

Study of 2-Chlorprocaine 1% with Adjuvants Fentanyl and Buprinorphine in Comparison with Plain 2-Chlorprocaine 1% for Subarachnoid Blocks in Perianal Surgeries

Mamatha Mishra¹, Shivakumar K. Marulappa², Ravi Madhusudhana³

¹Assistant Professor ²Assistant Professor ³Professor, Department of Anaesthesiology, Sri Devaraj Urs Medical College, R L Jalappa Hospital, SDUAHER, Tamaka, Kolar, Karnataka 563101, India.

Abstract

Introduction: This study aims at comparing the anaesthesia characteristics between Buprenorphine and Fentanyl when added as an adjuvant to intrathecal 2-Chlorprocaine 1% in an attempt to prolong the duration of spinal analgesia post operatively and are compared with the plain 2-Chlorprocaine 1% intrathecally for perianal and perineal surgeries. **Methods:** The study was conducted on 63 patients divided into 3 groups. The control A was given 30mg (3 ml) of 2-Chlorprocaine 1% with 0.5cc normal saline and study groups B and C were given 30mg (3ml) of 2-Chlorprocaine 1% with 0.5cc (25 μ) of Fentanyl and 0.2cc (60 μ) of Buprenorphine with 0.3cc of normal saline respectively. Study included ASA I and II patients and were subjected to the following perianal and perineal surgeries like haemorrhoids, fissure-in-ano, fistula-in-ano, perianal and scrotal abscess, carcinoma rectum for rectal biopsy, hydrocele, phimosis. Standard spinal anaesthesia techniques were chosen for all patients including lateral position, midline approach with 25G quincke spinal needle. **Results:** There was no significant difference in time of onset of sensory block and motor blockade between the 3 groups and also no significant haemodynamic changes between the 3 groups. But there was a significant difference in mean total duration of analgesia and VAS score between 3 groups post operatively. **Conclusion:** The study shows that 2-Chlorprocaine 1% provides an adequate block for perianal and perineal surgeries lasting 40-60 min. Addition of Buprenorphine 60 μ and Fentanyl 25 μ improves the quality of spinal anaesthesia and prolongs the duration of analgesia post operatively and Buprenorphine prolongation being much longer than Fentanyl.

Keywords: Adjuvants; Ambulatory Surgeries; 2-Chlorprocaine.

How to cite this article:

Mamatha Mishra, Shivakumar K. Marulappa, Ravi Madhusudhana. Study of 2-Chlorprocaine 1% with Adjuvants Fentanyl and Buprinorphine in Comparison with Plain 2-Chlorprocaine 1% for Subarachnoid Blocks in Perianal Surgeries. Indian J Anesth Analg. 2018;5(10):1662-67.

Introduction

2-Chlorprocaine 1% is an amino-ester local anaesthesia with a very short half-life and a favourable profile for short surgeries, approved by the Food and Drug Administration (FDA) for peripheral nerve blocks and epidural anaesthesia. It was first used for spinal anaesthesia in 1951 and has been successfully used since 1952 [1]. But due to neurological damage associated with its epidural use in 1980s it never gained widespread popularity

[2-4]. The drug was abandoned. Since then there was a continuous search for an ideal anaesthetic technique and an anaesthetic agent for all the short surgeries which can be taken as day care procedures. With the advent of many short acting drugs such as Remifentanyl and Propofol general anaesthesia was the preferred choice for short outpatient procedures. But the studies during those times was comparing regional with general anaesthesia with either long acting or intermediate acting local anaesthetic for spinal anaesthesia [5].

Corresponding Author: Shivakumar K. Marulappa, Assistant Professor, Department of Anaesthesiology, Sri Devaraj Urs Medical College, R L Jalappa Hospital, SDUAHER, Tamaka, Kolar, Karnataka 563101, India.
E-mail: drkmsshivakumar@yahoo.com

Received on 19.07.2018, Accepted on 09.08.2018

Aims and Objectives

To study the anaesthesia characteristics of Buprenorphine and Fentanyl when added as adjuvants to 2-Chlorprocaine 1% in comparison with plain 2-Chlorprocaine 1%, in terms of onset of time for sensory and motor blockage and duration of analgesia post operatively and side effects if any associated with administration of these two drugs as intrathecal adjuvants with 2-Chlorprocaine 1%. This is done by comparing the effect of intrathecal 2-Chlorprocaine 1% (30mg) with Fentanyl (25 μ) and Buprinorphine (60 μ) with that of plain 2-Chlorprocaine 1% (30mg) in terms of

1. Time of onset and duration of sensory and motor blockade
2. Time to two segment sensory regression
3. Duration of effective analgesia post operatively
4. Haemodynamic changes
5. Adverse effects.

