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Original Research Article

Comparative study of intrathecal fentanyl, tramadol, clonidine mixed with bupivacaine for peri and post operative pain relief in lower limb and lower abdominal surgery

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ABSTRACT

Background: Pain relief is of paramount importance in patients undergoing surgery during perioperative and post-operative period. After effective pain relief a smoother post-operative period and early discharge from the hospital is anticipated. Intrathecal and epidural narcotics have been widely used to relieve pain and provide post-operative analgesia. Here three drugs tramadol, fentanyl, and clonidine used as adjuvant with bupivacaine in intrathecal injection for post-operative pain relief and comparative study had been done.
Methods: After the study protocol was approved by the Ethical clearance committee of the DMCH, Laheriasarai, Bihar. Study design was prospective, randomized and double-blind techniques. A group of 80 patients undergoing lower abdominal and lower limb surgery were included in the study. Every patient was fully explained about the anaesthesia and surgical procedure before inclusion in the study. The patients were in the (25-65) years age group and belonged to the American Society of Anaesthesiologist (ASA) physical status class I-II and scheduled for lower abdominal and lower limbs surgery were randomly allocated to four groups with equal number: group B [Bupivacaine (35)% 3 cc + 0.4 cc normal saline], group BT [Bupivacaine (5)% 3 cc + 25 mg tramadol], BC [Bupivacaine (0.5)% 3 c.c + 30 µg clonidine], BF [Bupivacaine (0.5)% 3 c.c + 20 µg fentanyl]. All additive drugs used intrathecally were preservative free. All intrathecal punctures were performed in the lateral (Right or Left) position with a (25G) Quinke needle, using the midline approach at the L3-L4 intervertebral space.
Results: The study revealed that administration of additives in group BC and group BF did prolong analgesia. In group B, duration of analgesia and mean duration of rescue analgesic requirement was (3.57±0.45) hrs. For group BC it was (9.47±0.85) hrs, for group BF (7.6±1.14) hrs, for group BT (3.72±0.42) hrs.
Conclusions: Addition of adjuvants (Fentanyl, Clonidine) to intrathecal bupivacaine for perioperative pain relief does prolong postoperative analgesia and improves the intraoperative quality of analgesia than bupivacaine alone.

Keywords: Hyperbaric bupivacaine, Intrathecal clonidine, Intrathecal fentanyl, Lower abdominal surgery, Postoperative analgesia, Spinal anaesthesia

INTRODUCTION

Pain relief is of paramount importance in patients undergoing surgery during perioperative and post-operative period. The effective pain relief means a smoother post-operative period and early discharge from the hospital.

Post-operative pain relief can be obtained by many methods. Intrathecal and epidural narcotics have been

widely used to relieve pain and provide post-operative analgesia.[1] Pain relief by these methods have been shown to improve surgical outcome by excellent pain relief, decreased post-operative catabolism, decreased incidence of post-operative adverse manifestations, improved vascular graft blood flow and improved pulmonary function.

Intrathecal and epidural narcotics like morphine have the appeal of ease of administration, either at the time of spinal/epidural local; anaesthetic injection for surgical anaesthesia or as a separate technique of providing analgesia when general anaesthesia is administered. Although this method of pain relief has shown good results in clinical practice, it is still subject to certain drawbacks, the most serious of which appears to be delayed respiratory depression.[2] The other major problems with intra spinal opioids are development of tolerance and inefficiency against certain types of pain.

Hence some newer drugs of different chemical structures and different mode of actions are being tried and introduced either intrathecally or epidurally. Three such drugs are Fentanyl, tramadol, clonidine, of these three drugs - the first two are opioid receptor agonists and clonidine is alpha 2 adrenergic receptor agonist.

Alpha (α)-2 Adrenergic Receptor (AR) agonist have been the focus of interest for their sedative, analgesic, preoperative sympatholytic and hemodynamic stabilizing properties. Clonidine, a highly selective α2-AR agonist with a relative high ratio of α2/α1activity possesses all these properties but lack respiratory depression, making it a safe adjuvant.[3,4]

Intrathecal opioids are among the most popular, commonly combined with local anesthetics to improve the onset time of block, duration and quality of analgesia both intra operatively and post operatively.[5] The addition of morphine and fentanyl have been used regularly. Fentanyl a lipophilic opioid, has rapid onset of action following intrathecally administration. It does not tend to migrate to the fourth ventricle in sufficient concentration to cause delayed respiratory depression when administered intrathecally. In the present study, we have attempted to evaluate and compare the effect of intrathecal fentanyl, tramadol, clonidine mixed with bupivacaine for peri and post-operative pain relief and quality of block in lower limb and lower abdominal surgery.

