephrine tends to augment the duration of blockade, reduce the resultant local anaesthetic concentration, and recover intraoperative anesthetic quality; though statistical significance was not achived for any T10 was achieved within 15 minutes of administering the epidural injection in all patient groups.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1438-1443
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.53

Comparison Between Interscalene Block using 0.5% Ropivacaine with Low dose Dexmedetomidine and using 0.5% Ropivacaine Alone in Upper Arm Surgeries: An Observational Study

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Abstract

Background: Interscalene brachial plexuses block is one of the delicately done widely used blocks for upper humerus and shoulder surgeries. Ropivacaine, a newer Local Anaesthetic (LA), has been increasingly used nowadays in different concentrations for peripheral nerve blocks including brachial plexux block. Dexmedetomidine, a selective α2-receptor agonist has also been reported to improve the quality of intrathecal and epidural anesthesia when used along with LA as adjuvant. In this background, this study was undertaken to observe any alteration of the quality of brachial plexus block when dexmedetomidine used as an adjuvant along with ropivacaine in interscalene approach while performing upper arm surgeries. *Methods:* On obtaining Institutional Ethics Committee approval, sixty patients in total were studied when equally divided into two groups, R and RD. Thirty Patients for each group (either R or RD) were studied who fulfilled inclusion protocol and underwent surgery under brachial plexus block. Patients observed in group R received 30 ml of 0.5% ropivacaine and patients observed in group RD received 30 ml of 0.5% ropivacaine with 50 µg (0.5 ml) dexmedetomidine by electrical stimulations by using peripheral nerve stimulator (PNS) for brachial plexus block. All patients were primarily assessed for 24 hours for duration postoperative pain relief using VAS pain score (0-10centimeter). Secondarily onset and duration of sensory and motor blocks were assessed as well. Patient satisfaction scores (PSS) were also recorded by a specific scoring method for 24 h postoperatively where score 5=excellent, 4=very good, 3=good, 2=fair, and 1=poor. All patients were also monitored for hemodynamic parameters, oxygen saturation, respiratory parameters, sedation and any other adverse outcome for 24 hours. *Results:* The independent samples t test and Chi square test procedures were used to compare means and standard deviations for two groups of cases accordingly. Parametric and nonparametric data were assessed accordingly and p value < 0.05 was considered as significant. Patients observed in both groups were comparable with respect to baseline demographic characteristics. Total duration of analgesia in patients of group R was 540.21 ± 11.54 minutes and in group RD was 630.75 ± 10.67 min. The difference was statistically significant (p value <0.0001). Onset and duration of sensory and motor blockade were also found to be shortened and prolonged respectively in patients of group RD in comparison to group R. PSS were also found to be better in group RD. *Conclusion:* Dexmedetomidine when added in a relatively low dose as an adjuvant to bupivacaine for interscalene brachial plexus block, it was observed to shorten the onset time and prolongs the duration of both sensory and motor blocks with significant prolongation of duration of postoperative analgesia in patients undergoing upper humerus and shoulder surgery.

Keywords: Adjuvant; Low dose dexmedetomedine; Interscalene block; Duration of analgesia.

How to cite this article:

Jayanta Chakraborty, Soumen Mandal. Comparison Between Interscalene Block using 0.5% Ropivacaine with Low dose Dexmedetomidine and using 0.5% Ropivacaine Alone in Upper Arm Surgeries: An Observational Study. Indian J Anesth Analg. 2019;6(4): 1438-1443.

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Received on 23.05.2019, **Accepted on** 11.07.2019

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Introduction

Regional anesthesia is a recommended technique for upper and lower limb surgeries with better postoperative profile.[1,2] Interscalene approach brachial plexuses block is one of the most widely used blocks for upper end of humerus and shoulder surgeries.

Research have been continuing in the recent years for an ideal local anaesthetic drug that should possess a fast sensory onset, differential offset, with an earlier offset of motor than sensory blockade, enabling early ambulation with prolonged analgesia. Ropivacaine, a newer Local Anaesthetic (LA), has been increasingly used nowadays in different concentration for peripheral nerve blocks. It has lesser cardiac toxicity and higher safety margin when compared to bupivacaine.[3,4] It produces differential neural blockade with less motor block, hence well tolerated for postoperative analgesia and reduced cardiovascular and neurological toxicity.[5,6] However, it has been found that onset time for ropivacaine used in major nerve or plexus block is typically 20-30 mins with an average duration of block is 360-720 mins.[M]

Many drugs such as clonidine[8] and fentanyl [9] have been used successfully as adjuvant with different LAs for the early onset of the block and for prolonging the duration of the block. Dexmedetomidine, an α2-receptor agonist, with α2/α1 selectivity 8 times more than that of clonidine has also been reported to improve the quality of intrathecal and epidural anesthesia[10,11] when used along with LA as adjuvant. Use of dexmedetomidine as an adjuvant to 0.5% ropivacaine in interscalene approach brachial plexus block had been provided with relatively lesser amount of concrete data so far. Consequently a suitable dose of dexmedetomidine for brachial plexus blocks had still not been established convincingly. Hence in this study an optimal dose of 50 µg dexmedetomidine had been chosen based on few of the earlier studies.[12,13,14,15]

This observational study was primarily aimed to know whether 50 µg dexmedetomidine as an adjuvant to 0.5% ropivacaine in interscalene approach brachial plexus block using peripheral nerve stimulator can alter the quality of the block.

Objectives

Primary outcome: To compare total duration of analgesia following successful interscalene approach brachial plexus block between two groups.

Secondary outcome: To compare onset and duration of motor and sensory anesthesia along with patient satisfaction between two groups and also to compare any adverse outcome like sedation, bradycardia, hypotension and voice change etc. between these two groups.

Study design: Longitudinal comparative observational study.

Study period: October 2017 to September 2018

At orthopaedic Operation Theatre, Burdwan Medical College, Burdwan.

Materials and Methods

On approval from the Institutional Ethics Committee, sixty patients were observed following interscalene brachial plexus block when they were equally divided into two groups, R and RD for study convenience. Preoperatively patients were counseled and familiarized with the use of visual analog scale (VAS) pain score for the assessment of perioperative pain. All the patients participating in the study were explained clearly about the purpose and nature of the study in their own understandable language and written informed consent was taken.

Inclusion criteria

- American society of Anesthesiologists (ASA) physical status I and II.
- Aged between 18 and 60 years.
- Scheduled for upper limb surgery mainly upper end of humerus and shoulder surgeries.

Exclusion criteria

- Patients on beta blockers.
- Pregnant.
- With coagulopathy.
- Morbid obesity.
- Severe cardio-pulmonary disease.
- Neurological deficits in the operative arm.

Pre anaesthetic assessment was done for every patient following which patients in Group R received 30 ml of 0.5% ropivacaine and patients in Group RD received 30 ml of 0.5% ropivacaine with 50 µg (0.5 ml) dexmedetomidine by electrical stimulation with PNS. Same anaesthesiologists prepared study drug solutions and administered the block and were designed to observe the quality and duration

of the block and the hemodynamics and respiration postoperatively for 24 hours for each patient of both the groups. These anaesthesiologists collected and analyzed the data and were also involved in management of the patients perioperatively.

Each patient observed in the study were premedicated with tablet alprazolam 0.5 mg and tablet ranitidine 150 mg orally at bedtime the and kept fasting for 10 hours overnight.

In the following morning on arrival of each patient for surgery, 18 gauge intravenous cannula was inserted with infusion of Ringer's lactate. Each patient was thoroughly monitored for heart rate (HR), noninvasive measurements of systolic blood pressure (SBP), diastolic BP (DBP), mean arterial pressure (MAP) and continuous ECG, respiratory rate (RR), and oxygen saturation (SpO_2). The baseline SBP, DBP, MAP, and HR were recorded.

After positioning of each patient on operating table with the head turned to opposite side, interscalene groove was identified by rolling the finger posterior to sternocleidomastoid muscle between the bellies of the anterior and middle scalene muscle at the level of cricoid cartilage. Skin over the insertion site was infiltrated with 2% lignocaine.

Interscalene block was performed in all patients with the peripheral nerve stimulator (Stimuplex, B Braun) connected to 5 cm, 22 gauge, short bevel insulated stimulating needle by modified Winnies approach. The intensity of stimulating current was initially set to deliver 1 mA with impulse duration of 0.1 ms. Thereafter, current was gradually decreased to 0.5 mA. The localization of the plexus was considered optimal when an output current of <0.5 mA caused the contraction of pectoralis muscle, deltoid, biceps or triceps. After eliciting motor response of any of these muscles, 30 ml of 0.5% ropivacaine alone was given in patients of group R and and 30 ml of 0.5% ropivacaine with 50 mcg (0.5 ml) of dexmedetomidine in patients group RD as per study protocol in increments of 5 ml after fixing the stimulating needle aspirating in between to avoid inadvertent intravascular injection.

Hemodynamic parameters such as HR, SBP, DBP as well as SpO_2, and RR were monitored at every 20 min interval till 1 hour of LA injection and then every 30 min till 2 hour and thereafter every hour till the end of surgery and postoperatively one hourly till first 24 hour. Adverse events such as hypotension (20% decrease in relation to the baseline value), bradycardia (HR < 45 bpm), hypoxemia ($SpO_2 \leq 90\%$), perioperative nausea and vomiting, and development of change of voice (if any) were recorded. Clinically relevant bradycardia (heart rate < 45 bpm) spells were treated with atropine (0.6 mg IV). Sedation was evaluated by using the University of Michigan Sedation Scale (UMSS)[12] of 0 to 4 [0 = awake and alert; 1 = minimally sedated/ sleepy, appropriate response to conversion and/or sound; 2 = moderately sedated, somnolent/sleepy, easily aroused with tactile stimulation and/or simple verbal command; 3 = deeply sedated/deep sleep, aroused only with significant stimulation and 4 = could not be aroused].

Patient's perception of pain was assessed using VAS (0–10).

Block was considered inadequate when sensory anesthesia was not achieved within 30 min following which general anesthesia was considered and patient was not included in the study.

The following parameters were assessed.

Onset of sensory block

Sensory block was assessed by loss of sensation to pinprick over the C5T1 dermatomes using a 3points scale which is as follows:

0 sharp pain, 1 dull pain (analgesia), 2 no pain (anesthesia).

Sensory onset time was defined as the time interval between the end of LA administration and establishment of score 2 on 3 point scale on all nerve territories.

Onset of motor block

Motor block was assessed using Bromage scale.

0 Normal motor functions with full flexion and extension of the elbow, wrist, and fingers

1 Decreased motor strength with the ability to move fingers only

2 Complete motor blockade with the inability to move fingers.

Motor block onset time was defined as the time interval between the end of LA administration and complete motor block (score 2).

Duration of sensory block

Duration of sensory block was defined as the time interval between the end of LA administration and the complete resolution of anesthesia (score 0 on a 3 point scale) on all nerves.

Duration of motor block

Duration of motor block was defined as the time interval between the end of LA administration and the recovery of complete motor function (Score 0 on Bromage scale).

Patient satisfaction

Patient satisfaction score (PSS) was recorded after 24 h postoperatively as 5 excellent, 4 very good, 3 good, 2 fair, and 1 – poor.

Patients were monitored for 24 h postoperatively to assess total duration of sensory and motor blockade and VAS pain score.

Postoperatively rescue analgesia in the form of nonsteroidal anti-inflammatory drugs (injection diclofenac sodium 75 mg) was given when patient complained of VAS ≥ 3.

The patients were continuously monitored for any perioperative complications and adverse reactions and examined on the 3rd post operative week for any weakness in the concerned arm.

Statistical analysis

A sample size of 26 patients were to be needed in each group to detect an intergroup difference of duration of analgesia of at least 30 minutes with a power of 0.80 and α error of 0.05 with a pooled standard deviation of 10 minutes. In order to make good for attrition rate, a total number of 30 patients in each group were included for the study. Chi-square test was applied for age, weight, sex and ASA grades and independent samples *t* test procedures was used to compare means of standard deviation for two groups of cases for demographic data, hemodynamic parameters, onset and duration of sensory/motor blockade and duration of analgesia and any adverse effects. SPSS for windows (version 21.0, SPSS Inc., Chicago, IL, USA) was employed for data analysis. $P < 0.05$ was considered as significant.

Results

Sixty patients belonging to ASA physical status 1 and II and fulfilling other criteria of the study undergoing shoulder and upper humerus surgeries under interscalene block were included in the study. As shown in Table 1, patients in both groups were comparable with respect to baseline demographic characteristics.

Table 1: Demographic and surgical variables

Variables	Group R	Group RD	P Value
Age (years)	45.67 ± 9.8	44.18 ± 10.04	0.563
Weight (Kg)	55.16 ± 8.46	56.08 ± 8.32	0.673
Sex (M/F)	18/12	20/10	0.884
ASA (I/II)	17/13	18/12	0.951
Duration of surgery (min)	90.33 ± 21.96	87.16 ± 26.66	0.539

As shown in Table 2, the mean time for the onset of sensory block in Group R was 15.6 ± 1.06 min and in Group RD was 12.96 ± 1.18 min. The difference was statistically significant with earlier onset of sensory block in Group RD ($p < 0.0001$).

The mean time for the onset of motor block in Group R was 18.3 ± 1.877 min and in Group RD was 16.4 ± 1.1 min. The difference was statistically significant with earlier onset of motor block in Group RD ($p= 0.0268$).

The mean duration of sensory block in Group R was 506.77 ± 10.77 min and in Group RD was 598.5 ± 10.98 min. The difference was statistically significant in ($p <0.0001$).

The mean duration of motor block in Group R was 413.45 ± 14.75 min and in Group RD was 424.6 ± 20.89 min. The difference was statistically significant ($p<0.02$).

Table 2: Characteristics of brachial plexus block

Column1	Group R	Group RD	*p* Value
Onset time of sensory block (minutes)	15.6 ± 1.06	12.96 ± 1.18	<0.0001
Onset time of motor block (minutes)	18.3 ± 1.877	16.4 ± 1.1	0.0268
Duration of sensory block (minutes)	506.77 ± 10.77	598.5 ± 10.98	<0.0001
Duration of motor block (minutes)	413.45 ± 10.75	424.6 ± 12.89	0.02

Total duration of analgesia in Group R was 540.21 ± 11.54 min and in Group RD was 630.75 ± 10.67 min as shown in table 3. The difference was statistically significant (*p* value <0.0001).

Table 3: Characteristics of analgesia

Column1	Group R	Group RD	*p* value
Time to get first rescue analgesic	540.21 ± 11.54	630.75 ± 10.67	<0.0001

Patients in both the groups had an equally good PSS.

PSS	Group R	Group RD	*p* Value
PSS 5	17	23	0.757
PSS 4	7	12	0.688

Table 4: Suspected adverse drug reaction profile in the two study groups

Suspected adverse reaction	Ropivacaine plus dexmedne (RD)	Ropivacaine alone (R)	*p* value
Bradycardia (HR <45 bpm)	1	0	1.000
Hypotension (fall in MAP > 20% of base line)	8	6	0.766
SpO2 < 90%	0	0	
Sedation score (mean ± standard deviation)	2.2 ± 0.75	1.7 ± 0.53	< 0.236
Postoperative arm weakness	1	0	1.000

Discussion

Dexmedetomidine so far had been shown promising outcome in intravenous conscious sedation in ICU patients. Different studies done in different set ups also had shown that dexmedetomidine's use could prolong analgesia when used with local anaesthetics for neuraxial blocks by virtue of its effects on spinal α_2 receptors.