Materials and Methods

The study was conducted on 63 patients divided into 3 groups of 21 each, group A being the control group was given 30mg (3cc) of 2-Chlorprocaine 1% with 0.5cc of normal saline. Group B was given 30mg (3cc) of 2-Chlorprocaine 1% with 25 μ of fentanyl (0.5cc) and group C was given 30mg (3cc) of 2-Chlorprocaine 1% with 60 μ (0.2cc) of Buprinorphine and 0.3cc of normal saline. Taking into consideration of the limited study in group B and no studies at all in group C, the study was conducted initially as a pilot study with 5 patients in each group and once the results were satisfactory it was continued in the larger size.

ASA I and II were included in the study with the exclusion criteria being history of allergy to the study drug, contraindications to the spinal block like spine abnormalities, haemorrhagic diathesis, localised skin sepsis, neurological diseases and patients with head injury, raised intracranial pressures. The selected patients were subjected to those perianal and perineal surgeries which were likely to be of the duration ranging from 20-60 mins like haemorrhoids, fissure-in-ano, fistula-in-ano, perianal abscess, scrotal abscess, hydrocele, phimosis and carcinoma rectum for biopsy. Standard anaesthetic technique including premedication at night prior to surgery, preloading the patient with Ringer Lactate prior to the spinal anaesthetic procedure and monitoring was done for all. The spinal anaesthetic drug as allocated to the

groups were injected in left lateral position using 25G Quincke needle through midline approach. The time of injection of the spinal anaesthetic drug was noted and the patient was made supine. Time of onset of the sensory and motor blockade was noted the maximum height of sensory blockade was noted. The haemodynamic parameters in terms of systolic BP, diastolic BP, mean arterial pressure, heart rate, SPO₂ were recorded at 0min (time of injection of the drug into the intrathecal space) and every 3min for the first 10min and every 10min till the completion of the surgery. Any adverse effects throughout the procedure were looked for. After the completion of surgery patient was shifted to recovery room and monitored for the time to two segment regression of sensory block, recovery of motor blockade and the time when patient complained for pain were noted down. Quality of analgesia was assessed by the maximum height of the sensory block achieved and patients comfort throughout the surgical procedure intraoperatively and VAS post operatively. Duration of sensory and motor blockade was calculated from the time of onset of sensory and motor blockade to the time to two segment regression of sensory block and recovery of motor blockade respectively. Duration of analgesia was calculated from the time of injection of study drug till the patient complained for pain.

Results and Observations

The data was entered into Microsoft excel datasheet and was analysed using SPSS 22 version software. Chi-square test was used as test of significance as test for qualitative data. Continuous data was represented as mean and SD. ANOVA (Analysis of Variance) or Kruskal Wallis test was the test of significance to identify the mean difference between more than two groups for quantitative and qualitative data respectively. p value (probability that the result is true) of < 0.05 was considered as statistically significant after assuming all the rule of statistical tests.

In Group A, mean age of subjects was 41.05 \pm 14.30 years, 28.6% were females and 71.4% were males, 71.4% were ASA grade 1 and 28.6% were ASA grade 2, mean time of onset of sensory block was 3.81 \pm 1.99 min and mean time onset of motor blockage was 2.43 \pm 0.9 min.

In Group B, mean age of subjects was 45.29 \pm 14.53 years, 33.3% were females and 66.7% were males, 62.5% were ASA grade 1 and 37.5% were ASA grade 2, mean time of onset of sensory block was

3.10±1.34 min and mean time onset of motor blockage was 2.67 ± 1.20 min.

In Group C, mean age of subjects was 37.81±9.97 years, 23.8% were females and 76.2% were males, 61.9% were ASA grade 1 and 38.1% were ASA grade 2, mean time of onset of sensory block was 3.29±1.68 min and mean time onset of motor blockage was 2.71±1.90 min.

There was no significant difference in age distribution, gender and ASA grades.

Time of onset of Sensory Block and Motor Blockage between three groups showed no significant differences.

