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Research Article

A COMPARATIVE STUDY OF CLINICAL EFFECT OF HYPERBARIC BUPIVACAINE WITH FENTANYL VS HYPERBARIC LEVOBUPIVACAINE WITH FENTANYL FOR SPINAL ANAESTHESIA IN ADULT PATIENTS UNDERGOING ELECTIVE LOWER LIMB SURGERIES

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ABSTRACT

Objective: The aim of the present study was to compare the safety and efficacy of 2.5 mL of 0.5% hyperbaric bupivacaine with 25 mcg of fentanyl and 2.5 mL of 0.5 hyperbaric levobupivacaine with 25 mcg fentanyl when given intrathecally in adult patients undergoing elective lower limb surgeries.

Methods: Our study was carried out in the Department of Anaesthesiology and Intensive Care, Rajindra hospital attached to Government Medical College Patiala from January 2023 to January 2024. The study was conducted on 100 patients and randomly divided into two groups with 50 patients in each group.

Results: There was no significant difference in the age, sex, and weight distribution of the patients between the groups. The baseline data in both the groups were not statistically significant. In group I, Incidence of hypotension was 44% while it was 8% in group II and Incidence of bradycardia in group I was 48% while it was 8% in group II. Thus the difference between incidence of hypotension and bradycardia was found statistically significant as $p<0.05$. In group I, the mean time to onset of sensory block was 2.72±0.08 min while it was 2.76±0.08 min in group II which was statistically nonsignificant as $p>0.05$. In group I, the mean duration of sensory block was 247.90±24.12 min while it was 311.18±15.57 min in group II which was statistically highly significant as $p<0.001$. In group I, mean time to onset of motor block was 1.60±1.18 min while it was 2.27±0.064 min in group II which was statistically highly significant as $p<0.001$. In group I, mean duration of motor block was 144.32±18.48 min while it was 112.04±12.15 min in group II which was statistically highly significant as $p<0.001$. The mean Bromage scale at different intervals in group I and group II intraoperatively showed statistically significant results.

Conclusion: We concluded that in Lower limb surgeries, combination of levobupivacaine and fentanyl decreases the incidence of adverse effects such as hypotension and bradycardia, provides a better hemodynamic stability and offers shorter block time thus minimizing the risk and providing early mobility. Therefore, the combination of levobupivacaine with fentanyl could be preferred combination for lower limb surgeries.

Keywords: 0.5% hyperbaric bupivacaine, 25 mcg fentanyl, 0.5 hyperbaric levobupivacaine, Intrathecally spinal anesthesia, Elective lower limb surgeries.

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INTRODUCTION

Neuraxial anesthesia has greatly expanded the anesthesiologist's armamentarium. Spinal anaesthesia is distinguished by its ease of performance, cost effectiveness, safety, quick onset of action, good muscle relaxation and reduced blood loss [1]. Neuraxial anesthesia provides numerous advantages, particularly in terms of reduced systemic effects, better postoperative pain management, quicker recovery times, and fewer complications related to respiration, aspiration, and cognitive dysfunction [2].

Bupivacaine belongs to the amide class of local anesthetics. It works by reversibly blocking voltage-gated sodium channels in nerve fibers, thereby inhibiting the generation and transmission of nerve impulse and inducing local anesthesia (LA). It poses a considerable risk of hypotension and bradycardia post intrathecal injection, potentially leading to fatal cardiac toxicity due to its strong affinity for cardiac myocytes [3,4].

Levobupivacaine, the S-enantiomer of bupivacaine offers several advantages in terms of reduced cardiotoxicity while maintaining similar analgesic efficacy to bupivacaine [5,6]. The regression of motor block occurs earlier with levobupivacaine as compared with bupivacaine. At low concentrations (0.25%), levobupivacaine produces a differential neuraxial block with preservation of motor function. Which may be favorable for ambulatory surgery [7-9].

Neuraxial opioids are widely used as adjuncts with LAs as they allow lower dose of LAs. They improve the quality of intraoperative analgesia and prolong the duration of analgesia without compromising its benefits such as early mobilization and early voiding. The addition of fentanyl along with levobupivacaine and bupivacaine for spinal anesthesia has been shown to prolong the duration of analgesia in the early postoperative period and thereby improving the quality of anesthesia [10,11].

The aim of the present study was to compare the safety and efficacy of 2.5 mL of 0.5% hyperbaric bupivacaine with 25 mcg of fentanyl and 2.5 mL of 0.5 hyperbaric levobupivacaine with 25 mcg fentanyl when given intrathecally for spinal anesthesia in adult patients undergoing elective lower limb surgeries.