Drugs such as clonidine and fentanyl had been in use as successful adjuvant with bupivacaine and/or ropivacaine for the early onset as well as for prolonging the duration of brachial block. Dexmedetomidine for being a relatively more selective α_2 agonist with α_2 adrenoreceptors located in the CNS and spinal cord level had been found to be responsible for the sympatholysis, sedation, and antinociception mediated by G-protein inhibition of L-type calcium channels thereby producing a complex pattern of analgesia by both spinal and supraspinal mechanism. Dexmedetomidine had also been shown to exert an anti hyperalgesic action in neuropathic pain states involving the peripheral nervous system and so had been increasingly found to be used as an adjuvant with various local anaesthetics in peripheral nerve blocks to decrease the time of onset and increase the duration of analgesia. Although clonidine added to bupivacaine prolonged the duration of anesthesia and analgesia in brachial plexus block, but was found to be associated with bradycardia, hypotension, and respiratory depression and over the past few years dexmedetomidine had gradually replaced clonidine as an adjuvant of choice. Ropivacaine, a newer LA with less cardiac and neural toxicity than bupivacaine, had been in use currently as an ideal agent for neural blockade. However it was found that ropivacaine could be less effective at times and larger volumes of drug might be required for getting adequate block. Some recent randomized, double-blind trials had shown that dexmedetomidine 1 microgram/Kg as an adjuvant to 0.5% levobupivacaine for axillary brachial plexus blockade shortened block onset time, prolonged duration of motor and sensory effects, extended postoperative analgesia and decrease in total analgesic use.[15] Ropivacaine being a newer LA had been in use in various concentrations of 0.25%, 0.5%, and 0.75% for nerve blocks producing greater sensory and motor differential blockade than bupivacaine, in a dose dependent manner, with higher concentrations (1%) causing greater degree of motor blockade than lower concentration (0.5% and 0.75%).[4] In the present study 0.5% ropivacaine had been chosen with an idea to achieve maximum possible sensory blockade with minimum effect on motor movements and to minimise unnecessary side effects of inadvertent high block. Dexmedetomidine dose had been chosen to be 50 microgram to avoid untoward bradycardia, hypotension and sedation yet to achieve adequate adjuvant effect for a desired quality of block during surgery and post operative period as well. Some of the previous studies had reported that 50 microgram dexmedetomedine could produce significant prolongation of analgesia when added to ropivacaine in brachial blocks.[8, 10, 15] It was clearly found in the present study that there was no significant difference between the two groups R and RD as far as the demographic data are concerned while it was also observed that mean total duration of analgesia in patients of group RD (630.75 ± 10.67 minutes) was significantly longer than the patients of group R (540.21 ± 11.54 minutes) till the receipt of first dose of rescue analgesic which was very much in corroboration with another study of Agarwal S, Aggarwal R, Gupta P *et al.* where they had shown the adjuvant effect of dexmedetomedine with bupivacaine in brachial plexus block.[16] Present study also had shown to improve the onset of motor and sensory block in patients of group RD due the adjuvant effect of dexmedetomedine which was similar to many other studies. Total duration of sensory and motor block were also found to be significantly prolonged in patients of group RD for the use of dexmedetomedine and these findings could well be compared to other recent works done with dexmedetomidine in brachial block. One of the possible causes of prolongation of effect of local anaesthetic could be the vasoconstriction caused by dexmedetomedine at the injection site by its alpha 2 adrenoceptor agonist effect resulting delayed absorption of local anaesthetic (AM AbdElmaksoud and his colleagues).[8] Moreover it was also found that that patient satisfaction was also better in patients of group RD which was assessed by a specified protocol based scoring system and though not significant as such but found to be almost comparable to a previous study that showed similar kind of patient satisfaction pattern for patients receiving dexmedetomedine as an adjuvant.[17] Many other studies had also emphasized on the role of dexmedetomedne for its adjuvant effect on pain relief thereby prolonging the effect of brachial block in post operative period and reducing the requirement of opioid rescue analgesics especially. Although this study was not designed to comment on this perspective but as per the observations it was quite clear that diclofenac sodium, the rescue analgesic used in this study was needed after a longer period of post

operative time in patients of group RD receiving dexmedetomedine as an adjuvant with respect to the patients of group R without dexmedetomedine.

There were limitations in this study of which non availability of ultrasography machine guided interscalene brachial plexus block was the foremost one which was more of a technical issue in this medical college. This medical college being a peripheral college certain logistic shortcomings such as lack of proper post operative care facilities made the postoperative assessment of pain of each patient a little more difficult and unassuming on the basis of VAS scoring for 24 hours post operative period which could have been better otherwise. Variations in observations by anaesthesiologists could be another method related problem which could not be addressed properly.

Conclusion

This observation based comparable study had substantial data to conclude that low dose dexmedetomedine when added as adjuvant to 0.5% ropivacaine in interscalene brachial plexus block produced significant prolongation of duration of analgesia in the operated arm without much clinically concerning side effects.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1444-1448
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.54

Comparison of Preemptive Intraperitoneal Instillation and Nebulisation of 0.5% Ropivacaine in Laparoscopic Cholecystectomy for Post-operative Pain Relief

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Abstract

Objective: The etiology of postoperative pain in patients undergoing laproscopic cholecystectomy is multifactorial consisting of incisional and visceral pain from the operation itself and parietal pain from trauma and irritation to the peritoneum and diaphragm. *Design:* This randamozied single blind study was conducted on 60 patients of either sex undergoing laproscopic cholecystectomy under general anesthesia. Group A [n=30] received 15 ml of 0.5% ropivacaine by instillation and group B [n=30] received 15 ml of 0.5% ropivacane intraperitoneally by piston type of nebulization 10 minutes before surgery and both the groups got 5 ml [0.5%] ropivacaine at the trocar site at the end of surgery. Results: Patients in both the groups were comparable with respect to age, sex and weight [p>0.05]. VAS score for incisional pain was significantly lower in Group A at 1hour and 8 hrs postoperatively [p=0.02 and p=0.04] respectively. At all other intervals the incisional pain, Visceral pain and shoulder tip pain was comparable amongst the two groups [p>0.05]. Time to first analgesia was longer in group A [2.29 hrs] as compared to Group B [1.66 hrs] but was stastically insignifiacant [p>0.5]. Mean total number of analgesic used was 1.4 in both the groups [p=1]. *Conclusion:* Intraoperative subdiaphgramatic and intraperitoneal instillation of ropivacaine 0.5% is beneficial and better modality of pain relief because of ease of technique and better VAS scores as compared to intrperitoneal nebulization of ropivacaine.

Keywords: Intraperitoneal nebulization; Instillation; Ropivacaine; Laproscopic cholecystectomy; Preemptive.

How to cite this article:

Jyoti Pathania, Meenal Aggarwal, Anupam Sharma *et al*. Comparison of Preemptive Intraperitoneal Instillation and Nebulisation of 0.5% Ropivacaine in Laparoscopic Cholecystectomy for Post-operative Pain Relief. Indian J Anesth Analg. 2019;6(4): 1444-1448.

Introduction

Pain after laparoscopic surgery is the result of surgical manipulations and intraperitoneal insufflation of carbon dioxide causing peritoneal stretching, diaphragmatic irritation, changes in intra-abdominal pH, moreover retention of the insufflated gas in the abdominal cavity after surgery are all attributed for post operative pain.[1] The efficacy of intraperitoneal use of local anaesthetics for postoperative pain relief in laparoscopic

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Received on 23.05.2019, **Accepted on** 27.06.2019

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procedures is still debated. Some studies suggest that local anaesthetic infiltration does attenuate post operative pain after laparoscopic cholecystectomy[2]. Some suggest that it does not improve patient outcome in terms of post operative pain after laparoscopic surgery.[3]

Intraperitoneal aerosolization of local anaesthetics has proven efficient in spreading drugs homogenously throughout the peritoneum[4,5]. This technique combines the effect of gas conditioning and the analgesic benefits of local anaesthetic instillation[4]. Till now there have been only a few trials comparing the analgesic effects achieved with intra-peritoneal nebulisation with intra-peritoneal instillation of local anaesthetic agents in laproscopic cholecystectomy. Optimal management of postoperative pain is important as this procedure is now carried out in an ambulatory setting. Keeping the above factors in mind, the present study was conducted in our institution.

Material and Methods

After approval of Institutional Research and Ethical Committee a prospective randomized single blind [observer was blind to study] was carried out in 60 ASA I and ASA II patients posted for laproscopic cholecystectomy under general anesthesia. Patients were randomly allocated into into two groups of 30 each.

Group A: Subdiaphragmatic and Sub hepatic Instillation of Ropivacaine

Group B: Intraperitoneal Nebulisation of Ropivacaine using piston type air nebulizer

In both the groups, 15ml of 0.5% ropivacaine was given intraperitoneally (by instillation in group A and by nebulisation in group B) immediately after the insertion of trocars and 5ml of 0.5% ropivacaine was infiltrated into the port sites at the end of the surgery.

Exclusion Criteria: Patients with severe chronic obstructive airway disease, Patients with coronary artery disease, History of allergy to Local Anaesthetic agents, Conversion of Laparoscopic Cholecystectomy to Open Cholecystectomy, Intra Operative intra abdominal drain insertion, Age < 20 years and > 60 years.

Anesthesia Technique: Patients were kept nil per orally for at least 6 hrs. In the operation theatre, all patients were connected to monitors and baseline vital data (mean arterial pressure, heart rate, pulse oximetry and respiratory rate) were recorded. Intravenous line was secured and intravenous fluid was started in the contralateral arm. The patient was given Injection glycopyrolate 0.01 mg/kg i.v., injection butorphanol 0.02 mg/kg i.v. as analgesic after preoxygenation with 100% Oxygen for 3 minutes followed by induction with injection thiopentone 5 mg/kg intravenously followed by injection succinyl choline 2 mg/kg intravenously. Airway was secured with appropriate size endotracheal tube and anesthesia was maintained with N_2O (66%), O_2 (33%) and isoflurane (0-1%). Non depolarizing muscle relaxant atracurium (0.5 mg/kg) was used. After insertion of the trocar, in Group A sub diaphragmatic and sub hepatic instillation of 15 ml of 0.5% ropivacaine was done and surgery was started 10 min after the instillation of the drug. In group B, nebulisation with 15 ml of 0.5% ropivacaine was done intraperitoneally. The piston type air nebulizer was kept at a height of 6 ft to minimize contaminated air. Intraperitoneal pressure was maintained between 12-15 mm Hg and gas was vented if pressure increases. At the end of surgery, the port sites were infiltrated with 5 ml of 0.5% ropivacaine in both the groups and isoflurane was stopped, injection ondansetron 0.1 mg/kg was given and muscle relaxation was reversed with injection neostigmine 0.05 mg/kg i.v. and injection glycopyrrolate 0.01 mg/kg i.v. Patient was extubated and 100% O_2 was given via the mask for 5 minutes in operation theatre. Patients were monitored intra-operatively for Heart rate Mean blood pressure Arterial oxygen saturation. These parameters were noted at time of instillation or nebulisation (taken as 0 minutes), then at 3 minutes, 5 minutes, 10 minutes and thereafter every 10 minutes until the end of surgery. Patients were analyzed postoperatively for following parameters:

1. Incisional Pain (At 0, 1, 2, 3, 4, 5, 6, 8, 16 and 24 hrs)
2. Abdominal (Visceral) Pain (At 0, 1, 2, 3, 4, 5, 6, 8, 16 and 24 hrs)
3. Shoulder Pain (At 0, 1, 2, 3, 4, 5, 6, 8, 16 and 24 hrs)
4. Duration between time of extubation and first dose of analgesic (diclofenac)
5. Analgesic requirement for 24 hrs

The Intensity of pain was assessed on Visual Analogue Scale (VAS). Analgesic requirement was assessed in terms of administration of number of injections of diclofenac sodium [75 mg] on demand. Analgesic was given if patient has pain equivalent to VAS of 4 or more.

Results

The data obtained from both the groups was observed and statistically compared using computer software SPSS version 20 and Microsoft excel. Unpaired t- test was used for quantitative data and Mann Whitney U test for non parametric data. A *p*-value of < 0.05 was considered statistically significant.

Both the groups were comparable in demographic variable like age, sex and weight distribution. Mean age (in years) in group A was 41.5 and in group B was 42. The ratio of males: female in group A was 9:21 and group B was 11:19 [$p > 0.05$]. The baseline parameters like heart rate, mean B.P. and SpO_2 were also comparable in both the groups. There was no significant difference found in the heart rate, mean B.P. and SpO_2 at various time intervals during the surgery in group A and B which means that the two techniques had no variation in terms of hemodynamic effects.[$p > 0.05$]

The VAS score was statistically significant While comparing incisional pain at 1 hr (*p*-value 0.02) and 8 hrs (0.042) postoperatively. The pain scores recorded at all other time intervals were found to be comparable with a p-value > 0.05. (Table 1, Figure 1a). The values for visceral pain and shoulder tip pain were found to be statistically comparable at all time intervals [$p > 0.05$] (Table 2 and 3).

In our study, six patients in both the groups did not require any analgesic during the first 24 hrs after surgery. The mean time in group A was found to be 2.29 hrs (2 hrs 17 min) and that in group B was 1.66 hrs (1 hr 40 min) [$p = 0.35$]. There was no difference in the mean analgesic requirement in both the groups and it was 1.4 doses in 24 hrs. [Table 4]

Table 1: Table showing comparison of incisional pain scores at different time intervals in group A and B

	Group A			Group B			*p*-value
VAS	0	1-3	4 or more	0	1-3	4 or more	
0 hr	20	5	5	12	15	3	0.23 (NS)
1 hr	11	7	6	2	12	12	0.02 (S)
2 hr	6	6	4	1	8	3	0.581 (NS)
3 hr	3	9	0	1	8	0	0.669 (NS)
4 hr	1	10	1	2	7	0	0.405 (NS)
5 hr	1	9	0	2	7	0	0.448 (NS)
6 hr	1	8	1	1	6	2	0.296 (NS)
8 hr	0	7	1	1	6	0	0.042 (S)
16 hr	0	6	0	1	5	0	0.067 (NS)
24 hr	3	3	0	1	5	0	0.241 (NS)

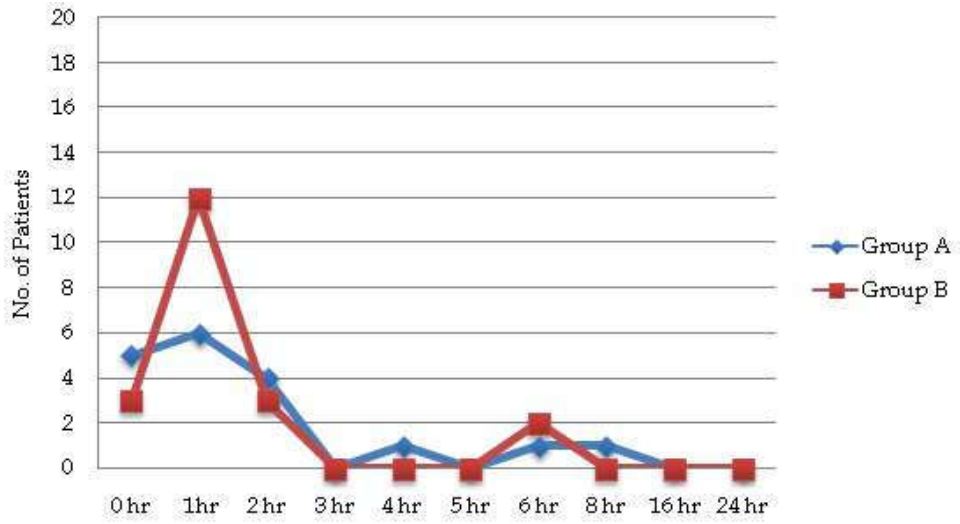

Fig. 1: No. of patients with severe incisional pain (VAS 4 or more)

Table 2: Table showing comparison of visceral pain scores at different time intervals in group A and B

	Group A			Group B			*p*-value
VAS	**0**	**1-3**	**4 or more**	**0**	**1-3**	**4 or more**	
0 hr	20	5	5	14	3	3	0.39 (NS)
1 hr	9	8	7	4	9	13	0.098 (NS)
2 hr	6	6	4	2	7	13	0.755 (NS)
3 hr	2	10	0	1	8	0	0.846 (NS)
4 hr	0	10	2	1	8	0	0.422 (NS)
5 hr	1	9	0	1	8	0	0.243 (NS)
6 hr	1	8	1	0	7	2	0.447 (NS)
8 hr	0	7	1	1	5	1	0.281 (NS)
16 hr	0	6	0	1	5	0	0.093 (NS)
24 hr	3	3	0	1	5	0	0.394 (NS)

Table 3: Table showing comparison of shoulder tip pain scores at different time intervals in group A and B

	Group A			Group B			*p*-value
VAS	0	1-3	4 or more	0	1-3	4 or more	
0 hr	29	1	0	30	0	0	0.317 (NS)
1 hr	23	1	0	25	0	1	0.977 (NS)
2 hr	16	0	0	12	0	0	1 (NS)
3 hr	12	0	0	8	1	0	0.248 (NS)
4 hr	12	0	0	8	1	0	0.248 (NS)
5 hr	10	0	0	8	1	0	0.292 (NS)
6 hr	9	0	0	9	0	0	1 (NS)
8 hr	8	0	0	7	0	0	1 (NS)
16 hr	6	0	0	6	0	0	1 (NS)
24 hr	6	0	0	6	0	0	1 (NS)

Table 4: Time of first analgesic dose and total analgesic requirement in the post-operative period

No. of doses	**0**	**1**	**2**	**3**	**Mean doses in 24 hrs**	**Mean time (hrs) to 1st analgesic**
Group A	6	9	12	3	1.4	2.29*
Group B	6	8	14	2	1.4	1.66*

*p=0.35

Discussion

Laparoscopic surgeries have become increasingly popular mainly due to the lower perioperative morbidity, less postoperative pain, reduced postoperative infections, less scar deformations and shorter length of stay in the hospital as compared to open surgery. Although local anaesthetic instillation intraperitoneally and at the site of incisions has been shown to reduce postoperative pain and analgesic requirement, but it is not enough to eliminate visceral and shoulder pain. One possible reason could be the non-uniform distribution of the local anaesthetic in the peritoneal cavity. This led to the use of nebulisation as a new modality to deliver drugs intraperitoneally. It has been reported to provide a homogenous spread of drug allowing a better distribution throughout the peritoneum.[6]

In our study, the duration of analgesic effect of 100 mg ropivacaine when instilled into the peritoneal cavity was found to be 2 hr 17 min as compared to Labaille T *et al.*[7], who found the duration of analgesia to be 1 hr 10 min while using 100 mg of ropivacaine. This could be attributed to the fact that the incision sites were not infiltrated with local anaesthetic and moreover, the rescue analgesic was administered to the patients at a VAS score of ≥ 3 by them we prescribed rescue analgesia at a VAS score of ≥ 4. Another reason for a shorter pain free period in their study could be a longer duration of surgery, mean duration being 125 min but in our study 20-50 min in most of the cases. They also used 300 mg of ropivacaine in one of the groups and found that a higher dose did not improve clinical effectiveness but lead to excessively large plasma concentrations of the drug.