Also there were no significant differences in haemodynamic parameters like Systolic BP, Diastolic BP, Mean Arterial Pressure, Heart Rate, SPO2 between the three groups at all intervals.

In the study among Group A, Group B and Group C, majority attained sensory level of T10 i.e. 52.4%, 47.6% and 57.1% respectively. There was no significant difference in Sensory level attained between three groups.

In Group A, mean total duration of surgery was 32.62±15.94 min, mean total duration of Sensory Regression by Two was 63.10±11.34 min and mean total duration of Motor Blockade was 72.90±16.37 min.

Onset of Sensory and Motor Blockage

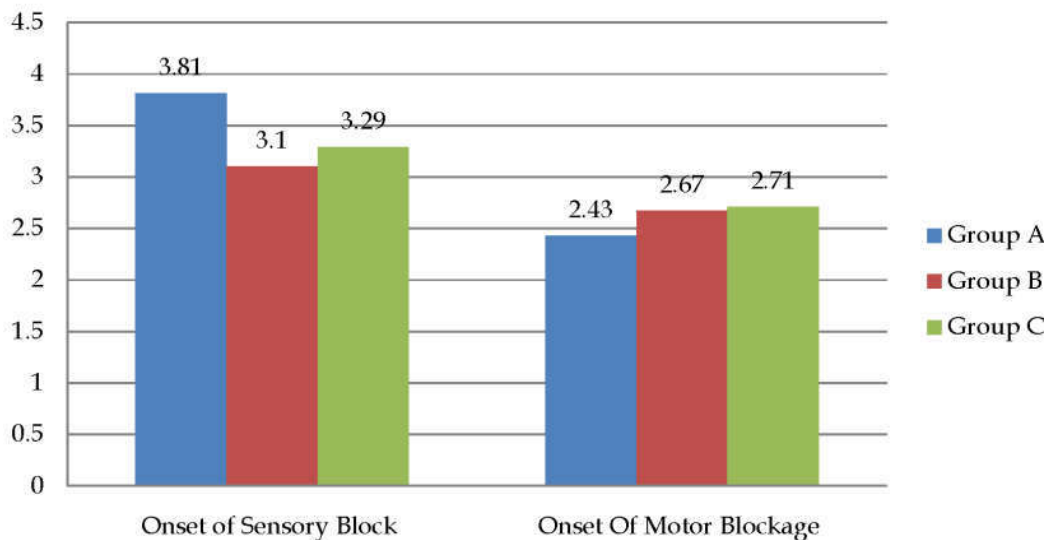


Fig. 1: Bar diagram showing Onset of Sensory and Motor Blockage between three group