Aims and objectives of the study were to evaluate the potency and duration of post-operative analgesic action of intrathecal drugs - Fentanyl, Tramadol, Clonidine with Bupivacaine and a comparative study in between the groups containing the respective drugs and Any adverse reaction caused by the drugs. The most important of side effects being, early and delayed respiratory depression, skin pruritus, urinary retention, post-operative nausea vomiting and shivering.

METHODS

After the study protocol was approved by the Ethical clearance committee of the DMCH Laheriasarai, a group of 80 patients undergoing lower abdominal and lower limb surgery in month of April 15 to November 16 were included in the study. Every patient was fully explained about the anaesthesia and surgical procedure before inclusion in the study.

Study design

Study design was prospective double blind, parallel randomized controlled clinical study. All the postoperative variables were assessed by the same post anaesthesia care unit person, who was unaware about the anaesthesia techniques and drugs used for the patients, to avoid individual variation in the assessment.

Sample size

The study population comprised of 80 patient of ASA grade 1 and 2, aged between 18 yr. and 60 yr. and wt. between 45-70 kg of either sex undergoing for elective surgery under spinal anaesthesia. Written informed consent was taken from each patient. The patients were randomly allocated to four groups (group B, BF, BT, BC) with equal numbers n=20.

Patients were excluded from the study if they have-

- A history of allergy or contraindication to any of the study drugs.
- Pregnant or nursing mothers.
- Any evidence of major Cardiovascular, Pulmonary, hepatic, renal, endocrinal or metabolic disorders.
- Suffering from bleeding diathesis and neurological disorders.
- Patients with gross spinal abnormality, on chronic analgesia therapy and under sedation were excluded.

Preparation

After fasting for at least (6-8) hours, the patients did not receive any sedatives, anxiolytics or analgesics orally or parenterally on the day of surgery.

Anaesthesia technique

In preoperative holding area, the dorsal vein of hand was cannulated with 18G cannula and all the patients were hydrated with lactated Ringers solution calculated on the basis of body weight of the patients and hours of preanesthetic fasting.

Monitors like pulse oximeters, Noninvasive Blood Pressure (NIBP), Electrocardiography (ECG), and capnography were attached before induction of

anaesthesia (spinal or intrathecal blockade) to see the baseline parameters.

All intrathecal punctures were performed in the lateral (Right or Left) position with a (25G) Quinke needle, using the midline approach at the L3-L4 intervertebral space. All additive drugs were given using a tuberculin syringe.

Then all the patients received intrathecal drugs (Local anasethetics and additive analgesics according to their groups).

There were four groups:

Groups	Drugs used intrathecally
B (group I)	Bupivacaine 2.5cc (0.5%) + (0.4cc) saline
BF (group II)	Bupivacaine 2.5cc (0.5%) + 25µg fentanyl (0.5cc)
BT (group III)	Bupivacaine 2.5cc (0.5%) + 20mg tamadol (0.4cc)
BC (group IV)	Bupivacaine 2.5cc (0.5%) + 30µg clonidine (0.3cc)

Intraoperative monitoring

Monitoring of Blood Pressure (BP), Oxygen Saturation (SPO2), End tidal Carbon dioxide (ETCO2), Respiratory Rate (RR), Heart Rate (HR), Electro Cardiography (ECG), Visual Analogue Scale (VAS Score), Sedation Score, Bromage Score, Onset of block was done. Other adverse effects e.g. observed. Nausea vomiting, respiratory depression, urinary retention, shivering and pruritus were also, treated accordingly (vasopressors, antiemetic etc.).

Every parameter was assessed before giving block and was consider as the baseline value (0-minute measurement), then measured at 5 minutes interval for first 30 minutes, then 15 minutes interval up to the end of surgical procedures.

After that patient was sent to postanesthetic care unit (PACU) for further assessment and treatment (based on aforementioned parameters).