In our study, the analgesic effect of ropivacaine, either instilled or nebulized into the peritoneal cavity, were almost comparable. However, at 1 hr and 8 hrs postoperatively instillation proved to be better than nebulization in terms of a lower VAS score. This is in accordance with the results of the study conducted by Buccerio M[6] *et al.* who also concluded that abdominal pain was comparable in instillation and nebulization group. But they found a significant difference in analgesic efficacy of the two techniques in terms of shoulder pain with nebulization being more effective than instillation. 25 patients of nebulization group as compared to no patient in the instillation group had shoulder pain. The possible reason for this reason could be the use of Aeroneb Pro system, which is a microvibration based nebulization device, by Buccerio M[6] *et al.* for nebulization. This device generates aerosol particles with mass median diameter < 5 microns, thus ensuring an efficient drug delivery. On the other hand, in our study, we used a custom made nebulization device using a piston nebulizer which generates comparatively larger size aerosol particles. Thus the complete delivery of drug into the peritoneal cavity could not be assured. Another difference was the use of 60 mg ropivacaine in their nebulization group in comparison to 100 mg used in our study. This could be a probable reason for a higher incidence of postoperative nausea and vomiting seen in the nebulization group of their study (22%) as compared to ours (3%). This study was in accordance with ours as they too did not use a control group. This was because previous studies have shown controversial benefits of intraperitoneal instillation.

In a study conducted by Bissgard T[8] *et al.*, both intraabdominal and shoulder pain after laparoscopic cholecystectomy decreased significantly in the ropivacaine instillation group for 2 hrs postoperatively. From 3 hr onwards, both shoulder pain and intraabdominal pain began to increase. However, this was not the case in our study. The difference could possibly be attributed to the lower concentration of ropivacaine used which was 0.2% in their study as compared to 0.5% ropivacaine used in our study. Moreover, in our cases, the drug was preferentially sprayed on the right hemidiaphragm but they instilled the drug on both sides of the diaphragm. Although they used a higher total dose of ropivacaine, i.e. 286 mg, most of it was given at the incision sites (210 mg) and a comparatively less dose was given intraabdominally. This well explains why incisional pain was well controlled even beyond 3 hrs whereas intraabdominal and shoulder pain increased at 3 hrs postoperatively.

In another study conducted by Goldstein A[2] et al., who used 150 mg of ropivacaine instillation, the mean number of rescue analgesic doses (morphine in this case) was 0.35, whereas in our study the mean number of rescue analgesic doses (diclofenac) was 1.4. This difference could be because of a higher dose of ropivacaine used in their study as compared to 100 mg in ours. However, the rescue analgesia usage was comparable to ours i.e. mean doses amounting to 1.5 in their study as compared to 1.4 in ours.

The incidence of postoperative nausea and vomiting in the study conducted by Goldstein A[2] *et al.* in the ropivacaine group was (15%) slightly higher than our study (10%). Because of study conducted in gynecological procedures with a more extensive surgical manipulation and a longer duration of surgery as compared to laparoscopic cholecystectomy. Moreover, tubal manipulation, which was required in a good number of cases, is known to cause more nausea and vomiting. In accordance with our study, this study also reported no hemodynamic adverse effects of ropivacaine in the patients.

In the study conducted by Callesen T[9] *et al.*, who used instillation of a total dose of 285 mg ropivacaine intraperitoneally, the incidence of postoperative nausea and vomiting was 13% which is comparable to that in our study i.e. 10% in the instillation group. The mean duration of analgesia in this study was around 4 hrs, whereas it was 2 hrs 17 minutes in the instillation group in our study. The difference could be because of the use of a significantly higher dose of ropivacaine i.e. 285 mg as compared to 100 mg in our study.

Conclusion

Our study concluded that intraperitoneal administration of ropivacaine is beneficial in controlling postoperative pain in patients undergoing laparoscopic cholecystectomy, with instillation being a better mode of administration of the drug as compared to nebulisation. In our study, the local anesthetic has been administered before the surgical dissection thus, its role is in "pre-emptive analgesia" which refers that previously administered medications modulate the arousal of nociceptive action in the postoperative period. Moreover, ropivacaine does not seem to have any adverse effects on the hemodynamics of the patient and as it provides analgesia for 2-3 hrs only as far as visceral pain is concerned thus, its combination with other drugs should be tried to prolong the duration of analgesia.

Limitation of the study

1. The number of patient taken was small as only 60 patients were enrolled in the study.
2. Piston type of air nebulization was used instead of aeroneb pro technology as it was not available in our institution.

Conflict of interest: This study did not receive any grant or help from any pharmaceutical company at any level.

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1450-1458
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.55

Real-time Ultrasound-Guided Catheterization of the Internal Jugular Vein: A Prospective Comparison with the Landmark Technique

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Abstract

Introduction: Conventionally central venous catheter is done utilising landmark technique. With increased availability of portable USG units, USG-guided intervention is fast gaining acceptance as a valuable tool in the critical-care setting. We designed this study to compare two methods of CVC insertion in terms of time taken, number of attempts, success rate and incidence of complications. This study will help us evaluate real time ultrasound in comparison to landmark technique. *Material and Methods:* 100 ASA I and II patients of either sex of ≥ 18 years of age, admitted to ICU or underwent surgery, requiring CVC placement were included in the study. Patients were randomly divided into two groups. Primary outcome measures were Successful insertion of a CVC. Secondary outcomes were (a.) Number of attempts for successful insertion of CVC (b.)Time taken to insert, (c.) Failure rate in insertion (d.) Incidence of complications. *Result*: The study was conducted in patients with a variety of disease processes. The distribution of age and sex was comparable in both the groups. Success rate was more in case of USG guided CVC insertion than landmark technique. In landmark technique successful cannulation was done in 86% patients vs 98% in USG group. The time taken during the procedure between group A (landmark technique) was 42.59 ± 16.54 seconds which was higher than the time taken to catheterised by ultrasound guided technique 16.69 ± 9.80 seconds. p value was found to be less than 0.001, which was statistically significant. In group A incidence of hematoma formation was 14% and intra-arterial insertion of needle was 6% out of 20% overall complications. In group B incidence of hematoma formation was 8% and intra-arterial cannulation was 2% out of overall 10% complications. It was found that overall complication was more in group A patients than group B patients. But P value was found to be 0.161, and was statistically not significant. *Conclusion*: Considering the findings of the study, we concluded that USG guided CVC insertion has a better success rate, less failure, required less number of attempt and time taken to insert the CVC was significantly less. However, there was less complication with USG guided CVC insertion in present study, but it did not achieve statistical significance

Keywords: Ultrasound guided catheterization; Central venous catheter; Seldin.

How to cite this article:

Shahbaz Alam, Pallavi Ahluwalia. Real-time Ultrasound-Guided Catheterization of the Internal Jugular Vein: A Prospective Comparison with the Landmark Technique. Indian J Anesth Analg. 2019;6(4): 1450-1458.

Introduction

Central venous catheter (CVC) placement has become integral part in intensive care units. It is an innovative technique developed by Seldinger for insertion of large bore catheter. Access to central circulation using CVC is very useful in CVP measurement for evaluating hemodynamic

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Received on 09.05.2019, **Accepted on** 08.06.2019

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status of the patient. CVC may be required for administration of hyperosmolar or vasopressor, parenteral nutrition, rapid infusion of fluid boluses or continuous monitoring of various physiological parameters[1,2]. CVC is also indicated when peripheral lines catheter insertion is not possible[3].

Conventionally, CVC insertion is done using landmark technique (LMT) in internal jugular vein, subclavian vein or femoral vein. IJV is more commonly used because of its ease of accesssibility and less chances of complications. However infection rate has been reported to be least in subclavian approach[4,5]. Many anatomic landmark guided techniques for IJV puncture have been described since 1966[6,7]. With increased availability of portable USG units, USG-guided intervention is fast gaining acceptance as a valuable tool in the critical-care setting[8]. Ultrasonography-guided procedures can save time and increase the accuracy, safety and efficacy of many interventions commonly performed in ICUs, including CVC insertion. There is abundant evidence that USG-guided catheter placement increases the safety and efficiency of the procedure. The benefits of using USG guidance over LMT for CVC insertion have been reported as far back as 1978, and the body of literature supporting the use of USG continues to increase[9]. The advantages of USG guidance over LMT in CVC insertion include risk reduction[5,10,11], improved success rates[5,11,12], quicker insertion, a reduction in the number of attempts required and the ability to cannulate in difficult situations[6,7,13-18]. Hence it designed this comparative study of Real-time ultrasound-guided catheterisation of the internal jugular vein with the landmark technique.

Aims and Objectives

Primary outcome measures were Successful insertion of a CVC.

Secondary outcomes were (a.) Number of attempts for successful insertion of CVC (b.) Time taken to insert, (c.) Failure rate in insertion (d.) Incidence of complications

Material and Methods

After obtaining approval from Ethical Committee, the present study was conducted in Department of Anesthesia of Teerthanker Mahaveer Medical College & Research Centre, Moradabad. After taking prior informed consent from the either patient or patient's relative we included 100 ASA I and II patients of either sex of ≥ 18 years of age, admitted to ICU or underwent surgery from August 2017 to August 2018, requiring CVC placement were included in the study. The patients not giving consent, patients with coagulopathies or prolonged bleeding time [International Normalisation ratio>1.5, platelets count<50,000/mm^3], infection at the site of needle insertion, patients with CVC placement for cardiopulmonary resuscitation or trauma patients in whom the cervical spine could not be cleared clinically or radiologically before line insertion were excluded from the study.

The patients were randomly divided into two groups using computer generated random number table. A minimum number of 50 patients were enrolled in each group after taking consent from patient or his/her relative.

Group A (n = 50): Anatomical land mark technique central approach

Group B (n = 50): USG guided two person technique

In group A the CVC insertion done by Landmark technique and in group B CVC was inserted by USG guided technique.

Intervention and approach

The Operator had an experience of insertion of more than 10 CVC in each group. The right internal jugular vein was taken as first choice for cannulation. Left IJV could be cannulated only if right IJV was not available for cannulation due to the presence of a previously inserted CVC, dialysis catheter, infection, haematoma formation by previous attempt. CVC insertion using the anatomical technique had been performed through the central approach. USG guided CVC insertion had been performed with two person technique.

Landmark Technique

The patient was positioned in Trendelenberg position to decrease the risk of air embolism. This also helps to distend the IJV. Under all aseptic conditions triangle formed by two head of sternocleidomastoid muscle and the clavicle was identified. Infiltration with local anaesthetic was given at the apex of the triangle. A 25 gauge needle was advanced along the medial border of the lateral head of sternocleidomastoid towards the ipsilateral nipple, at an angle of 30° to the skin. Aspiration of venous blood confirmed the vein location. An 18 gauge needle was introduced along the same path as locator needle. When free flow of blood was

achieved, vein puncture confirmed and a guide wire introduced. The needle was removed and a dilator advanced over the wire. Then dilator removed and the catheter advanced after flushing all the ports with saline and distal ports capped except the central through which guide wire passed. The guide wire then removed and the line connected to IV line. The CVC then secured properly and sterile dressing applied.

USG Guided Approach

A portable ultrasound machine "MTURBO®" with a 7.5-10 MHz, 38 mm linear array probe used. Aseptic measures included cleaning of the lead and transducer with an antiseptic solution and gel was used to cover the probe. After patient positioning the neck was draped and sterilized with antiseptic solution. Keeping in mind the anatomical landmarks, the transducer was placed at right angle to the vessels at the tip of the triangle formed by the two heads of the sternocleidomastoid muscle and the clavicle.

The vein was recognised by its large lumen and confirmed by checking its easy compressibility. Artery was distinguished by its thicker walled and pulsatile nature. Transducer was placed in such a way that vein would be seen at centre of ultrasound monitor. After infiltration with local anaesthetic [2 ml of 1% lignocaine] if patient was not sedated, the introducer needle was directly inserted along the centre of the probe towards the centre of the vein, under USG guidance. On the monitor, the needle was seen either puncturing the vein or compressing the vessel. Once puncture of the vein occurred, the modified Seldinger technique followed as described above in anatomical approach to insert a CVC.

No. of attempts and Failure

The procedure considered a failure if the operator was unable to cannulate the vein within three attempts. An attempt was defined as the introducer needle entry into the skin and its removal from the skin. If the initial method was unsuccessful after a maximum of three attempts, an alternative method was used. If three unsuccessful attempts were made by anatomical landmark technique then USG guided technique was used or help taken from more experienced operator or an alternative site chosen.

Time Taken for the Procedure

For Anatomical land mark technique: Time taken to perform CVC was measured from insertion of the pilot needle for vein location to easy aspiration of blood through the central venous catheter. For USG guided technique:

Time taken to perform CVC was measured from the beginning by transducer to easy aspiration of blood through the central venous catheter.

Observations

All patients in both the groups were independently observed for the following effects:

A) Successful insertion of a CVC, B) Time taken during the procedure, C) Number of attempts in both the groups, D) Number of failures in both the groups, E) Incidence of complications such as hematoma formation, pneumothorax, artery puncture, nerve injury etc.

Statistical Analysis

Statistics

Results were statistically analysed using latest version of SPSS 16.0. The means of the continuous variables between two groups were compared using the student t-test and categorical variables were compared using chi-square test. A p-value of < 0.05 was considered statistically significant.

Sample Size

A sample size of 50 in each group was based on power analysis in which alpha level was fixed at 0.05, anticipated effect size (Cohen's d) of 0.6 and for a desired statistical power level of 0.8, a minimum required sample size per group was calculated to be 45 and minimum total required sample size was calculated to be 90.

Data Analysis

Continuous data was presented as means ± standard deviation. Ordinal data are presented as medians (quartiles), and categorical data are presented as numbers and frequencies. Demographic Data between the groups were analyzed using chi square, unpaired t-test etc.

Results

The study was conducted in patients with a variety of disease processes. The distribution of age and sex was comparable in both the groups so it did not influence our result.

Table 1 shows distribution of patients according to sex in group A and group B was comparable.

Table 2 demonstrates the distribution of age between two groups. The difference of the Mean was not statistically significant.

Table 3 demonstrates the successful insertion of CVC in each group.

Table 4 depicts the time taken during the procedure between group A and group B. Among the two technique time taken to catheterized for landmark technique was 42.59±16.54 seconds which is higher than the time taken to catheterised by ultrasound guided technique 16.69±9.80 seconds. p value was found to be less than 0.001(CI -31.43 to -20.37), which was statistically significant.

Table 5 depicts incidence of individual complications in group A and group B.

In group A incidence of hematoma formation was 14% and intra-arterial insertion of needle was 6% out of 20% overall complications. In group B incidence of hematoma formation was 8% and intra-arterial cannulation was 2% out of overall 10% complications.

It was found that overall complication was more in group A patients than group B patients. But p value was found to be 0.161, and was statistically not significant.

Table 6 demonstrates comparison of the two groups.

In group A CVC was successfully inserted 43 (86%) out of 50 patients, and in group B CVC was successfully inserted in 49 (98%) out of 50 patients. P-value was 0.027 and was statistically significant. Similarly, in group A failure occurred in 7 (14%) out of 50 patients, while in group B failure occurred in 1 (2%) out of 50 patients. *p*-value was 0.027 and was statistically significant.

In group A CVC was inserted successfully in one attempt in 8 patients, two attempts in 24 patients and three attempts in 12 patients, whereas in group B it was inserted in one attempt in 26 patients, two attempts in 20 patients, in three attempts in 3 patients. *p*-value was <0.001, which was statistically significant. In group A time taken to insert CVC Mean ±SD was 42.59 ± 16.54 seconds compared to group B Mean±SD was 16.69 ± 9.80 seconds. *p*-value found to be <0.001 which was statistically significant.

Complication was found in 10 patients out of 50 in group A, and 5 patients out of 50 in group B. P-value found to be 0.161 which was not statistically significant.