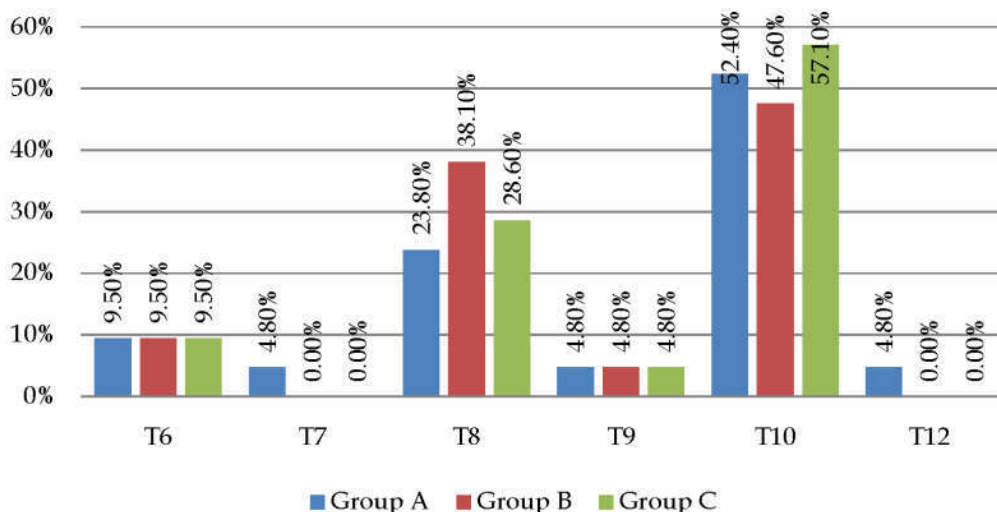


Fig. 2: Sensory level attained comparison between three groups

Table 1: Comparison of Profile of subjects between three groups

		Group A		Group B		Group C		P value
		Count	%	Count	%	Count	%	
Age (Mean ± SD)		41.05 ± 14.30		45.29 ± 14.53		37.81 ± 9.97		0.188
Sex	Female	6	28.6%	7	33.3%	5	23.8%	0.792
	Male	15	71.4%	14	66.7%	16	76.2%	
ASA Grade	1	15	71.4%	10	62.5%	13	61.9%	0.775
	2	6	28.6%	6	37.5%	8	38.1%	
Onset of Sensory Block (Mean ± SD) in min		3.81 ± 1.99		3.10 ± 1.34		3.29 ± 1.68		0.372
Time Onset Of Motor Blockage (Mean ± SD) in min		2.43 ± 0.93		2.67 ± 1.20		2.71 ± 1.90		0.780

Table 2: Comparison of Durations between three groups

	Group A		Group B		Group C		P value
	Mean	SD	Mean	SD	Mean	SD	
Total Duration of Surgery	32.62	15.94	41.90	18.87	37.14	17.93	0.241
Total Duration of Sensory Regression by Two	63.10	11.34	62.52	18.06	69.33	13.81	0.256
Total Duration of Motor Blockade	72.90	16.37	69.29	15.15	69.86	13.32	0.704
Total Duration of Analgesia	96.38	17.90	109.33	33.77	123.00	42.90	0.041*
VAS Score	6.14	0.91	5.38	0.86	5.24	1.00	0.006*

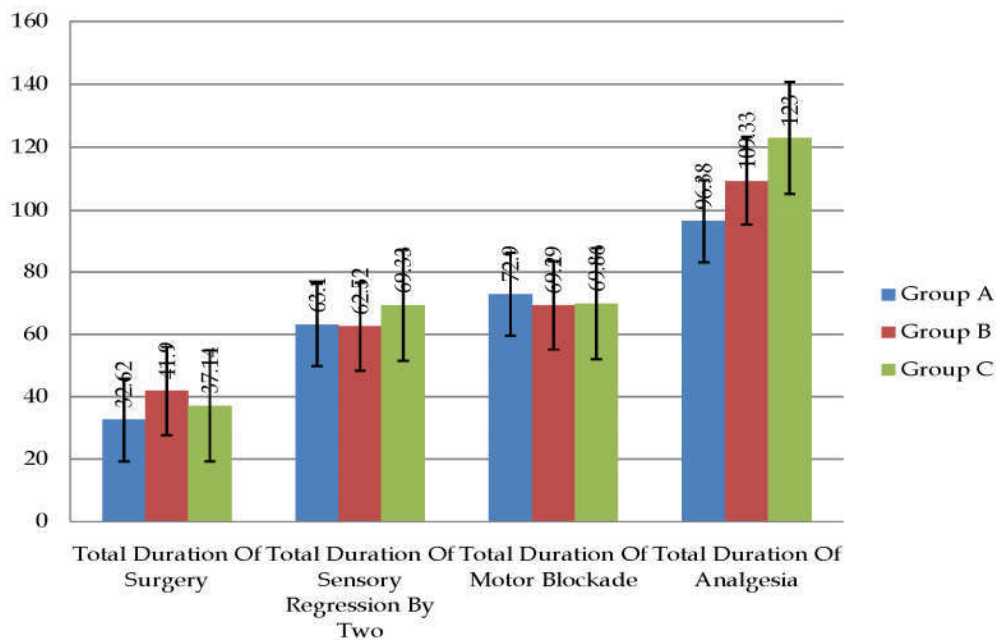


Fig. 3: Bar diagram showing Comparison of Durations between three groups

In Group B, mean total duration of surgery was 41.90±18.87 min, mean total duration of Sensory Regression by Two was 62.52±18.06 min, mean total duration of Motor Blockade was 69.29±15.15 min.

In Group C, mean total duration of surgery was 37.14±17.93 min, mean total duration of Sensory Regression by Two was 69.33±13.81 min, mean total duration of Motor Blockade was 69.86±13.32 min. There was no significant difference in mean total duration of Sensory Regression by Two and Motor Blockade between the three groups post operatively.