Monitoring in PACU

In PACU, all vital parameters monitoring and special monitoring like sedation score, pain- VAS Score, Bromage score, any other adverse effects, retention of urine, respiratory depression, pruritus, PONV were assessed by trained anaesthesia personnel and other trained paramedical personnel.

All scoring system were assessed and calculated by trained personnel in the PACU at 1st, 2nd, 4th, 6th, 8th, 12th, 24th postoperative hours.

Whenever the patient required analgesia in post-operative period, patient was given analgesic according to patient demand or pain-VAS Score (rescue analgesia). Rescue analgesia was provided by injection Diclofenac-Na (75 mg) i.m (if pain on VAS Score was between (40-50) and in severe break through (VAS >50) pain then pentazocine (30 mg) was given i.m.

The following scoring systems were used for assessment of potency and duration of analgesic action of intrathecally administered drugs.

Visual Analogue Scale (VAS)

Score: 0 ◄—— 100 (mm)
(No pain) (Worst pain)

Bromage Scale (Motor Blockade) - (0-3)

0 = Able to straight leg raise against resistance (No motor block)
1 = Unable to straight leg raise but able to flex knee
2 = Unable to flex knee but able to dorsiflex ankle
3 = Unable to move hip, knee or ankle

Sedation score (0-3)

0 = Patient is awake and talkative
1 = Patient is awake but uncommunicative
2 = Patient is drowsy, quiet and easily arousable
3 = Patient is asleep

As the effects of subarachnoid block dissipated, they were encouraged to drink and to try voiding in a standardized manner. When the patients were fully able to take oral fluid (if no contra indication for oral feeding), Intravenous (IV) drip was omitted. A 24 hour follow up was made. After that the patients were shifted to general ward.

RESULTS

Table 1 shows different patient data in different groups. Each group consisted of 20 patients. There was no statistically significant difference in the values between the groups with respect to age, body weight, height and duration of surgery. The difference between the means and between the study groups and control groups is statistically significant. Student ‘t’ test used for comparison. Regarding ASA status, when compared statistically (X2 test) no significant different was found.

Table 2 shows that, there is no significant difference between the groups with time of onset of sensory block. There was no significant difference in the Highest sensory level achieved (T4-T10) and Sensory regression to L1 from highest sensory level (min) is not significantly different In groups B(120±6.2 m) BT(124±8.6 m), BC (126±9.2m), but is prolonged in group BF (176±6.8) mins.

Table 1: Demographic data of each group (Mean+SD).

Items	Group B	Group BT	Group BC	Group BF	't' test 'p' value
No. of patients	20	20	20	20	*
Age (years)	41.3±9.1	40.25±8.6	39.65±8.6	44.5±6.7	*
Body w. (kg.)	56.2±7.6	54.8±9.5	59.6±3.6	59.30±5.17	*
Height (cm.)	154.35±3.6	154.5±3.7	155.7±3.1	154.55±3.3	*
Duration of surgery (hour)	1.64±0.25	1.69±0.25	1.6±0.24	1.73±0.26	*
Asa status (i/ii)	19/1	18/2	19/1	18/2	*

[p<0.01].

Table 2: Onset of sensory block in different groups.

Group	Onset of sensory block (min.)
Group B	3.1±1.87
Group BT	3±1.22
Group BC	3.2±1.43
Group BF	3.0±1.36

Table 3: Time of administration of rescue analgesic (vas 50) mean duration+SD.

Group	(Mean±SD) of R. A.
B	(3.57±0.45) hrs.
BT	(3.72±0.42) hrs.
BC	(9.47±0.85) hrs.
BF	(7.6±1.14) hrs.

Conclusion: p<0.001 in groups BC, BF implying statistical significance.
p>0.05 in group BT implying statistical insignificance.

Table 3 Shows that mean duration of administration of first rescue analgesic differs in the groups. In the group BC it is (9.47±0.85) hours and in the group BF it is (7.6±1.14) hrs compared to the control group B (3.57±0.45) hours. It shows significant (p<0.5) prolongation of analgesic effect in the groups BC and BF, compared to the group B and Group BT.

Since there was no statistically significant difference (p>0.05) between groups B and BT, BT was not included in further analysis with anova. The mean duration of analgesic action or mean duration of first analgesic administration has been statistically compared by student's t test, ANOVA.

According to student's t test

T values between groups are as follows:

Table 4: 't' value and 'P' value between the groups.