Table 1: Distribution of Patients According to Sex in the Groups

Sex	Group A		Group B		Test of significance
	N	%	N	%	
Male	27	54.0	29	58.0	$\chi 2$=0.162
Female	23	46.0	21	42.0	*p*= 0.687
Total	50	100.0	50	100.0	

Table 2: Distribution of Age Between Group A and Group B

Age (in years)	Group A		Group B		Test of significance
	N	%	N	%	
<30	15	30.0	23	46.0	
30–44	17	34.0	8	19.0	t= 0.8845
45–59	8	16.0	12	24.0	
>60	10	20.0	7	14.0	Standard error of difference=2.980
Total	50	100.0	50	100.0	
Age (Years)	Group A		Group B		*p*= 0.3786
Mean±SD	39.9 ± 15.80		36.92 ± 17.83		

Table 3: Successful Insertion of Central Venous Cathrter

	Group A		Group B		
	N	%	N	%	
Success	43	86.0	49	98.0	$\chi 2$=4.89
Failure	7	14.0	1	2.0	
Total	50	100.0	50	100.0	*p*=0.027

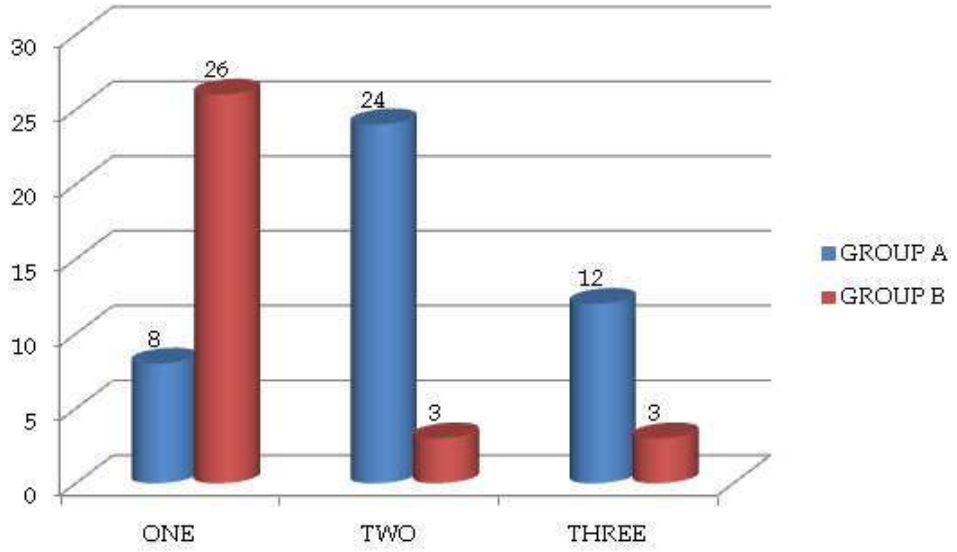

Fig. 1: Shows the Graphical Representation of Number of Attempts Taken to Insert Central Venous Catheter in Both the Groups.

Table 4: Time Taken During the Procedure in Successful Patients

Time in seconds	Group A		Group B		
	N	%	N	%	
<15	0	0.0	20	40.82	
15–29	10	22.73	28	57.14	t value=9.297
30–44	20	45.45	0	0.0	*p* value<0.001
45v60	10	22.73	0	0.0	
>60	3	9.09	1	2.04	95% CI 31.43 to 20.37
Total	43	100.00	49	100.00	
Mean±SD	42.59 ± 16.54		16.69 ± 9.80		

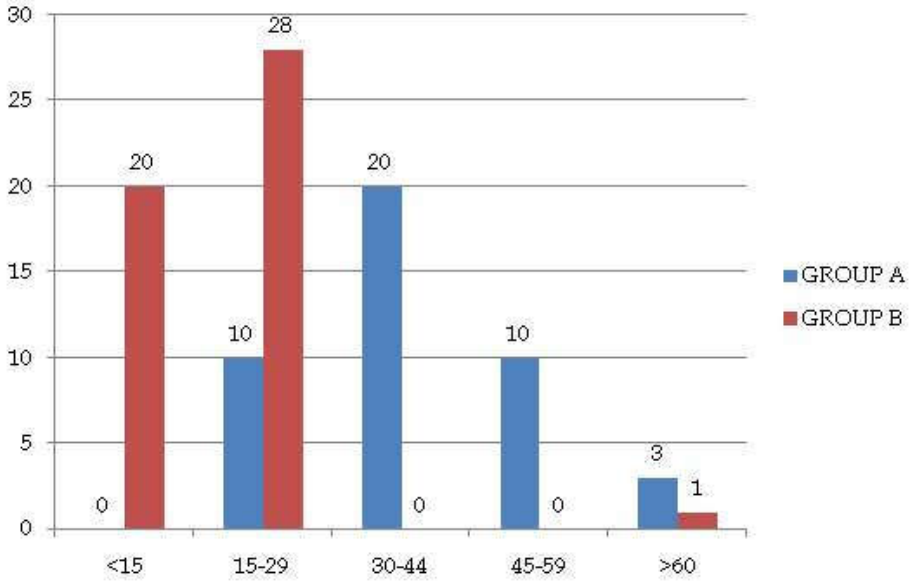

Fig. 2: Graphical Representation of Time Taken During the Procedure in Both the Groups in Successful Patients

Table 5: Incidence of Individual Complications in Group A and Group B

	Complication		No Complication		
	Hematoma	Intra-Arterial	N	%	
Group A	14%	6%	40	80%	$\chi 2=1.96$
Group B	6%	4%	45	90%	$p=0.161$

Table 6: Comparison of the Two Groups Considering All the Parameters

	Success/ Failure (No. of patients)	No. of Attempt	Time Taken (in seconds)	Complication (No. of patients)
Group A	Success = 43 (86%) Failure = 7 (14%)	One-8 (18.60%) Two-24 (55.81%) Three-12 (25.58%)	Mean±SD 42.59 ± 16.54	Complication-10 patients No complication-40 patients
Group B	Success = 49 (98%) Failure = 1 (2%)	One-26 (53.06%) Two-20 (40.82) Three-3 (6.12)	Mean±SD 16.69 ± 9.80	Complication-05 No complication-45
Significance	*p*-value 0.027	*p*-value <0.001	*p*-value <0.001	*p*-value 0.161

Discussion

Benefits and utility of CVC placement is well established but evidences has shown that landmark based approach in CVC insertion is associated with significant complications, including arterial puncture, hemothorax, pneumothorax, brachial plexus injury, hematoma formation, catheter malposition[13,14]. A review by Le frant et al.[15] described an overall complication rate of 15% in landmark technique. Central venous catheter cannulation is associated with a number of technical complications. The common ones are arterial puncture (10.6–13%)[16,17], hematoma formation (4–8.4%)[16,17], brachial plexus injury (1.7%)[18], pneumothorax (0–6.6%)[19,20], and hemothorax (1%)[4]. The procedure is also associated with some rare but serious complications, including arterial rupture (<1%)[21], arteriovenous fistula formation (0.2%)[22], guidewire loss (0.5%)[23], chylothorax and chylopericardium.

Various studies have shown that incidence of success is more in case of USG guided CVC insertion than landmark technique.[5,12,18] In case of USG guided CVC catheterisation the path of needle can be visualised. Thus it becomes easier to perform catheterisation under ultrasound guidance. In case of landmark technique anatomic aberration cannot be ruled out so there is more chance of failure and complication. The image quality offered by 2-dimensional USG allows the user to clearly see variations in anatomy and to assess the patency of a target vein.

Similar results were reported by G.C. Clagett[24], J. Leung *et al.*[25] and Dimitrios karakitsos *et al.*[26] . They concluded that ultrasound-guided catheterisation of the internal jugular vein in critical care patients is superior to the landmark technique and therefore should be the method of choice in these patients. C. Froehlic *et al.*[27] demonstrated that there was no difference in the overall success rates (88.2% LM vs. 90.8% US) between landmark and USG guided technique. Ninfa Mehta *et al.*[28] found that the ultrasound was significantly (p=0.02) more successful at eventually placing CVCs into a internal jugular vein with a relative success (RS) rate of RS=1.19, higher success rate for the USG78% compared with the LMT- 55%. In present study success rate was more in case of USG guided CVC insertion than LMT. In LMT successful cannulation was done in 86% patients which was in agreement to previous studies. Whereas cannulation was done in 98% patients, and was in accordance to previous studies. p-value was 0.027 and was statistically significant. Hence it was concluded that USG guided CVC insertion is better than landmark technique.

In present study it was found that failure occurred in 14% patients in landmark technique, whereas 2% failure occurred in USG guided technique. p-value was 0.027 and was statistically significant. Our result was in accordance with previous studies.

It has been shown in many studies that use of ultrasound decreases number of attempts.[25,29-31] Variations in external landmarks and internal anatomy can make landmark-guided cannulation challenging.

E.Koski *et al*.[31] compared the conventional method with the ultrasound-aided technique. The venous lumen was reached with fewer punctures while using the ultrasound-aided technique. Similarly, Randolph *et al*.[30] evaluated the effect of real-time ultrasound guidance using a regular or Doppler ultrasound technique for placement of central venous catheters. They found that USG significantly decreases the need for multiple catheter placement attempts when compared with the standard LMT.

C. Froehlic *et al*.[27] demonstrated median number of attempts were fewer with USG for all CVCs attempted. Ultrasound identified the vein size and location, anomalies, and vessels patency, thus avoiding futile attempts in patients with absent or thrombosed veins and congenital anomalies such as persistent left superior vena cava.M. Bruzoni *et al*.[32] also compared and reported success at first attempt in 65% of patients in the ultrasound group vs 45% in LMT (p = 0.021). Ultrasound reduced the number of cannulation attempts necessary for venous access.

In the present study out of 50 patient's cannulation was done in 1 attempt in 8 (18.60%) patients, two attempts in 24 (55.81%) patients and three attempts in 11 (25.58%) patients by LMT. In USG guided technique CVC inserted in one attempt in 26 (52%) patients, in two attempts in 20 (40%) patients, and in three attempts in 3 (6%) patients out of 50 patients. There was a statistically significant difference between the two groups. It was found in previous studies that use of USG decreases the time taken to puncture IJV as compared to traditional LMT. U. Teichgraber et al[33] showed that access time was markedly shorter with the sonographically guided technique (mean, 15.2 sec: range, 8-76 sec) than with the anatomic LMT (mean, 51.4 sec; range, 3-820 sec)/p = .001). In ultrasound lumen of vein could be visualised which probably reduces the time taken from skin puncture to aspiration of blood. Thus time taken to cannulate the vessel decreases.

C. Froehlic *et al*.[34] demonstrated mean time with USG (median 919 seconds vs. 405 seconds, p = 0.02) and Henjarappa *et al*.[35] reported the mean access time in USG technique lesser than in LMT. Similarly in the present study it was found that mean time taken to cannulate IJV was significantly lower in USG guided technique as compared to LMT. In group A time range was 18-96 seconds while in group B it was between 8-76 seconds. In group A time taken to catheterise was Mean± SD=42.59 ± 16.54, was significantly higher as compared to group B, which was Mean± SD=16.69 ± 9.80.

Randolph *et al*.[12] evaluated that ultrasound guidance significantly decreases complications during catheter placement. U. Teichgraber *et al*.[31] demonstrated that complications were fewer with USG (neck hematoma, 2% versus 10%; plexus irritation, 4% versus 6%; carotid artery puncture, 0% versus 12%).J. Leung *et al*.[26] observed that there was a 10.8% complication rate, with 16.9% complications in LMT and 4.6% in the ultrasonographic group, a difference of 12.3%. However in the present study we found that out of 50 patient's complications occurred in 10 (20%) patients in LMT while in 5 (10%) patients in USG guided technique. Although the difference in incidence of complication between two groups was not statistically significant, the incidence was less in USG guided group.

Limitations

As with most of the studies our study is not exceptional. It has some limitations and weaknesses which were inevitable. It could not be double blinded, this limitations has an inborn chance of being biased. The study was randomised on the basis of technique of insertion of central venous catheter. However, the strength of the study was the sample size, and populations with various disease process.

Conclusion

Considering the findings of the study, we concluded that USG guided CVC insertion has a better success rate, less failure, required less number of attempt and time taken to insert the CVC was significantly less. However, there was less complication with USG guided CVC insertion in present study, but it did not achieve statistical significance.

Hence, we suggest that as per the NICE guideline Central Venous Cannulation should be done under the USG guidance, if available especially in patients who are critically ill. This will increase the success rate; decrease the number of attempts, duration of insertion, duration of insertion and complications.

Source(s) of support: Nil.

Conflict of interest: None

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1465-1473
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.56

A Comparative Study of Intrathecal Levobupivacaine and Levobupivacaine with Midazolam in Lower Abdominal and Lower limb Surgeries

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Abstract

Context: Intrathecal midazolam as an adjuvant to levobupivacaine provides excellent intraoperative hemodynamic stability and also good postoperative analgesia. Present study was done to evaluate the efficacy, duration of pain relief, the incidence of adverse effects and complications when midazolam is given along with levobupivacaine intrathecally. *Aims:* To compare between intrathecal levobupivacaine (Group LB) and intrathecal levobupivacaine with adjuvant midazolam 1 mg (Group LBM) with respect to onset and duration of analgesia, motor blockade, intraoperative discomfort and postoperative analgesia requirement and complications like nausea, vomiting, respiratory depression etc. *Methodology:* In this prospective, randomized, double blind, placebo controlled study a total of 100 patients of American Society of Anaesthesiologists (ASA) grade I and II, undergoing elective lower abdominal and lower limb orthopaedic surgery under sub-arachnoid block were randomized into two groups. Group LB (n=50) received 3 ml of 0.5% isobaric levobupivacaine with 0.2 ml of normal saline and Group LBM (n=50) received 3 ml of 0.5% isobaric levobupivacaine with 0.2 ml midazolam (1 mg) (preservative free) as intrathecal anesthesia. Assessment of sensory blockade, motorblockade, duration of analgesia, intraoperative hemodynamics, discomfort and postoperative analgesia estimated. After surgery, patients were asked to score their pain at 2, 4, 6, 12, 18 and 24 hr by VAS score. The presence of postoperative nausea vomiting (PONV), pruritus and respiratory depression were recorded and compared between the two groups. *Statistical analysis:* For continuous variables the summary statistics of N, mean, standard deviation (SD) were used. For categorical data,the number and percentage were used in data summaries.Chi-square($\chi 2$)/ Fisher exact test was employed to determine the significance of differences between groups for categorical data. The difference of the means of analysis variables was tested with unpaired *t*-test. *p*-value <0.05 was considered significant. Data were analysed using SPSS software v.23.0. *Results:* Group LBM had superior quality of analgesia,prolonged duration of analgesia, reduced postoperative analgesic requirement and minimal hemodynamic changes compared to Group LB. *Conclusions:* Intrathecal midazolam potentiates levobupivacaine effect leading to better quality and longer duration of analgesia, better sedation, better postoperative outcome with minimum side effects.

Keywords: Midazolam; PONV; Visual Analogue Pain Scale; Adjuvants, Anesthesia; Assessment, Pain.

How to cite this article:

Siddesh N Kadur, Ravi kumar M, Abhishek M Patil. A Comparative Study of Intrathecal Levobupivacaine and Levobupivacaine with Midazolam in Lower Abdominal and Lower limb Surgeries. Indian J Anesth Analg. 2019;6(4): 1465-1467.

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Received on 03.07.2019, **Accepted on** 22.07.2019

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Introduction

Subarachnoid block is one of the most versatile regional anesthesia techniques available today. Subarachnoid block provides adequate anesthesia for patients undergoing lower abdominal and lower limb surgeries. In order to maximize quality of anesthesia and post operative analgesia, a number of adjuvants have been added to local anaesthetics. The benefits of intrathecal opioids and non-opioids as adjuvants in spinal anesthesia are well documented. The addition of intrathecal opioids is however associated with dose related adverse effect such as respiratory depression, nausea, vomiting, urinary retention, pruritus and sedation.[1] So, use of non-opioids such as ketamine, clonidine, neostigmine, magnesium sulphate, midazolam have become popular adjuncts for postoperative analgesia.[2]

Hyperbaric bupivacaine is one of the common local anaesthetic used for spinal anesthesia in patients undergoing lower abdominal and lower limb surgeries. However, it has considerable adverse effects on the cardiovascular and central nervous system. Enantiomers of bupivacaine may have the same desired pharmacological properties, but fewer side effects. Levobupivacaine, the S(-)-enantiomer of bupivacaine has been shown to provide a more selective neuraxial blockade than racemic bupivacaine.[3] Intrathecal midazolam abolishes pain of somatic origin, produces selective sensory block and depresses somatosympathetic reflexes without any neurotoxicity. It potentiates the blocking actions of local anaesthetics. It improves the quality of sensory and motor block, without prolonging the recovery and also provides good postoperative analgesia.

The subarachnoid midazolam was originally shown to have anti-nociceptive properties in studies performed in animals in early 1980's.[4] The subarachnoid midazolam has been used in humans since 1986 and doses up to 2 mg have been described.[5] There are many clinical studies in favour of intrathecal midazolam which has added advantages of sedation, amnesia and anti-nociceptive effects without any neurotoxicity or other side effects.

Hence, this study was designed to evaluate the efficacy, to know the duration of pain relief, to know the incidence of adverse effects and complications when midazolam (preservative free) is given along with levobupivacaine intrathecally.

Materials and Methods

This prospective, randomized, double-blind study was conducted at Department of Anaesthesiology, Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapur from December 2014 to June 2016. The study included 100 patients of ASA Grade I and II, age 20-45 years, body weight 50-80 kg who underwent elective lower abdominal and lower limb surgery. The study was approved by the institutional ethical committee.

Patients belonging to ASA grade III and IV, pregnant women, patients on long term analgesic therapy and chronic alcoholics, had any deformity or local pathology in lumbar spine region, history of convulsions, allergy to the drugs used, bleeding disorders, were uncooperative and with severe neurological deficit were excluded from the study. Patients with severe hypovolemia, anemia, receiving steroid medication and patients in whom spinal anesthesia failed and general anesthesia was required were also excluded from the study.