There was significant difference in mean total duration of Analgesia and VAS score between three groups, mean total duration of Analgesia was 96.38±17.90 min and mean VAS score was 6.14±0.91 in Group A, mean total duration of Analgesia was 109.33±33.77 min and mean VAS score was 5.38±0.86 in Group B and mean total duration of Analgesia was 123.00±42.90 min and mean VAS score was 5.24±1.00 in Group C. Median VAS score in Group A was 6, in Group B and Group C was 5.

The duration of Analgesia post operatively was more prolonged in Group C than that in Group B and Group A.

As far as adverse effects are considered, like itching, nausea, vomiting and urinary retention only one patient in group B had mild itching post operatively which was treated with antihistamines. There was no incidence of urinary retention in any of the opioid group.

Discussion

Subarachnoid Lidocaine 5% was popular for spinal anaesthesia for short surgeries lasting up to 60 mins because of its predictable duration and dense sensory and motor blockade. With development of preservative free 2-Chlorprocaine 1% this drug has got an increasing popularity as an intrathecal agent for day care surgeries. 2-Chlorprocaine 1% has similar onset time and rapid resolution for both sensory and motor blockade and also has advantage of decreased incidence of Transient Neurological Symptoms, which is 10-40% with Lignocaine 5% [6,7]. In comparison with long acting spinal anaesthetic like Bupivacaine 0.5%, 2-Chlorprocaine 1% has a short and predictable duration of sensory block thus making it a preferred drug for day care surgeries [8].

Various dose ranges have been studied of 2-Chlorprocaine 1%, ranging from 30-60mg showing minimum effective dose for surgeries of 40-60min duration is 30mg, below this dose it did not produce adequate sensory and motor blockade and also the level achieved was not sufficient to perform the surgeries comfortably [9,10]. Also various drugs such as morphine, pethidine, phenylephrine, neostigmine, ketamine, buprenorphine, fentanyl have been used as adjuvants to various local anaesthetics, but none proved ideal for this purpose [11,12,13,14].

Though 2-Chlorprocaine 1% has shown a better anaesthetic drug for short procedures like perianal surgeries with lower incidence of residual motor block and postoperative urinary retention, there are incidence of severe pain in the immediate post-operative period which needs to be taken care of in these kinds of surgeries.

Various adjuvants have been used to improve the quality of surgical block with minimum side effects to the patients and to increase the duration of analgesia post operatively. These studies are mainly comparing long acting local anaesthetics with combinations of opioids. Use of 2-Chlorprocaine

1% with opioids has been into question. There have been studies showing the antagonism of 2-Chlorprocaine 1% with epidural morphine [15] and epidural clonidine [16]. Conversely addition of fentanyl with 2-Chlorprocaine 1% found to be synergistic [17].

In his study, Kopacz studied the effect of adding fentanyl intrathecally, on the quality, duration and recovery from 2-Chlorprocaine 1% spinal anaesthesia. This was a volunteer based study with 8 volunteers. Buprenorphine is an opioid of the phenanthrene morphine class with extremely high binding affinity at the μ and kappa receptors. It has partial agonist activity at μ and kappa receptor, partial or full agonist activity at delta opioid receptor and competitive antagonist activity at the k-opioid receptor. These multifaceted properties of buprenorphine has formed basis for its use intrathecally with various spinal anaesthetics in comparison with fentanyl [18]. Intrathecal buprenorphine enhances sensory blockade of the local anaesthetics without affecting the sympathetic activity. The benefits of this opioid are far more than the side effects like vomiting and nausea. It is easily available, easy to perform and most predictable drug [19]. No study has been done with the short acting 2-Chlorprocaine 1%.

A dose-ranging study using fentanyl and buprenorphine as an additive to 2-Chlorprocaine 1%, has shown that the addition of these two drugs as adjuvants this short acting local anaesthetic improves the quality of spinal anaesthesia intraoperatively in that the patient could tolerate the surgery well for upto 60-70 minutes in few of cases of haemorrhoids and multiple fistula-in-ano, where as few patients with plain 2-Chlorprocaine 1% were uncomfortable when the surgery was extended 3-5 minutes beyond 30 minutes, though the maximum sensory block achieved in all cases were same. And post operatively patients were more comfortable in additives groups for longer periods of time with reduced VAS scores, the buprenorphine group having longer duration of post operative analgesia.

Conclusion

2-Chlorprocaine 1%, a short acting local anaesthetic with additives like fentanyl and buprenorphine can be used safely in place of long acting spinal anaesthetic, Bupivacaine 0.5% for all short surgical procedures and can be a drug of choice for all day care procedures. These

combinations of drugs can be used in other lower limb surgeries of short durations and lower abdominal procedures, more studies needs to be conducted.