Groups	't' value *	'p' value
B-BF	14.778	0.0001
B-BC	27.527	0.0001
BF-BC	5.881	0.0001

*The above 't' values in between groups are highly significant (p<0.001)

Table 4 shows 't' value and 'p' value between the groups and these are highly significant.

According to ANOVA

Groups B, BF, BM are analyzed.

Table 5: ANOVA table.

Source	DF	Sum of squares	Mean sum of squares	F
Between columns	2	363.5	181.75	242.76*
Within columns	57	42.67	0.74	

*Highly significant at p<0.001

Table 5 shows ANOVA analysis between columns and within columns.

The duration of motor blockade is slightly prolonged in group BF (5.1±2.1) hours and also in group BC (5.8±1.8) hours than in the control group B (4.2±0.96) hours.

The sedation score is significantly (p<0.05) prolonged in groups BC (9.8±1.8) hours and group BF (7.2±1) hours than control group B (4.1±2.4) hours. The sedation score is also not only prolonged but higher in score in group BC than in others.

In the hemodynamic changes, Heart rate was maximally affected with group BC and control group B. In order of providing hemodynamic stability, the groups are as BF, BT >B >BC. With regard to changes in systolic blood pressure, maximum hemodynamic stability was observed in group BT. In order of hemodynamic stability of the different groups, they are as follows: group (BT >BF >B >BC).

Table 6 shows that, Shivering was maximum in control group B(10%), least in group BC(0), less in group BF(5%) and group BT(5%). Incidence of Pruritus was maximum in group BF(10%), then group BT(5%), group B(5%), group BC(0). PONV was maximum in patients of group BT(20%).

Followed by group BF(10%). It was less in the control group B(5%) and absent in group BM. Incidence of Urinary retention was also higher in group BF(15%) and group BT(10%). Early respiratory depression was also observed in group BF(20%), group BT(10%). Amnesia was observed in 3 patients in group BC.

Table 6: Side effects seen in different groups.

	Shivering	Pruritus	PONV	Urinary retention	Early respiratory depression	Complaint of discomfort
Group B	10%	5%	5%	5%	0%	5%
Group BT	5%	5%	20%	10%	10%	15%
Group BF	5%	10%	10%	15%	20%	5%
Group BC	0%	0%	0%	0%	0%	0%

DISCUSSION

This is the study of prospective pain relief using intrathecal anaesthesia with local anesthetic Bupivacaine combined with opioid group of drugs like fentanyl, tramadol and α2 receptor agonist like clonidine.

Fentanyl acts through opioid receptors at pre-synaptic and post-synaptic sites in CNS and spinal cord. Tramadol is a synthetic opioid. It relieves pain by opioid as well as additional mechanism, while clonidine mediates its analgesic effects primarily through the spinal dorsal horn α2-receptors on primary afferents and interneurons, as well as the descending noradrenergic pathway.

As observed by Morgan, saline retains isobaricity of a local anesthetic solution. Therefore, a volume of (0.4 cc) of normal saline was added to the control group of bupivacaine as the other groups also received an extra volume of (0.4 cc) of each drug in the other three groups, namely-BT, BC, BF.

Dose of Bupivacaine was fixed at 12.5 mg or 2.5 cc of (0.5%) bupivacaine as that dose was needed for lower abdominal surgeries and also covered for lower limb surgeries. The dose of intrathecal fentanyl used in this study is 25 µg. Intrathecal lipophilic opioids (Fentanyl) and clonidine have been studied as adjuvant with local anesthetic (bupivacaine) in spinal anaesthesia and may provide improved intra and post-operative analgesia.[6,7]

Fentanyl acts on µ receptors in substantia gelatinosa in spinal cord, at presynaptic and postsynaptic sites in CNS (brainstem and spinal cord). Fentanyl prolongs the sensory bupivacaine spinal block as observed from the study of H Singh, J Yang et al, 1995. The mean duration for rescue analgesics in the group-BF was (7.6±1.14) hrs. longer than that in the control group (3.57±0.45) hrs. but less than that in the group-BC (9.47±0.85) hrs. Intraoperatively, as observed during gynecological procedures it causes less discomfort and less vagal stimulation and eliminates visceral pain effectively.