Preanaesthetic check-up was done on the day before surgery, and included a complete history and any known drug allergy, general and systemic examination and local examination of lumbar spine region. Pulse rate, blood pressure, respiratory rate, and weight and height of the patient were noted. Relevant investigations were done in all the patients.

The anaesthetic procedure was briefly explained to the patient. The patients were also introduced to Visual Analogue Scale (VAS) and taught how to use it. An informed written consent was obtained from the patient or his/her relatives.

The patients were randomized on the day of surgery into two groups of 50 each. Hundred pieces of paper, 50 with 'saline' written on them and 50 with 'midazolam' written were put in a box and the patients were asked to pick one piece of paper. This piece of paper was handed to an anaesthesiologist unconnected to the study who prepared the medications. Group LB patients received 3 ml of 0.5% isobaric levobupivacaine with 0.2 ml of normal saline and Group LBM patients received 3 ml of 0.5% isobaric levobupivacaine with 0.2 ml of midazolam (1 mg) (preservative free) intrathecally. [1 ml midazolam ampoule (preservative free) consisted 5 mg, of which 0.2 ml = 1 mg was given intrathecally].

On arrival in the operating room fasting status (at least for 8 hours), and written consent was checked,

the patient was connected to the routine monitors which included non invasive blood pessue, pulse oximeter and electrocardiogram. Base line pulse rate, blood pressure, respiratory rate, SpO_2 were recorded.

All resuscitation equipments like intubation trolley with airways, laryngoscopes, endotracheal tubes along with drugs like atropine, mephentermine were kept ready. The anesthesia machine was also checked along with the oxygen delivery system.

A18 or 20 gauge intravenous access was obtained and secured. All patients were preloaded with 15 ml/kg of Ringer's lactate prior to spinal anesthesia. The patients were then put in sitting position. Under strict aseptic precautions, lumbar puncture was performed by midline approach by using disposable Quincke spinal needle (25G) at L_3–L_4/ L_2-L_3 intervertebral space.

Patients were continuously monitored using sphygmomanometer, pulseoximeter and electrocardiogram. After spinal anesthesia, the patient's pulse rate and blood pressure were recorded at 0, 5, 10, 20, 30, 45, 60, 90 and 120 minutes.

Assessment of sensory blockade was tested by pin-prick method.

The time of onset: Time of injection of the drug into the subarachnoid space to loss of pin-prick sensation.

Maximum sensory block: Time of injection of drug to loss of pin-prick sensation at highest dermatomal level.

The time for two dermatomal segments regression of sensory level was noted.

Duration of sensory blockade: time of onset to time of return of pin prick sensation to L_2dermatomal area.

Assessment of motor blockade was done by Bromage scale.

Bromage Scale:

Grade-I (No block): Full-flexion of knees and ankle joint possible

Grade-II (Partial block): Just able to flex knees, but still full flexion of ankle joint possible

Grade-III (Almost complete block): Unable to flex knees. Flexion of ankle joint possible.

Grade-IV(Complete block): Unable to flex knees or ankle joint

The time of onset: The time interval between injections of drug into subarachnoid space to the patient's inability to lift the straight extended leg.

Maximum motor blockade: time of injection of the drug to maximum degree of motor block.

Sedation score was assessed every 15 min both intra and postoperatively using a four point scale (1= awake, 2=drowsy but responding to verbal commands, 3=drowsy but responding to physical stimulus, 4=unresponsive to verbal/ physical stimulus).

Postoperative pain was measured and recorded using a 10 point Visual Analogue Scale (VAS). VAS consisted of a 10 cm line, one end labelled as No pain and other end as Worst possible pain. Patients marked on the scale as per severity. Patients were asked to score the pain both at rest and during movement at 2, 4, 6, 12, 18, and 24 hours after surgery.

The duration of effective analgesia :time of intrathecal drug administration to the time of first supplementation with rescue analgesic. Intavenous Diclofenac 75 mg was given as the rescue analgesic if VAS was found to be 4 or more.

The incidence of hypotension, bradycardia were noted during intraoperative period and also in the recovery room. Patients were monitored for any adverse event (e.g. nausea, vomiting, urinary retention etc.) during the following time periods 0–3, 3–6, 6–12, and 12–24 h.

Statistical analysis: For continuous variables the summary statistics of N, mean, standard deviation (SD) were used. For categorical data, the number and percentage were used in data summaries. Chi-square($\chi 2$)/Fisher exact test was employed to determine the significance of differences between groups for categorical data. The difference of the means of analysis variables was tested with unpaired t-test. p-value <0.05 was considered significant. Data were analysed using SPSS software v.23.0.

Results

Our study consisted of 100 patients of ASA I and II divided into 2 groups. Group LB received 3ml of levobupivacaine and 0.2ml saline and group LBM received 3ml levobupivacaine and 0.2ml midazolam (preservative free 1mg).

Patient characteristics across the groups

The patients studied across the group did not vary much with respect to age, sex or height. The

type of surgeries performed were almost identical in both the groups. These parameters were kept identical in both the groups to avoid variations in the intraoperative and postoperative outcome of the patients (Table 1-3).

The mean age, sex, height, ASA grading and duration of surgery were similar in both the groups

Table 1: Percent Distribution of Age in two study groups

Age group	Group LB		Group LBM	
	N	%	N	%
21–25	12	24.0%	12	24.0%
26–30	10	20.0%	11	22%
31–35	12	24.0%	11	22.0%
36–40	6	12.0%	7	14.0%
41–45	10	20.0%	9	18.0%
Total	50	100.0%	50	100.0%

Table 2: Percent Distribution of Sex in two study groups

Sex	Group LB		Group LBM	
	N	%	N	%
Male	29	58.0%	25	50.0%
Female	21	42.0%	25	50.0%

Table 3: Percent Distribution of ASA grade in two study groups

ASA Grade	Group LB		Group LBM		*p* value
	N	%	N	%	
I	40	80.0%	32	64.0%	
II	10	20.0%	18	36.00%	0.075
Total	50	100.0%	50	100.0%	

Time of onset of sensory block was 153.2 ± 8.7 secs in group LB and 173.0 ± 5.8 secs in group LBM which was statistically significant (p<0.001). Time of onset of motor blockade between groups was statistically significant (p<0.001). The duration of analgesia was 139.6 ± 8.7 min in group LB and 263.80 ± 35.8 min in group LBM (P<0.001) and statistically significant. Two segment regression was 87.2 ± 3.4 min in group LB and 122.6 ± 3.6 min in group LBM (p<0.001) and statistically significant. The difference between the groups was statistically highly significant (Table 4).

VAS scores between groups LB and LBM at 3hrs was 0.43 ± 0.78 and 0.02 ± 0.43,at 6 hrs 4.22 ± 0.51 and 0.62 ± 0.65, at 12 hrs 5.41 ± 0.42 and 1.73 ± 0.76 respectively, which was statistically significant (p<0.001). The difference between the groups was statistically highly significant (Table 5).

The means of sedation score between the groups was comparable (Table 6).

There were 3 episodes of badycardia and hypotension in each of the 2 groups (p=0.999) (Table 7)

The difference in heart rate between the groups at different time intervals were statistically insignificant (*p*>0.05) (Fig. 1).

Systolic blood pressure comparison showed to be statistically insignificant (Fig. 2 and 3).

Means of sedation score were comparable in both the groups (Fig. 4).

Table 4: Variables in study (mean ± SD)

Variables	Group LB (n=50)	Group LBM (n=50)	*p* value	Significance
Duration of Analgesia (min)	139.6 ± 8.7	263.80 ± 35.8	<0.001	S
Onset of sensory block (sec)	153.2 ± 8.2	173.0 ± 5.8	<0.001	S
Onset of motor block (sec)	220.4 ± 7.3	240.4 ± 4.6	<0.001	S
Two segment regression (mins)	87.2 ± 3.4	122.6 ± 3.6	<0.001	S

Table 5: Comparison of Visual Analogue Scores at different time interval between two study groups

Time in hours	Group LB		Group LBM		Mean Difference	*p* value
	Mean	SD	Mean	SD		
3	0.43	0.78	0.02	0.43	0.5	<0.001*
6	4.22	0.51	0.62	0.65	-19.8	<0.001*
12	5.41	0.42	1.73	0.56	-20.0	<0.001 *

Table 6: Comparison of Means of Sedation Score in two study groups by different time (Min)

Time	Group LB		Group LBM		Mean Difference	*p* value	95% Confidence Interval	
	Mean	SD	Mean	SD			Lower	Upper
3''	0.0	0.0	0.0	0.0	-	-	-	-

6''	0.0	0.0	0.0	0.0	-	-	-	-
9''	0.0	0.0	0.0	0.0	-	-	-	-
12''	0.0	0.0	0.0	0.0	-	-	-	-
15''	0.0	0.0	0.0	0.0	-	-	-	-
20''	0.0	0.0	0.0	0.1	0.0	0.320	-0.1	0.0
25''	0.0	0.0	0.0	0.1	0.0	0.320	-0.1	0.0
30''	0.0	0.1	0.0	0.2	0.0	0.562	-0.1	0.0
40''	0.1	0.2	0.0	0.1	0.0	0.312	0.0	0.1
50''	0.0	0.0	0.1	0.2	-0.1	0.080	-0.1	0.0
60''	0.0	0.0	0.0	0.1	0.0	0.320	-0.1	0.0
90''	0.0	0.0	0.0	0.1	0.0	0.320	-0.1	0.0
120''	0.0	0.0	0.0	0.0	-	-	-	-
180''	0.0	0.0	0.0	0.0	-	-	-	-

Table 7: Percent Distribution of Complications in two study groups

Complications	Group LB		Group LBM		p value
	N	%	N	%	
Bradycardia	3	50.0%	3	50.0%	
Hypotension	3	50.0%	3	50.0%	0.999
Total	6	100.0%	6	100.0%	

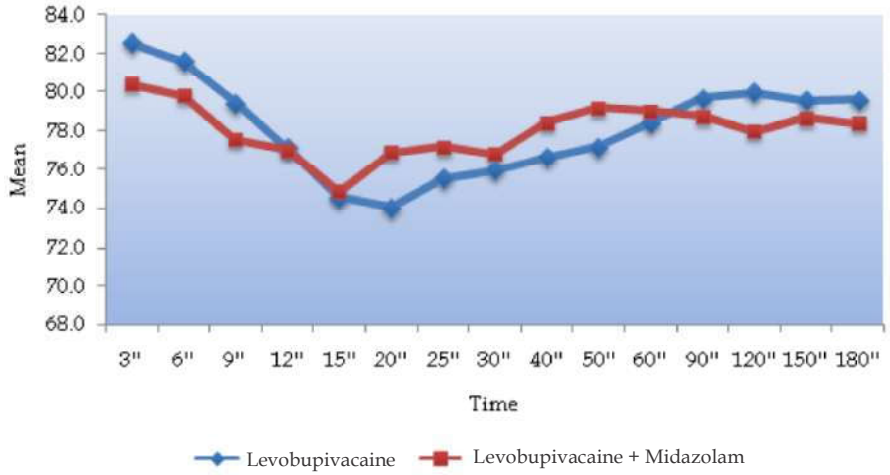

Fig 1: Comparison of means of heart rate in the two groups

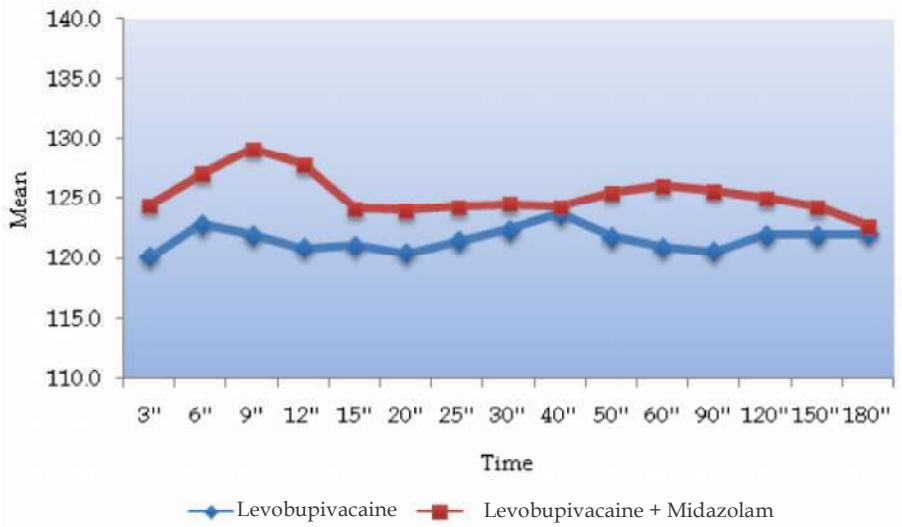

Fig 2: Comparison of Means of Systolic Blood Pressure in two study groups by different time (Min)

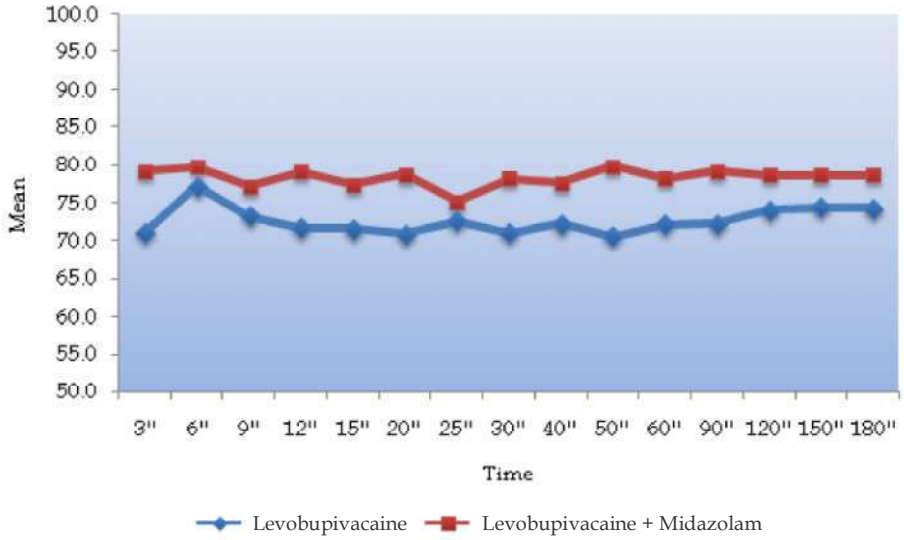

Fig. 3: Comparison of Means of Diastolic Blood Pressure in two study groups by different time (Min)

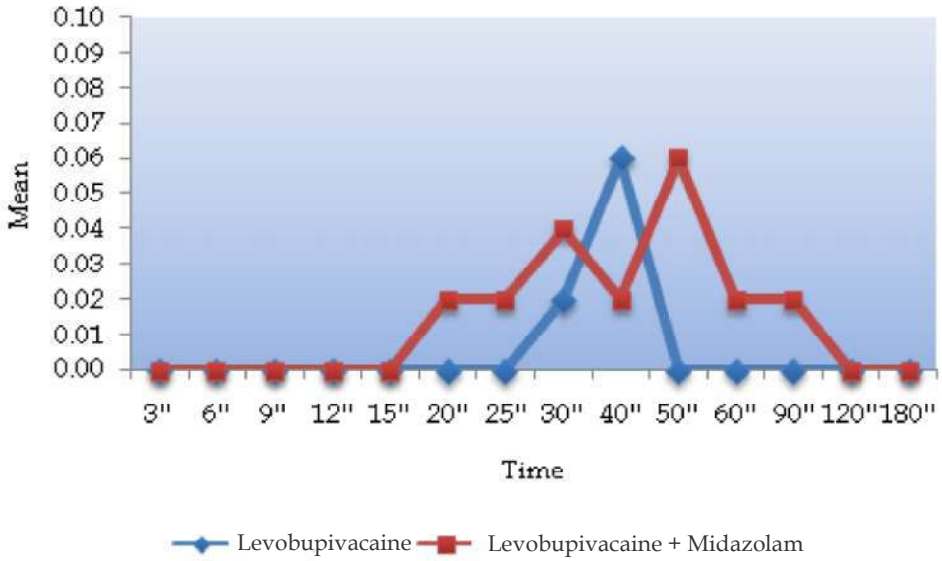

Fig. 4: Comparison of Means of Sedation Score in two study groups by different time (Min)

Discussion

The subarachnoid blockade is the common form of centrineuraxial blockade performed for lower abdomen and lower limb surgeries.Intrathecal midazolam has been used as an adjuvant to local anaesthetics since 1980s. It has been tried widely and antinociceptive effect with neurological safety has been well established in animals and humans.

The intrathecal benzodiazepine induced analgesia is spinally mediated. The binding sites of midazolam are GABA receptors which are abundant in dorsal root nerve cells of spinal cord. The maximum concentration of GABA receptors are found within lamina II of dorsal nerve cells, a region which plays prominent role in processing nociceptive and thermoceptive stimulation. Acting over the GABA receptors benzodiazepines induce changes in chloride conductance and enhance GABA induced presynaptic inhibition of primary afferent terminals.