Source(s) of Support: Nil

Presentation at a meeting: Nil

Conflicting Interest: None

References

1. Foldes FF, McNall PG. 2-Chlorprocaine: a new local anesthetic agent. *Anesthesiology* 1952;13:287-96.
2. Reisner LS, Hochman BN, Plumer MH. Persistent neurologic deficit and adhesive arachnoiditis following intrathecal 2-chlorprocaine injection. *Anesthesia & Analgesia* 1980;59:452-4.
3. Ravindran RS, Bond VK, Tasch MD, Gupta CD, Luerssen TG. Prolonged neural blockade following regional analgesia with 2-chlorprocaine. *Anesthesia & Analgesia* 1980;59:447-51.
4. Moore DC, Spierdijk J, VanK leef JD, Coleman RL, Love GF. Chlorprocaine neurotoxicity: four additional cases. *Anesthesia & Analgesia* 1982;61:155-9.
5. Liu SS, Strodtbeck WM, Richman JM, Wu CL. A Comparison of Regional Versus General Anesthesia for Ambulatory Anesthesia: A Meta-Analysis of Randomized Controlled Trials. *Anesth Analg.* 2005;101:1634-42.
6. Schneider M, Ettlin T, Kauffmann M, Schumacher P, Urwyler A, Hampl K, Von Hochstetter A. Transient neurologic toxicity after hyperbaric subarachnoid anesthesia with 5% lidocaine. *Anesth Analg* 1993;76:1154-7.
7. Tarkkila P, Huhtala J, Tuominen M. Transient radicular irritation after spinal anaesthesia with hyperbaric 5% lignocaine. *Br J Anaesth* 1995;74:328-9.
8. Camponovo. C, Wulf. H, Ghisi. D. Intrathecal 1% 2-Chlorprocaine Vs. 0.5% Bupivocaine in Ambulatory Surgery: A Prospective, observer-blinded, Randomized Controlled Trials. *Acta Anaesthesiol Scand.* 2014;58 : 560-6.
9. V. Gebhardt L. Mueller Hansen A. Schwarz. Chlorprocaine 10 mg/ml for low dose spinal anaesthesia in perianal surgery - a randomised dose finding study. *Acta Anaesthesiol Scand.* 2017;61: 241-49.
10. Kopacz DJ. Spinal 2-chlorprocaine; minimum effective dose. *Reg Anesth Pain Med* 2005;30:36-42.
11. Hirota K, Lambert DG. Ketamine: Its mechanism (s) of action and unusual clinical uses. *Br J Anaesth* 1996;77:441-4.
12. Vaida GT, Moss P, Capan LM, Turndorf H. Prolongation of lidocaine spinal anesthesia with phenylephrine. *Anesth Analg* 1986;65:781-5.
13. Ho KM, Ismail H, Lee KC, Branch R. Use of intrathecal neostigmine as an adjunct to other spinal medications in perioperative and peripartum analgesia: A meta-analysis. *Anaesth Intensive Care* 2005;33:41-53.
14. Arvinder Pal Singh, Ravinder Kaur, Ruchi Gupta, Anita Kumari. Intrathecal buprenorphine versus fentanyl as adjuvant to 0.75% ropivacaine in lower limb surgeries. *J Anaesthesiol Clin Pharmacol.* 2016; 32:229-33.
15. Karambelkar DJ, Ramanathan S. 2-Chlorprocaine antagonism of epidural morphine analgesia. *Acta Anaesthesiol Scand* 1997;41:774-8
16. Huntoon M, Eisenach JC, Boese P. Epidural clonidine after cesarean section. Appropriate dose and effect of prior local anaesthetic . *Anesthesiology* 1992;76:187-93
17. Vath JS, Kopacz DJ. Spinal 2-chlorprocaine: the effect of added fentanyl. *Anesth Analg* 2004;98:89-94.
18. Arvinder Pal Singh, Ravinder Kaul. Intrathecal buprenorphine versus fentanyl to 0.75% ropivocaine in lower limb surgeries. *J Anaesthesiol Clin Pharmacol,* 2016;32:229-33
19. Lalla RK. Lower dose of intrathecal buprenorphine for post operative analgesia. *Indian J Anaesth.* 1997; 41:38-9.