Mild modulation of motor blockade may be due to its action through peripheral tissues and its analgesic action. Mild sedation is also observed. It may be due to the systemic absorption of the drug. Arterial hypoxemia and hypercarbia may develop despite normal breathing rate. It may manifest as excessive sedation as depressed level of consciousness (produced by hypercarbia). Moreover, lipid soluble opioids like fentanyl are limited in their cephalad migration by uptake into the spinal cord (CSF tabes 1-2 hrs. to reach cisterna magna and 3-6 hrs. to reach 4th and lateral ventricles from lumb as region). Therefore, delayed respiratory depression was not observed in any of the cases. Ventilatory depression (as evidenced by decreased SpO2, (<90 mm Hg) rising ETCO2) was early and was observed in 2 cases. Systemic absorption of fentanyl depresses carotid sinus baroreceptor reflex control of heart resulting in bradycardia. In this study, after the initial hemodynamic effect of the spinal block, more hemodynamic stability and a few (2) cases of bradycardia at 40 minutes were seen. Shivering was only found in 1 case. It was less compared to control group B. Pruritus was observed in 2 cases in group-BF. Only 1 patient complained of discomfort during operation. Urinary retention seen in 3 cases passed away with conservative treatment in group-BF.

The use of intrathecal tramadol in group-BT did not cause any difference in the onset of block, attainment of height of block or no significant prolongation of VAS score as compared to the control group. Motor blockade was not affected. No sedation was observed except for 1 case. Early respiratory depression was observed in 2 cases. Urinary retention was observed in 2 cases, PONV was observed in 4 cases. Pruritus was observed in 1 case, shivering was also observed in 1 case in group-BT. After the initial effects of spinal block, there was more hemodynamic stability in group-BT.

α2-Agonists are now assuming greater importance as anesthetic adjuvants and analgesics. α2 receptor agonist like clonidine mediates its analgesic effects primarily through the spinal dorsal horn α2-receptors on primary afferents and interneurons, as well as the descending noradrenergic pathway. The α2 agonists produce their

sedative-hypnotic effect by an action on α2 receptors in the locus caeruleus and an analgesic action at α2 receptors within the locus caeruleus and within the spinal cord. Their primary effect is sympatholytic. They reduce peripheral norepinephrine release by stimulation of prejunctional inhibitory α2-adrenoreceptors. They inhibit central neural transmission in the dorsal horn by presynaptic and postsynaptic mechanisms and also have direct sympatholytic effects on spinal preganglionic sympathetic neurons Data suggest that oral, intravenous, epidural, and intrathecal administration of clonidine potentiates the anesthetic action of other anesthetics, volatile or injectable, and reduces general and regional anesthetic requirements with correspondingly fewer side effects. Although dose-dependent adverse effects such as hypotension and sedation and idiosyncratic adverse effects such as bradycardia do occur, clonidine does not induce profound respiratory depression and only mildly potentiates opiate-induced respiratory depression. Patients with intractable pain that is unresponsive to maximum doses of oral or epidural opioids benefit from oral, patch, intramuscular, or neuraxial administration of clonidine as do patients with reflex sympathetic dystrophy and neuropathic pain.

Intrathecal Clonidine has been shown to be practically free of any neurotoxicity by many anesthetists. They observed that no adverse or irreversible damage to spinal cord and meninges after administration of clonidine through intrathecal route.

In group-BC, there was no difference noted in the time of onset of analgesia, highest sensory level attained. There was significant prolongation of postoperative analgesia and mean duration of rescue analgesics was (9.47±0.85) hrs. than the control group-B, also the group-BF. Intraoperatively also the reflexes to visceral pain were diminished as assessed by increased levels of comfort, lack of PONV. There was no complaint of any discomfort during operation. Duration of motor block was also prolonged. Sedation score was higher and more prolonged than in other groups. Amnesia was observed in a few patients. Hemodynamically, there was more fall in BP, and HR in group-BC than group-BF and group-BT. There was no incidence of shivering, pruritus, PONV, respiratory depression. Therefore, it is observed that group-BC causes the most significant prolongation of postoperative analgesia along with less incidence of adverse effects and better sedation intra and postoperatively.[8-11]

CONCLUSION

With the principle objective of reducing postoperative pain and distress in the group of patients, the study "Comparative study of intrathecal fentanyl, tramadol, clonidine mixed with bupivacaine for peri- and post-operative pain relief in lower limb and lower abdominal surgery" was carried out in the department of Anesthesiology, Darbhanga Medical College and Hospital, Laheriasarai. The study was to evaluate the potency and duration of analgesic action of the drugs when administered intrathecally and a comparative study in between them.