Changes in the perioperative cardiovascular parameters

In the present study, the incidence of hypotension was equal, with 3 patients in each group had a fall in blood pressure. Hypotension was corrected by administration of injection mephentermine 6 mg

IV in incremental doses and giving IV fluids. Heart rate, systolic and diastolic blood pressure in both the groups did not vary significantly. Goodchild CS, Noble J in 1987[5], Bahar M, Cohen ML *et al.* in 1997[6], Batra YK and *et al.* in 1999[7] and Bharti N and *et al.* in 2003[8] found no difference in the hemodynamic responses to the drugs used. Our study correlated with. Rosa Herrera and *et al.*[9] study of stable hemodynamics with isobaric levobupivacaine.

Changes in respiratory parameters

None of the patients in the present study had respiratory depression. Bahar M and *et al.* in 1997[6] found no changes in the arterial blood gases or respiratory rate when given intrathecal midazolam in animal model. Sen A and *et al.* in 2001[10] found that intrathecal midazolam produces better tranquility of patients of caesarian section delivery without much sedation and respiratory depression. Apgar score of baby in 1st and 5th minute of delivery was found to be normal.In our study we did not include caesarian section deliveries. Bharti N and *et al.* in 2003[8] studied the effect of intrathecal 1 mg of midazolam with hyperbaric bupivacaine in patients undergoing lower abdominal surgery and found no change in oxygen saturation.

The above observations were similar to our study results. We conclude that intrathecal midazolam 1 mg is safe to use without causing respiratory depression.

Changes in the onset of sensory and motor blockade

In our study the onset of sensory blockade in group-B was 153.2±8.2 seconds compared to 173.0±5.8 seconds in group-II which was statistically highly significant ($p < 0.001$). It shows that addition of midazolam to local anaesthetic delays the onset of analgesia. Similarly the onset of motor blockade in group-B was 220.4 ± 7.3 compared to 240.4 ± 4.6 seconds in group-BM which was also statistically highly significant ($p < 0.001$) i.e., the addition of midazolam to local anaesthetic delays the onset of motor blockade. Yegin A and *et al.* 2004[11] did not find anydelay in onset of sensory and motor blockade with addition of 2 mg of midazolam to hyperbaric bupivacaine in spinal anesthesia in patients undergoing perianal surgery. But in our study we used isobaric levobupivacaine instead of bupivacaine.

From the above study we conclude that there is variation in the onset of sensory and motor blockade in different studies. Though it is statistically significant in our study it does not have any clinical implications.

Time for two dermatomal segments regression of sensory level

In our study, the two segment regression of sensory level in group LB was 87.50 ± 4.4 minutes compared to 122.00 ± 3.6 minutes in group LBM which was statistically highly significant ($p < 0.001$). This shows that addition of midazolam increases the duration of sensory blockade.

Bharti N and *et al.* in 2003 found that duration of sensory block (ie., time to regression to S_2 segment) was significantly longer in the midazolam group than the control group (218 min vs 165 min, $p < 0.001$). Venkatesh Selvaraj, Tapan Ray in 2015[12] had similar finding with midazolam as an adjuvant to intrathecal lignocaine. So we can conclude that intrathecal midazolam increases the duration of sensory blockade.

Time of first request of analgesics

In our study, the time of first request of analgesics in group LB was 139.00 ± 8.77 minutes compared to 263.8 ± 35.8 minutes in group LBM which was statistically highly significant ($p < 0.001$). This shows that there was significantly longer period of analgesia with intrathecal midazolam. Kim MH and *et al.* in 2001[13] found significantly greater time to first analgesia in the midazolam group in patients undergoing haemorrhoidectomy. Amr M and *et al.* in 2003[14] had similar finding in patients undergoing knee arthroscopy. Valentine J.M. J and *et al.* in 1996[15], Shah FR *et al.* in 2003[16] found prolonged duration of postoperative pain relief with midazolam as adjuvant. These studies validate our findings of prolonged first request of supplemental analgesics in the postoperative period.

Visual Analogue Score

In our study, there was significant reduction in the visual analogue score of the patients in group LBM in comparison with higher VAS in group LB recorded at 3 hours, 6 hours and 12 hours of spinal anesthesia. Shah FR and *et al.* in 2003 showed that patients treated with intrathecal midazolam had better pain relief judged by visual analogue scroe on coughing ($p = 0.0013$) and a nursing mobility score ($p < 0.0001$). Yegin A and *et al.* in 2004 found significantly lower visual analogue pain scores in midazolam group at the first 4 hours.

Above studies support that intrathecal midazolam potentiates the sensory blockade of levobupivacaine, there by reduce the visual analogue scores in the early post operative period bringing about better post operative outcome.

Sedation Score

The sedation score was assessed by scoring system of Chernic *et al.*[17]

In our study the sedation score ranged from 0 to 1 in both the groups. Most of the patients in group LBM were calm and sleeping comfortably were as most of the patients in the group LB were awake and alert. Nishiyama T 1995[18] studies used midazolam for pre and post operative sedation which showed the sedation scores were higher in the patients receiving midazolam by the epidural or intrathecal route. Vaswani *et al.*[19] found sedation scores were less but more sustained when the midazolam is administered intrathecally. Anjana Sen *et al.* also reported the higher sedation scores with intrathecal midazolam.

The results of present study are consistent with both the authors though the duration of the sedation is less. This may be because of different doses of the drug.

Adverse Effects

In the present study, 3 patients had hypotension and bradycardia, 1 patient had shivering and nausea vomiting in group LBM compared to 3 patients of hypotension, 2 patients of shivering and 1 patient of nausea & vomiting in group LB. This signifies that adverse effects are minimal with intrathecal midazolam.

Studies in humans by Valentine JMJ *et al.* in 1999, Sen A and *et al.* in 2001, Bharti N and *et al.* in 2003, Shah FR and *et al.* in 2003, Amr M and *et al.* in 2003, Tucker AP and *et al.* in 2004, found no adverse neurological symptoms in those received intrathecal midazolam. They also found that intrathecal midazolam has mild sedative and antiemetic effect.

Conclusion

With all the above observations we conclude that addition of midazolam to levobupivacaine provides prolonged analgesia, superior pain relief and better sedation with minimal side effects compared to levobupivacaine alone in spinal anesthesia**.**

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1474-1482
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.57

Attenuation of Hemodynamic Response to Laryngoscopy and Endotracheal Intubation by using Oral Ivabradine

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Abstract

Introduction: Laryngoscopy gives rise to a stress response that is seen as rise in heart rate and blood pressure and as dysrhythmia. Such changes are at peak immediately after intubation and can be dangerous for those having already limited or compromised cardiovascular reserve. They can lead to increased risk of myocardial infarction (MI), stroke, congestive cardiac failure or sudden death. *Aims and Objectives:* To study the effect of oral Ivabradine in attenuating the hemodynamic stress response to laryngoscopy; and to endotracheal intubation and extubation. *Materials and Methods:* A randomized double blinded study was done. Total number of 140 patients (adult patients undergoing ENT surgery) were randomly taken into two Groups. The first group was labelled as Test Gropu (A) and the second group was called Control Group (B). Each group had 70 patients. The Test group (A) received 5 mg oral Ivabradine and the Control group (B) received placebo. Patients were monitored for hemodynamic changes as per the protocol. *Result:* Mean heart rate, SBP, DBP and MAP reading at intubation, post-intubation period till 10 mins, at extubation and till 10 minutes post-extubation were significantly less in test group i.e. in patients who received oral Ivabradine as compared to control group (p<0.05). *Conclusion:* We conclude that Ivabradine is an extremely useful drug to prevent abnormal tachycardias during the procedure of laryngoscopy and intubation. Its stabilizing effect of haemodynamics also extends up to extubation and immediate post-operative period.

Keywords: Ivabridine; Heart Rate; Diastolic Blood Pressure; Systolic Blood Pressure; Mean Arterial Pressure.

How to cite this article:

Vikas Bedi, Gaurav Chopra, Ashutosh Singh *et al.* Attenuation of Hemodynamic Response to Laryngoscopy and Endotracheal Intubation by using Oral Ivabradine. Indian J Anesth Analg. 2019;6(4): 1468-1476.

Introduction

Endotracheal intubation is a very common procedure, where the anesthesiologists have an important role to play.

Stress response with laryngoscopy manifest as tachycardia, hypertension and dysrhythmias and may have deleterious respiratory, neurological and cardiovascular effects[1]. These changes are maximum immediately after intubation and lasts for 5-10 minutes.

These effects are generally well tolerated by overall healthy patients but can be lethal to patients with preexisting conditions such as coronary

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Received on 16.04.2019, **Accepted on** 14.05.2019

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artery disease, recent myocardial infarction, hypertension, geriatric population, pre-eclampsia, and cerebrovascular pathology such as tumours, aneurysms or increased intracranial pressure and are at increased risk of morbidity and mortality.[2]

Geriatric and elderly patients are more susceptible to coronary artery disease and cerebrovascular disease as they have elevated baseline blood pressure, making them especially susceptible to variations in blood pressure, and heart rate during the procedures of laryngoscopy and endotracheal intubation, which can become critical for patients with compromised cardiovascular reserve with the resultant risk of myocardial infarction (MI), stroke, congestive heart failure or sudden death.[3]

Ivabradine also known as a cardiotonic agent is a highly selective inhibitor of 'If' channels which causes a reduction in the slope of spontaneous depolarisation. This results in an increase in the time interval between successive action potentials in the SA node, which in turn leads to slowing of heart rate.

Ivabradine slows down the heart rate but it does not cause sudden fall in blood pressure and for this reason it is desirable to use it in patients with pre-exsisting heart conditions like angina pectoris, coronary artery disease, heart failure, obstructive cardiomyopathies and other conditions where the myocardial perfusion is reduced.[4]

The α-2 receptors are present at various sites in peripheral and central nervous system, in visceral organs such as liver, kidney, pancreas, in eyes, the media of vessel walls, and also in platelets.[5]

It is difficult to classify the α-2 receptors on the basis of anatomical location as these receptors are present in presynaptic, postsynaptic and extrasynaptic locations.[6]

These receptors are divided into three subtypes and each type has unique actions of α-2 receptors. Within the CNS, the subtype A receptors are more common and are responsible for the sedative, analgesic and sympatholytic effect. The peripheral vessels and vasculature house the subtype B receptors that are responsible for the short term hypertensive response. The CNS also has subtype C receptors which play a role in anxiolysis.[7]

The α-2 adrenergic receptor mediates its effect by activating guanine-nucleotide regulatory protein (G proteins) which modulate cellular activity by signalling a second messenger system, which when activated leads to inhibition of adenylate cyclase which in turn, results in decreased formation of 3, 5- cyclic adenosine monophosphate (c-AMP).

This leads to hyperpolarization of the excitable cell membranes and provides effective means of suppressing neuronal firing. Stimulation of α-2 receptor also suppresses calcium entry into the nerve terminal, which may be responsible for this inhibitory effect on secretion of neurotransmitters.[8]

Aims and Objectives

1. To study the effect of oral Ivabradine on the hemodynamics (Heart rate, SBP, DBP and MAP) at the time of laryngoscopy and endotracheal intubation and also during extubation, in patients undergoing surgical procedures under general anesthesia.
2. To study the incidence of side effects (bradycardia, hypotention) and complications, if any, due to study drug.

Material and Methods

Study Area

Department of Anesthesia, Shri Mahant Indresh Hospital, the associated hospital of Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun (Uttarakhand).

Study Population

Adult patients undergoing ENT Surgery at our hospital

Study Design

A randomized double blinded study.

Sample Size

A total of 140 patients were studied. They were randomly put in two groups labelled as Test group and Control so that each group had 70 patients. The opaque, sequentially numbered sealed envelopes were stored in the preoperative room. Randomization of the patients to one of the 2 treatment arms was done using computer generated random numbers. Each patient picked up an envelope which contained a folded card. Those marked with 'A' were randomized to receive 5 mg oral ivabradine and those marked received 'B' placebo (sugar coated tablet).

Group-A or the Test Group: Had 70 patients, and they were given oral Ivabradine, 5 mg tab one hour before intubation.

Group-B or the Control Group: Had 70 patients, and they were given placebo (sugar coated tablet) one hour before intubation.

Study Duration

Dec 2016 - May 2018

Inlusion Criteria

Adult patients undergoing ENT Surgery, ASA Grade-1 and Grade- 2 and Age group of 20-50 years

Exclusion Criteria

Patients who refused to participate in the study, patients with low base line heart rate of less than 60 beats per minute, base line SBP <100 mm Hg, those having abnormal ECG readings, patients with previous history of angina or chest pain, or palpitations or history of syncope or any visual disturbances.

Patients already taking calcium channel blockers, azole antifungals, antiretroviral drugs, and macrolide antibiotics were excluded.

ASA Grade 3 and 4 were excluded.

Pregnant and breastfeeding females were excluded.

Patients with difficult intubation that took more than 20 seconds to intubate were also excluded.

Methodology

The premedication, induction agent and muscle relaxant to facilitate intubation were standardized for both the groups.

Intravenous cannulation with 18G cannula was done once the patients were shifted into the preoperative room and a drip of ringer lactate solution was started.

Premedication was done with Midazolam 1mg and Ondansetron 4 mg slowly intravenously, just before induction.

Injection fentanyl in a dose of 2 mcg/kg body weight was given as an analgesic.

Patient was connected to non- invasive blood pressure monitors, pulse oximeter probe and electrocardiographic leads. All patients were pre oxygenated with 100% oxygen for 3 minutes.

Injection Propofol (2 mg/kg body weight) was used for induction of ptients.

Vecuronium 0.1 mg/kg intravenously was used to facilitate the intubation. The lungs were ventilated with 100% oxygen for 3 minutes.

For both the groups, intubation was timed at 60 minutes after Ivabradine pre-treatment. Intubation was performed with an appropriate size oral cuffed, portex endotracheal tube by the aid of Macintosh laryngoscope blade.

Care was taken to ascertain that the time taken for intubation did not exceed 20 seconds. Anesthesia was maintained with Vecuronium bromide 0.02 mg/kg top-up doses; inhalational agent Isoflurane and intermittent positive pressure ventilation with nitrous oxide and oxygen in the ratio of 60%: 40% using circle absorber system connected to the Anesthesia work station (Drager fabius plus).

Recording of hemodynamic parameters were done as the patient was being cleaned and draped followed by commencement of surgery.

The recording of hemodynamic parameters was taken throughout the intra operative period.

At the end of the surgery, neuromuscular blockade was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.008 mg/kg). All the patients were thoroughly followed in the post-operative period.

In the postoperative period, both the groups were checked for any incidence of adverse effects of Ivabradine for 4 hours.

Any incidence of severe bradycardia (Heart Rate <50 bpm) was treated with injection Atropine 0.6 mg intravenously stat and hypotension (BP < 90/60 mm hg) was treated with injection ephedrine 6 mg intravenously stat.

The parameters that were recorded were

Heart rate, Systolic Blood Pressure, Diastolic Blood Pressure and Mean Arterial Pressure.

The above parameters were recorded at specific intervals as follows

Pre-operatively i.e. after premedication (for the basal line value).

At the time of induction/intubation, 1 minute after intubation 3, 5, 8 minutes and 10 minutes after intubation.

At the time of extubation, 1 minute after extubation, 3, 5, 8 minutes and 10 minutes after extubation.

Instruments Required

Anesthesia work station (Drager fabius plus) with circle absorber.

Multipara monitor for NIBP, SPO_2, heart rate, ECG, Resuscitatory equipments (Laryngoscope with Macintosh blade, oral cuffed portex endotracheal tube etc.)

Statistical Analysis

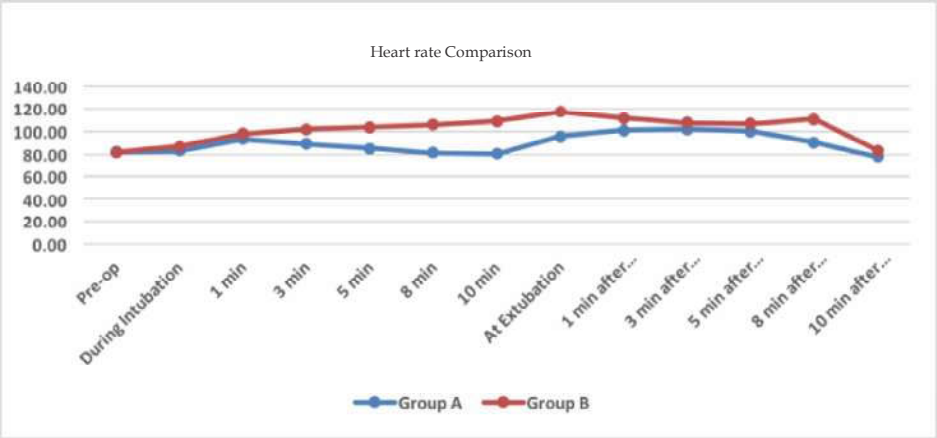
The quantitative data was represented as their mean ± SD. Categorical and nominal data was expressed in percentage. The t-test was used for analysing quantitative data, or else non parametric data was analyzed by Mann Whitney test and categorical data was analyzed by Chi-square test. The significance threshold of p-value was set at <0.05. SPSS software version 21 was used to analyse the data.

Results

Mean heart rate in test and control group were comparable at baseline i.e. pre-op period (82.47 vs 81.76/min; p-0.414). At intubation, post-intubation period till 10 mins, at extubation and till 10 minutes post-extubation, mean heart rate was significantly less in test group i.e. in patients who received oral Ivabradine as compared to control group (p<0.05). (Graph 1 and Table 1).

Table 1: Comparison of mean changes in heart rate between the two groups during the procedure

Heart Rate	Group	N	Mean	SD	p- value
Pre-op	A	70	82.47	4.46	0.414
	B	70	81.76	5.76	
During Intubation	A	70	83.04	6.06	<0.05
	B	70	87.23	6.26	
1 min	A	70	93.99	8.85	<0.05
	B	70	98.23	10.48	
3 min	A	70	89.27	8.84	<0.05
	B	70	102.10	8.56	
5 min	A	70	85.64	8.29	<0.05
	B	70	104.01	8.61	
8 min	A	70	81.40	7.20	<0.05
	B	70	105.93	10.81	
10 min	A	70	80.61	7.17	<0.05
	B	70	108.99	12.29	
At Extubation	A	70	96.00	14.86	<0.05
	B	70	117.49	18.30	
1 min after extubation	A	70	101.23	13.90	<0.05
	B	70	111.86	13.69	
3 min after extubation	A	70	101.97	12.85	<0.05
	B	70	107.89	10.18	
5 min after extubation	A	70	100.46	12.17	<0.05
	B	70	106.89	9.34	
8 min after extubation	A	70	90.91	7.81	<0.05
	B	70	111.00	9.34	
10 min after extubation	A	70	77.80	5.63	<0.05
	B	70	83.49	4.82	

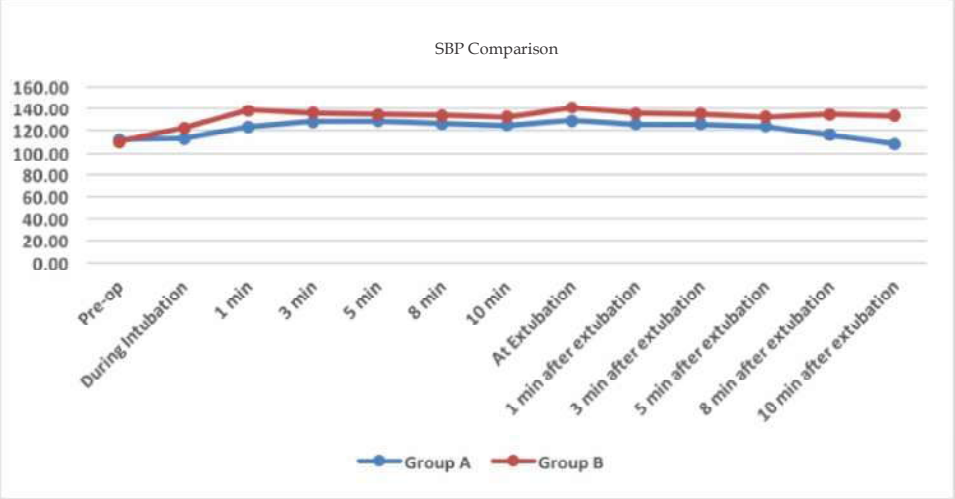


Graph 1: Comparison of mean changes in heart rate between the two groups during the procedure

Mean SBP in test and control group were comparable at baseline i.e. pre-op period (112.1 vs 110.47 mm Hg; p = 0.69). At intubation, post-intubation period till 10 mins, at extubation and till 10 minutes post-extubation, mean SBP was significantly less in test group i.e. in patients who received oral Ivabradine as compared to control group ($p < 0.05$) (Graph 2 and Table 2).

Table 2: Comparison of mean changes in systolic blood pressure between the two groups during the procedure

Systolic Blood Pressure	Group	N	Mean	SD	*p*-value
Pre-op	A	70	112.10	8.83	0.69
	B	70	110.47	12.42	
During Intubation	A	70	112.97	6.11	<0.05
	B	70	122.43	10.28	
1 min	A	70	123.61	6.97	<0.05
	B	70	138.50	12.66	
3 min	A	70	128.01	7.74	<0.05
	B	70	135.81	8.35	
5 min	A	70	128.44	6.47	<0.05
	B	70	134.81	5.97	
8 min	A	70	126.33	6.39	<0.05
	B	70	133.89	4.56	
10 min	A	70	125.00	6.42	<0.05
	B	70	132.10	6.06	
At Extubation	A	70	129.13	4.97	<0.05
	B	70	140.57	7.85	
1 min after extubation	A	70	125.94	5.34	<0.05
	B	70	135.71	5.49	
3 min after extubation	A	70	125.57	5.49	<0.05
	B	70	135.17	4.37	
5 min after extubation	A	70	123.97	6.60	<0.05
	B	70	132.31	8.23	
8 min after extubation	A	70	116.57	10.50	<0.05
	B	70	134.63	16.06	
10 min after extubation	A	70	108.43	13.45	<0.05
	B	70	133.06	8.44	

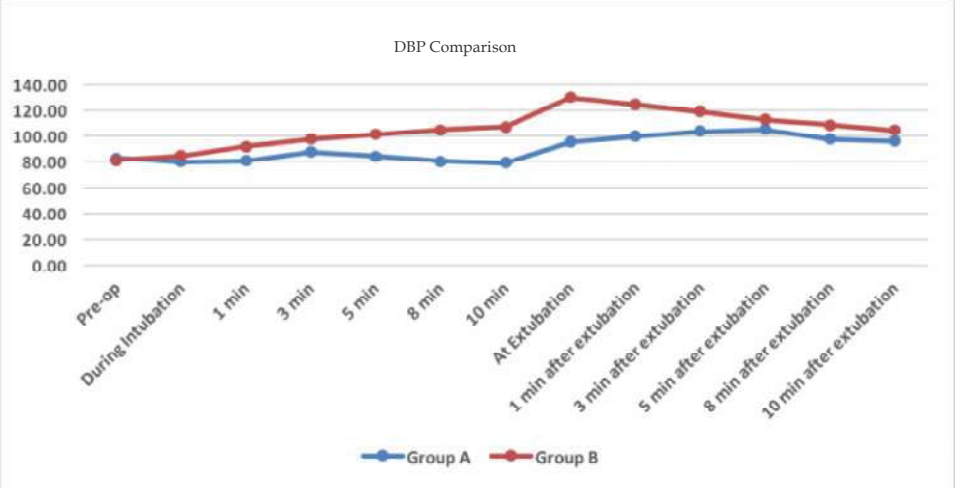


Graph 2: Comparison of mean changes in systolic blood pressure between the two groups during the procedure

Mean DBP in test and control group were comparable at baseline i.e. pre-op period (82.47 vs 80.71 mm Hg; p = 0.21). At intubation, post-intubation period till 10 mins, at extubation and till 10 minutes post-extubation, mean DBP was significantly less in test group i.e. in patients who received oral Ivabradine as compared to control group (p<0.05) (Graph 3 and Table 3).

Table 3: Comparison of mean changes in diastolic blood pressure between the two groups during the procedure

Diastolic Blood Pressure	Group	N	Mean	SD	p- value
Pre-op	A	70	82.47	5.75	0.57
	B	70	80.71	5.47	
During Intubation	A	70	79.51	6.81	<0.05
	B	70	84.27	7.01	
1 min	A	70	80.21	6.63	<0.05
	B	70	91.50	6.36	
3 min	A	70	87.43	7.03	<0.05
	B	70	97.21	8.92	
5 min	A	70	83.97	6.62	<0.05
	B	70	101.10	10.63	
8 min	A	70	80.17	5.92	<0.05
	B	70	104.74	12.94	
10 min	A	70	78.96	6.16	<0.05
	B	70	106.91	14.84	
At Extubation	A	70	95.17	16.65	<0.05
	B	70	129.66	17.72	
1 min after extubation	A	70	99.54	16.23	<0.05
	B	70	123.97	13.81	
3 min after extubation	A	70	103.57	15.99	<0.05
	B	70	118.74	11.02	
5 min after extubation	A	70	105.14	16.13	<0.05
	B	70	112.57	9.66	
8 min after extubation	A	70	97.13	10.98	<0.05
	B	70	108.37	10.42	
10 min after extubation	A	70	95.66	7.33	0.22
	B	70	104.26	6.07	

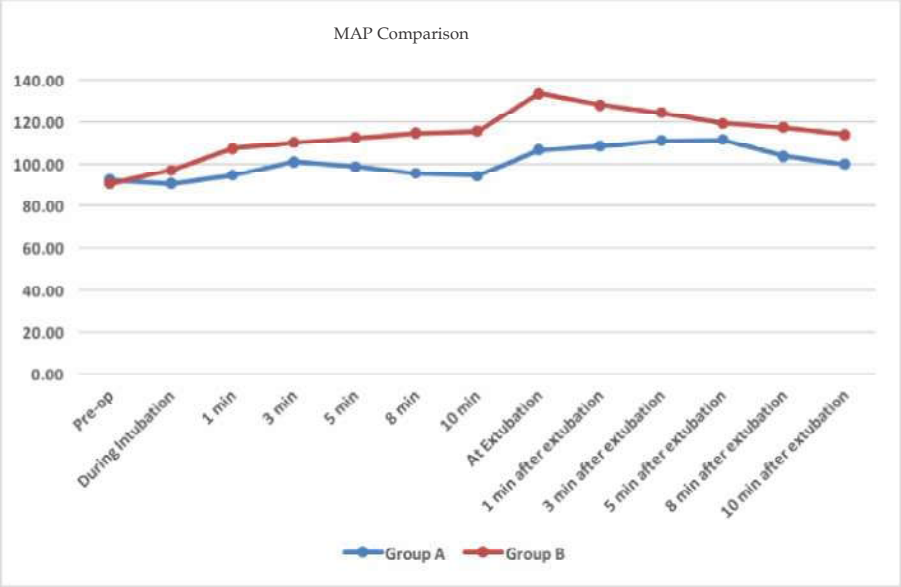


Graph 3: Comparison of mean changes in diastolic blood pressure between the two groups during the procedure

Mean arterial pressure in test and control group were comparable at baseline i.e. pre-op period (92.35 vs 90.63 mmHg; p = 0.54). At intubation, post-intubation period till 10 mins, at extubation and till 10 minutes post-extubation, mean arterial pressure was significantly less in test group i.e. in patients who received oral Ivabradine as compared to control group ($p < 0.05$) (Graph 4 and Table 4).

Table 4: Comparison of mean changes in mean arterial blood pressure between the two groups during the procedure

Mean Arterial Pressure	Group	N	Mean	SD	*p*- value
Pre-op	A	70	92.35	5.41	0.54
	B	70	90.63	9.38	
During Intubation	A	70	90.67	4.91	<0.05
	B	70	96.99	7.23	
1 min	A	70	94.68	5.98	<0.05
	B	70	107.17	9.00	
3 min	A	70	100.96	5.71	<0.05
	B	70	110.08	6.86	
5 min	A	70	98.80	4.99	<0.05
	B	70	112.34	6.96	
8 min	A	70	95.56	4.90	<0.05
	B	70	114.46	6.95	
10 min	A	70	94.30	4.95	<0.05
	B	70	115.31	8.24	
At Extubation	A	70	106.49	10.56	<0.05
	B	70	133.30	22.43	
1 min after extubation	A	70	108.34	9.37	<0.05
	B	70	127.89	17.63	
3 min after extubation	A	70	110.90	7.85	<0.05
	B	70	124.22	13.12	
5 min after extubation	A	70	111.42	7.10	<0.05
	B	70	119.15	9.51	
8 min after extubation	A	70	103.61	8.91	<0.05
	B	70	117.12	7.96	
10 min after extubation	A	70	99.91	4.06	<0.05
	B	70	113.86	10.91	



Graph 4: Comparison of mean changes in mean arterial blood pressure between the two groups during the procedure

Discussion

The parameters of Mean heart rate, systolic and diastolic blood pressure and mean arterial pressure in test and control group were similar and comparable at baseline i.e. pre-op period (p>0.05) (Table & Graph 1, 2, 3, 4).

After intubation, the placebo group showed a significant rise in heart rate and blood pressure (p<0.05). Whereas, the Ivabradine group showed only a slight increase in heart rate (82.47 to 83.04/ min) and SBP (112.1 to 112.97 mm Hg) was observed post-intubation while a decrease was observed in DBP (82.47 to 79.51 mm Hg) and MAP (92.35 to 90.67 mm Hg) (Table & Graph 1, 2, 3, 4).

After induction and intubation a gap period of ten minutes (duration of observation) was taken wherein the surgeon was asked to wait and not start the surgery. Ivabradine has no analgesic properties and immediate skin incision if given would raise the heart rate and blood pressure giving false results.

In the post-intubation observation period of 10 mins, mean heart rate, SBP, DBP and MAP readings were significantly less in oral Ivabradine group as compared to the control group that was given placebo (p value < 0.05). (Table & Graph 1, 2, 3, 4).

Mean heart rate, SBP, DBP and MAP readings were found to be significantly less in oral Ivabradine group when compared to control group of placebo at extubation and post-extubation observation period of 10 mins (p < 0.05) (Table & Graph 1,2,3,4).

In a similar study by Kunwer R *et al.*[9], mean heart rate which was 102.86 at preoperative time was gone up to 120.88 during intubation and it was still at 110.64/min. after 10 minutes, while in test group it was 82.6/min. which rose only up to 85.43 during intubation and came down to 73.46 at 10 minutes. Similar pattern was observed with mean SBP, DBP and MAP. The study results showed that haemodynamic parameters (during intubation and after 1, 3, 5, 8 and 10 min.) were found to be significantly lower in cases pre-treated with Ivabradine as compared to placebo.

Ibrahim *et al.*[10] in their study evaluated oral Ivabradine and oral propranolol in achieving a hemodynamic stability in microlaryngoscopic surgeries. Study observed that the changes in blood pressure and heart rate in both groups were mild after intubation, laryngoscope fixation for surgery and extubation but the changes in Ivabradine group were significantly less than the changes in propranolol group (p < 0.05). The authors concluded that premedication with oral Ivabradine in a dose of 5 mg or oral propranolol in a diose of 10 mg prior to microlaryngoscopic surgeries was effective in conferring good hemodynamic stability but that between the two, Ivabradine was more effective.

The advantage of Ivabradine noted in present study were – it gave good attenuation of heart rate response and blood pressure response during the process of intubation, the cardiovascular response in intraoperative period was smooth without any deviations, and also it was effective during extubation too.

No observed side effects with the dosage of Ivabradine were seen during the study. We thus conclude that Ivabradine is simple, safe, economical and easy to use drug that gives adequate and satisfactory haemodynamic stability during induction, laryngoscopy and intubation. Haemodynamic stability was also well maintained during intraoperative and immediate postoperative period.

Conclusion

We conclude that Ivabradine is an extremely useful drug and can be used to prevent tachycardia during laryngoscopy and intubation. Its stabilizing effect of haemodynamics also extends up to extubation and immediate postoperative period. There were no side effects seen with the dose of Ivabradine given in our study.

Recommendations

We recommend the routine use of Ivabradine to prevent the abnormal increase in heart rate and blood pressure seen during laryngoscopy and endotracheal intubation.

Acknowledgement

I am extremely thankful to my wife Dr Srishti Thakur for her support. I even want to extend my thanks to the patients and hospital for their cooperation.

Funding: Self

Conflict of interest: none

Ethical Approval: granted

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Original Research Article

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1483-1486
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.58

Comparison of Laryngeal Mask Airway and Endotracheal Intubation in Paediatric Patients: A Comparative Study

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Abstract

Aim: The aim of the present study was to compare the subsequent factors that take place during laryngeal mask airway insertion and endotracheal intubation for surgical procedures under general anesthesia. The parameters compared were: Ease of insertion and number of efforts and Postoperative complications like laryngospasm, bronchospasm and sore throat. *Materials and Methods:* The study participants included 80 paediatric patients between the ages of 2–8 years. All the participants were schedule to experience optional surgeries under general anesthesia in the medical hospital. *Results:* LMA had advantages over the tracheal tube in the form of lower incidence of cough during appearance and lower occurrence of postoperative sore throat, though offered no advantage more than tracheal tube in occurrence of bronchospasm or laryngospasm during appearance. *Conclusion:* The LMA provides a reliable airway in children. Incidence of postoperative complications is also less with LMA than endotracheal tubes. Therefore, LMA is a appropriate option to endotracheal intubation for possible short surgical procedures in pediatric patients.

Keywords: Laryngeal mask airway; Endotracheal tube; Pediatric.

How to cite this article:

Viral Prakashkumar Patel, Rekha bayer. Comparison of Laryngeal Mask Airway and Endotracheal Intubation in Paediatric Patients: A Comparative Study. Indian J Anesth Analg. 2019;6(4): 1477-1480.