Eighty patients with physical status of ASA grade I and II, scheduled for lower abdominal and lower limbs surgery were randomly allocated to four groups with equal number: group B [Bupivacaine (0.5)% 2.5 cc + .4 cc normal saline], group BT [Bupivacaine (0.5)% 2.5 cc + 20 mg tramadol], BC [Bupivacaine (0.5)% 2.5 c.c + 30µg Clonidine], BF [Bupivacaine (0.5)% 2.5c.c + 25 µg fentanyl]. All additive drugs used intrathecally were preservative free.

Addition of adjuvants (fentanyl, clonidine) to intrathecal bupivacaine for perioperative pain relief does prolong postoperative analgesia and improves the intraoperative quality of analgesia than bupivacaine alone. The side effects observed with groups for example PONV, pruritus with group-BF, amnesia with group-BC were easily manageable. There were no remarkable effects on respiratory system and hemodynamic stability. Addition of tramadol to bupivacaine did provide hemodynamic stability but there was no significant prolongation of analgesia and side effects like PONV was observed. With respect to intraoperative quality of analgesia, both Clonidine and fentanyl provided excellent results as adjuvants to bupivacaine.

Therefore, in view of providing better and prolonged postoperative analgesia with better sedation, Clonidine is the adjuvant of choice.

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REFERENCES

1. Bujedo BM, Santos SG, Azpiazu AU. A review of epidural and intrathecal opioids used in the management of postoperative pain. J Opioid Manag. 2012 May;8(3):177-92.
2. Rawal N. Epidural and spinal agents for postoperative analgesia. Surg Clin North Am. 1999 Apr 1;79(2):313-44.
3. Agarwal D, Chopra M, Mohta M, Sethi AK. Clonidine as an adjuvant to hyperbaric bupivacaine for spinal anesthesia in elderly patients undergoing lower limb orthopedic surgeries. Saudi J Anaesth. 2014 Apr;8(2):209.
4. Singh RB, Chopra N, Choubey S, Tripathi RK. Role of Clonidine as adjuvant to intrathecal bupivacaine in patients undergoing lower abdominal surgery: A randomized control study. Anesth, Essays Res. 2014 Sep;8(3):307.

5. Hindle A. Intrathecal opioids in the management of acute postoperative pain. Contin Edu anaesthesia, Critical Care Pain. 2008 May 2;8(3):81-5.
6. Nazareth M, Ghoshal P, Namshikar V, Gaude Y. Addition of intrathecal fentanyl to bupivacaine clonidine mixture effect on quality of subarachnoid block and postoperative analgesia. Anesthesia, Essays Res. 2013 Jan;7(1):76.
7. Chopra P, Talwar V. Low dose intrathecal clonidine and fentanyl added to hyperbaric bupivacaine prolongs analgesia in gynecological surgery. J Anaesthesiol, Clin Pharmacol. 2014 Apr;30(2):233.
8. Routray SS, Raut K, Pradhan A, Dash A, Soren M. Comparison of intrathecal clonidine and fentanyl as adjuvant to hyperbaric bupivacaine in subarachnoid block for lower limb orthopedic surgery. Anesthesia, Essays Res. 2017 Jul;11(3):589.
9. Bajwa BS, Singh AP, Rekhi AK. Comparison of intrathecal clonidine and fentanyl in hyperbaric bupivacaine for spinal anesthesia and postoperative analgesia in patients undergoing lower abdominal surgeries. Saudi J Anaesth. 2017 Jan;11(1):37.
10. Ahmed F, Khandelwal M, Sharma A. A comparative study of the effect of clonidine, fentanyl, and the combination of both as adjuvant to intrathecal bupivacaine for postoperative analgesia in total abdominal hysterectomy. J Anaesthesiol, Clin Pharmacol. 2017 Jan;33(1):102.
11. Singh R, Kundra S, Gupta S, Grewal A, Tewari A. Effect of clonidine and/or fentanyl in combination with intrathecal bupivacaine for lower limb surgery. J Anaesthesiol, Clin Pharmacol. 2015 Oct;31(4):485.

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