Introduction

The laryngeal mask airway (LMA) is wrought like a large endotracheal tube on the proximal end that connects to an elliptical mask on the distal end. It is intended to sit in the patient's hypopharynx and cover up the supraglottic structures, thus allows comparative isolation of the trachea.[1,2] A laryngeal mask airway (LMA) — also known as laryngeal mask— is a medical device that keeps a patient›s airway open during anesthesia or unconsciousness. It is a type of supraglottic airway.[3] A laryngeal mask is composed of an airway tube that connect to an elliptical mask with a cuff which is inserted through the patient's mouth, down the windpipe, and once deployed forms an airtight seal on top the glottis permits a secure airway to be managed by a health care provider.[4] Laryngeal mask airways come in several types, as follows: The LMA Classic is the original reusable design, The LMA Unique is a disposable version, making it ideal for emergency and prehospital settings and The LMA Fastrach, an intubating LMA (ILMA), is designed to serve as

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Received on 22.05.2019, **Accepted on** 19.06.2019

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a conduit for intubation. They are largely used by anaesthetists to channel oxygen or anesthesia gas to a patient›s lungs during surgery and in the pre-hospital setting for unconscious patients.[5]

The LAM, with its advantages over both the face mask/nasal hood and endotracheal intubation, potentially has a place in oral and maxillofacial surgery by increasing the safety and efficacy of outpatient general anesthesia in specific situations. The LAM also has an important role in acute airway management in the trauma setting or during anesthetic emergencies. Airway control may be established with the LAM when the patient can neither be intubated nor ventilated. In managing the difficult airway, the laryngeal mask airway can be considered before either transtracheal jet ventilation or establishing a surgical airway.

The progress of small sized laryngeal masks authorized its utilize in anesthesia for the paediatric surgical patients. These patients have diverse airway characteristics such as high larynx, large tongue, funnel shaped laryngeal cartilaginous skeleton, lack of teeth, and short neck which makes the likelihood of tricky intubation higher than in adult patients. Added to this is the quick development of hypoxemia during trials of intubation in a some what hard airway of few kilograms infant.[6]

The LMA has many recompense over the endotracheal tube with more hemodynamic stability, and condensed occurrence of perioperative complications such as coughing, bucking, laryngospasm, soft-tissue trauma, laryngeal edema, and sore throat.[7] Adding up the occurrence of postoperative sore throat connected with placement of LMA is fewer than that connected with ETT.[8] The aim of present study is to evaluate the subsequent factors that take place during laryngeal mask airway insertion and endotracheal intubation for surgical procedures under general anesthesia. The parameters compared are: Ease of insertion and number of attempts and Postoperative complications like laryngospasm, bronchospasm and sore throat.

Materials and Methods

The study participants included 80 paediatric patients between the age of 2 – 8 years. All the participants were schedule to undergo elective surgeries under general anesthesia in the medical hospital. The institute ethical committee were informed about the study and the ethical clearance certificate was obtained from them. All the surgeries were short procedures of less than 40 mins. All the study paediatric patients were alienated into two groups with 40 patients each. Study group 1 (group L): LMA of appropriate size was inserted and cuff inflated with appropriate volume of air. Study group 2 (group E): Laryngoscopy and endotracheal intubation with appropriate sized endotracheal tubes was done.

A detailed preanesthetic assessment was finished for all the paediatric patients a day prior the surgery time. A detailed history, airway assessment and physical examination was done to rule out for the exclusion criteria. Exclusion criteria: Patients in ASA grade III and IV, emergency surgeries, Presence of cardiac and pulmonary problems. Inclusion criteria: Paediatric patients between 2 – 8 years, Belonging to ASA I and II grade, Schedule for elective short surgeries.

Induction agent utilized for surgery was 3 mg/kg propofol given over 1 min. For all the patients the IV line is secured, all the children premedicated with inj. Glycopyrollate and inj. Midazolam. Analgesia was provided with Inj. Fentanyl 2 micrograms/kg IV, following which patients were calm with Inj. Scoline 2 mg/kg IV to facilitate insertion of LMA or endotracheal tube. The appropriate sized LMA was chosen based upon the weight of the children as follows: size 1.5 for 5-10 kgs, size 2 for 10-20 kgs, size 2.5 for 20-30 kgs. • The ease of insertion of LMA/ETT was graded as easy, difficult, impossible and number of attempts of insertion of LMA/ETT was noted. With the help of bilateral chest lift and ausculatation of breath sounds the position of ETT/LMA was confirmed. Monitoring of vital signs i.e. heart rate, noninvasive blood pressure, pulse oximetry, EKG lead II was completed in perioperative period. Hemodynamic changes in HR, BP, MAP, SpO_2 were watched just previous to induction (baseline), just following intubation/insertion 0 minute and then at 1, 3, 5, 10, 15, 20 minutes after intubation / insertion of LMA. Postoperative complications like laryngospasm, bronchospasm and sore throat was recorded postoperatively.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA).

Descriptive statistics included computation of percentages, means and standard deviations. For all tests, confidence level and level of significance were set at 95% and 5% respectively. Statistical

comparisons were performed by repeated measures of variance followed by Students '*t*' test. A probability value "*p*" less than 0.05 was regarded as statistically significant.

Results

Our study consisted of 80 children belonging to ASA grade 1 and 2 of either sex, aged between 2-8 years, posted for elective short surgical procedures under general anesthesia. These children were arbitrarily owed to LMA group (40 patients) in whom appropriate size LMA was inserted and ETT group (40 patients) in whom direct laryngoscopy and endotracheal tube was used to secure the airway (Table 1).

Table 1: Demographic data of the patients

Variable	Particulars	LMA	ETT	T	*p*
Age	Mean ± SD	3.6 ± 1.4	4.1 ± 1.4	1.36	0.30 NS
	Range	2–5 years	2–8 years		
Weight	Mean ± SD	15.4 ± 3.25	15.8 ± 2.36	0.25	0.74 NS
	Range	8–25 kg	8–28 kg		
Duration of the surgery	Mean ± SD	30.17 ± 6.8	30.17 ± 6.8	0.55	0.52 NS
	Range	18–40	18–40		

Unpaired t test

In the LMA group, a total of 7 patients belong to ASA class II and 33 patients were ASA class I. In the ETT group, 10 patients belong to ASA II and 30 patients were in ASA I grade (Table 2).

Table 2: ASA grade

ASA	ETT	LMA
I	30	33
II	10	7
Total	40	40

In the ETT group, endotracheal intubation was easy in 81.2% of patients and difficult in 19.7% of patients. In LMA group LMA insertion was graded easy in 95% of patient and difficult in 5% cases. In none of the case was LMA insertion difficult (0%). In none of the patients was endotracheal intubation impossible. In both groups, the ease of insertion is statistically comparable and $p = 0.233$ which is not significant (Table 3).

Table 3: Ease of insertion

	LMA (%)	ETT (%)	*p*
Easy	95	81.2	0.233
Difficult	5	19.7	
Impossible	0	0	

Table 4: Postoperative complications

	LMA	ETT	*p*
Cough	16	0	0.01*
Difficult	7	0	0.001*

In the ETT group 16 children had cough while in LMA group none of the children had cough. The *p* value was < 0.001 which is significant.

In the ETT group 7 children had sore throat post operatively, where as none of the children in LMA group had sore throat. The *p* value was < 0.01 that is statistically significant (Table 4).

In both the groups none of the children had any laryngospasm and bronchospasm.

Discussion

The laryngeal mask was invented by British anaesthesiologist/anaesthetist Archibald Brain in the early 1980s and in December 1987 the first commercial laryngeal mask was made available in the United Kingdom. The laryngeal mask is still extensively utilized today worldwide and a diversity of particular laryngeal masks exist.[9]

A laryngeal mask has an airway tube that attached to an elliptical mask with a cuff. The cuff can either be of the inflating type, or self-sealing.[10] Once inserted accurately the mask conforms to the anatomy with the bowl of the mask facing the space between the vocal cords. After accurate insertion, the tip of the laryngeal mask sits in the throat against the muscular valve that is situated at the upper portion of the esophagus.

Jamil SN, *et al.* reported that the LMA was easily inserted in 94% patients; where as endotracheal intubation was performed effortlessly in only 53% of patients. These results are comparable to our study and also carry the utilization of muscle relaxants to improve the ease of insertion of laryngeal mask airway.

The laryngeal mask airway has fundamentally transformed paediatric anesthesia practice and has become a chief constituent of airway management in children. Our study constituted 80 patients, ASA I or II physical status, aged between 2 and 8 years, who were randomly allocated into 2 groups; the LMA group and ETT group. These patients were posted for elective short surgical procedures under general anaestheisa, using either the LMA or endotracheal tube for airway management. In our study, it was observed that the LMA was easily inserted in 95% of patients, where as the ETT was inserted easily in 81.2% patients.

Respiratory problems in the form of laryngospasm or bronchospasm through emergence or postoperative sore throat and cough are chief regions of concerns whereas opting a tool for paediatric airway management. In our study the occurrence of postoperative complications like cough and sore throat was considerably lower with use of LMA than ETT. However in our study, we did not encounter any incidence of bronchospasm or laryngospasm in any groups.

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Case Report

Indian Journal of Anesthesia and Analgesia
2019;6(4) (Part - II): 1487-1489
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.59

Preventable Anesthesia Mishaps: An Overview

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Abstract

We report a case of malposition of the vaporizer on the selectatec manifold of the anesthesia workstation leading to interruption in the fresh gas flow at anesthesia machine outlet. We emphasize the importance of checking the anaesthetic vaporizer after mounting it on the backbar of the anesthesia workstation.

Keywords: Interruption in fresh gas flow; General anesthesia; Tilted vaporizer; Selectatec manifold.

How to cite this article:

Renuka R, Anshumali. Preventable Anesthesia Mishaps: An Overview. Indian J Anesth Analg. 2019;6(4): 1481-1483.

Introduction

Anesthesia workstations have come a long way since the ancient Boyles apparatus. The main focus of research in these machines has been to improve the safety features, in order to prevent delivery of hypoxic gas mixtures and alert the anesthesia care provider of any other problems. Modern anesthesia machines have several safety features, for patient as well as user safety. Ultramodern anaesthetic machines have additional safety features and are programmed with a computerized safety self checkout feature which is initiated at start up which needs to be repeated before every case and ideally not to be bypassed.

Inspite of all the advances and safety features, the occurrence of anaesthetic misadventures is still a problem of concern. We report a case of interruption in the fresh gas flow (FGF) during general anesthesia caused by incorrectly mounted vaporizer on the Selectatec manifold of the Blease Sirius Spacelabs anesthesia workstation (Blease Medical Equipment Limited, Washington, USA).

Case Report

A 42 year old male patient, ASA grade 1 with diagnosis of subacute intestinal obstruction was scheduled for emergency laparotomy. An automated checkout was performed for Blease Sirius Spacelabs anesthesia workstation (Blease Medical Equipment Limited, Washington, USA) before the case and it passed all the tests. On table, standard monitors were attached to the patient and

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Received on 10.05.2019, **Accepted on** 11.07.2019

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the baseline parameters recorded. Preoxygenation was done with 100% oxygen for 3 mins. After preoxygenation, rapid sequence induction was performed using 1.5 mg/kg of propofol and rocuronium 1 mg/kg used as muscle relaxant to aid intubation. Airway was secured with 8.5 mm portex cuffed oral endotracheal tube, bilateral equal air entry confirmed and patient connected to accoma ventilator for volume controlled ventilation with tidal volume of 500 ml, frequency of 12 /min, I:E ratio of 1:2. Anesthesia plan for maintainance included air–oxygen mixture, isoflurane, intermittent doses of rocuronium and fentanyl. Around 3-5 minutes after connecting to the ventilator, there was a low minute volume alarm and the bellows started collapsing. Immediately we looked for any cuff leak, circuit disconnections, loosening of CO_2 canister and malfunctioning of the valves but couldnot find any fault with them. So, an attempt to ventilate was made by changing to manual ventilation with increased FGF and later tried by connecting the Bain's system to auxiliary common gas outlet but there was inadequate filling of the reservoir bag. The bag could only be filled by activating the oxygen flush which was also short lived as enough pressure could not be generated. This guided us to have a strong suspicion about anesthesia machine malfunction to be the cause for ventilation failure and the patient was immediately disconnected from the workstation and was ventilated with a manual resuscitator until another workstation was ready for use. Simultaneously, we watched the patients vital parameters with a vigilant eye and found it to be stable throught this period. Meanwhile the previous anesthesia workstation was inspected and we could not found anything functionally wrong except that the isoflurane vaporizer was slightly lifted up and tilted to one side and the locking lever was not in place. The concentration control dial could be turned on and when the test lung was attached, it barely inflated. The vaporizer was removed, remounted properly, checked again for any leak by attaching the test lung and after confirming for its proper functioning by complete inflation of the test lung it was reconnected to the patient and the

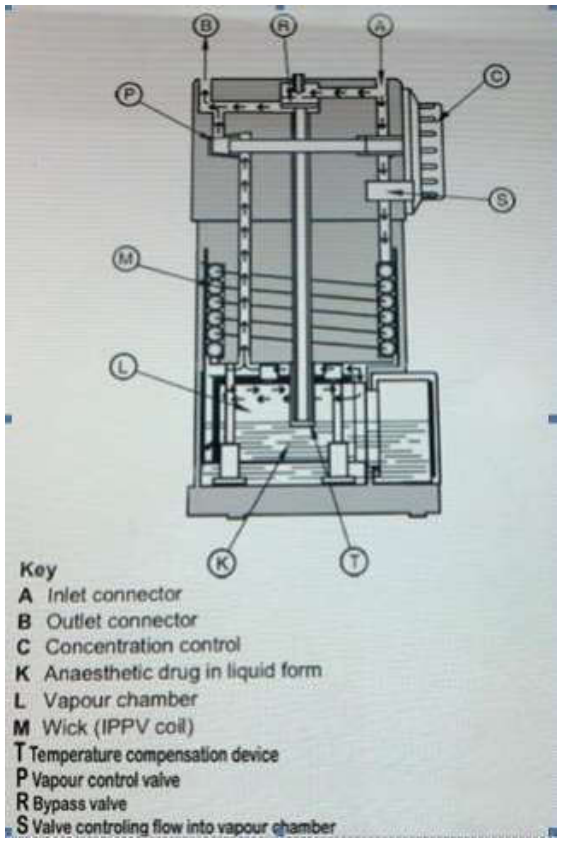

Fig. 1:

Fig. 2:

surgical procedure was carried out successfully. At the end of surgery, patient was extubated with an uneventful recovery and he did not experience any consequence like awareness as a result of this momentary loss of FGF.

Discussion

There are 2 types of vaporizer mounting systems: permanent mounting and detachable mounting. Detachable mounting systems are the standard on most anesthesia machines as they allow the vaporizer to be mounted and removed without the use of tools. The Selectatec system and a Plug-in system from Drager Medical are the most widely-used detachable mounting systems. The Selectatec system consists of a pair of port valves for positioning of each vaporizer[1]. The Blease Datum cage mount vaporizer has a special mounting bracket containing two plungers (spindles) which fits over the port valves. Weight of the vaporizer and an O-ring around each port valve creates a seal between the mounting system and the vaporizer. The interlocking extension rods prevent more than one vaporizer being used simultaneously (Fig. 1). Swinging the locking lever clockwise to 90 degrees is necessary to secure the vaporizer on the manifold and the concentration control dial cannot be moved unless the locking lever of the system is engaged. The FGF through the vapour chamber to produce the required concentration is regulated by the concentration control C (Fig. 2). When the concentration dial is in the zero position the bypass valve R opens isolating the FGF from the vapour chamber. When the dial is turned past zero, valve S opens allowing flow into the vapour chamber[2]. In the modern designs the vapour concentration supplied by the vaporizer is virtually independent of the FGF between 0.5 and 15 litres/minute.

There are three reported cases of anesthetic vapor leakage from unlocked vaporizers. In two of them, awareness with recall was identified after surgery[3,4] while in one there was desaturation and hypercapnia[5]. Accidental removal or damage of the O-ring due to frequent changing of the vaporizers in the Selectatec system increases the potential for leaks leading to alteration in the fresh gas composition and flow, operating room pollution, hypoventilation, rebreathing, desaturation and awareness in patients[1] is known. In our case and the case reported by Kim and Kim,[5] the concentration dial could be opened even when there was a faulty mounting of the vaporizer on the manifold leading to interruption in the FGF at the outlet. However, because of quick detection and rectification of the problem there was no signs of hypoxemia or hypercarbia noticed in our case. This case report highlights about the fault which is not detectable by performing the routine anesthesia machine check as recommended by the manufacturers and also the importance of anaesthetic agent monitors in detection of such faults. It also provides an insight into the lapses and lacunae in the level of training, alerts us about equipment malfunction, human errors and emphasizes that constant vigilance of the anesthetist is highly essential for the safe conduct of anesthesia.

Conclusion

Vaporizer malfunction may not be detected during conventional anaesthetic machine check and human errors can recur. We would like to highlight that the vaporizer interlock safety mechanism is not a part of routine safety check but needs incorporation in the revised safety checklist with the advent of newer technology.

Consent: Consent was obtained directly from the patient to allow for discussion and review in this case report.

Declaration of interest: None

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