METHODS

Our study was carried out in the Department of Anaesthesiology and Intensive Care, Rajindra hospital attached to Government Medical

College Patiala from January 2023 to January 2024. In this study, simple random sampling was used where each patient was randomly selected as per the inclusion criteria. Sample size has been calculated by referring to the results of previous study "A randomized clinical study comparing spinal anaesthesia with isobaric levobupivacaine with fentanyl and hyperbaric bupivacaine with fentanyl in elective cesarean sections" [12]. The study was conducted on 100 patients and randomly divided into two groups with 50 patients in each group.

Group I – spinal administration of 2.5 mL 0.5% hyperbaric bupivacaine with 25 mcg fentanyl.

Group II – spinal administration of 2.5 mL 0.5% hyperbaric levobupivacaine with 25 mcg fentanyl.

Patients were enrolled after checking eligibility. After getting informed consent, spinal anesthesia was given using either 2.5 mL of 0.5% hyperbaric bupivacaine with 25 mcg fentanyl or 2.5 mL of 0.5% hyperbaric levobupivacaine with 25 mcg fentanyl.

Inclusion criteria
- ASA grade I, II
- Between 20 years and 60 years of age of either sex
- Body mass index (calculated as weight in kilograms divided by square height in meters) of <30
- Normal coagulation profile
- Patient who gives consent for the surgery.

Exclusion criteria
- ASA grade III, IV
- Patient's refusal
- Having abnormality of spine
- Any skin infection or local cellulitis
- Any coagulation defect
- Recent myocardial infarction
- Patients with neurological disorders
- Unstable angina.

Informed consent
After taking Institutional Ethical Committee approval, written informed consent was obtained from each patient after explaining the technique prior to inclusion in this study in their own vernacular language. Patients were randomly divided into 2 groups of 50 each.

Visual analogue scale (VAS)
Patients were familiarized with the VAS (0 - No pain, 10 - Worst pain) 1 day before surgery and asked to grade their pain on this scale in the postoperative period. The assessment of pain was done every hour till 6 h and then every 2 h till 24 h and vitals recorded at the same time intervals. Duration of analgesia was taken as the time from onset of analgesia up to the time when VAS reached 5. Intramuscular Diclofenac (75 mg) was administered to the patient as rescue analgesia.

Pre-anesthetic check-up
While performing the pre-anesthetic check-up, the patients were asked for any systemic illnesses such as hypertension, diabetes, seizure disorder, and bronchial asthma. A history of any allergic reaction to any drug or any chronic use of the drug was taken. The patients satisfying the inclusion criteria were then investigated for hematological profile, LFTs, RFTs, serum electrolytes, chest X-ray, and ECG.

Premedication
Patients were advised overnight fasting and Tab Rabeprazole 20 mg and Tablorazepam 1 mg orally was given as premedications at 6 am in the morning on the day of surgery with as ip of water.

Baseline record
In the operation theater, the baseline blood pressure and pulse rate was recorded in every patient.

Pre-loading
In the operation room, after attaching routine monitors (electro-cardiogram, non-invasive blood pressure, pulse oximeter), intravenous access was secured with an 18 G cannula. All patients were preloaded with 15 mL/kg of Ringer's lactate solution. Diabetic patients were loaded with normal saline solution.

Spinal block
Patients were placed in a sitting position or lateral spinal position. Under complete aseptic precautions lumbar puncture were performed in L2–L3 or L3–L4, intervertebral space using a midline approach with a 23 gauge Quincke's spinal needle. After ensuring a free and clear flow of CSF, patientsin group I were given 2.5 mL of 0.5% hyperbaric bupivacaine with 25 mcg fentanyl; patients in group II were given 2.5 mL of 0.5% hyperbaric levobupivacaine with 25 mcg fentanyl. Immediately after the spinal injection, the patient was turned supine and oxygen was administered through a facemask. The level of anesthesia was assessed and then surgery was started.

Intraoperative
Clinically patients were monitored and the following observations were recorded intraoperatively.

Sensory block
The level of the sensory neural blockade was assessed by checking the touch sensation using cotton swab or by loss of pin prick sensation. Onset of sensory block was taken as the time from T0 to loss of pin prick sensation at T10 dermatome. Duration of sensory block was taken as the time from onset of sensory block till complete recovery of T10 dermatome.

Motor block
Motor neural blockade was assessed by using the Bromage scale. Motor block was assessed from T0 every 5 min till 20 min then every 20 min till recovery from motor block. The onset of motor block was Bromage Scale ≥2. Duration of motor block was taken as the time from onset of motor block till the recovery from motor block (defined as Bromage Scale 0).

Sedation
Grades of sedation during surgery were assessed by the Modified Ramsay's Sedation Scale every 5–30 min and then every 15 min till the end of surgery.

Post-operative pain
Postoperatively, the assessment of pain was done with the help of VAS score, every hour till 6 h and then every 2 h till 24 h and vitals were recorded at the same time intervals. Duration of analgesia was taken as the time from onset of analgesia up to the time when VAS reached 5. Intramuscular Diclofenac (75 mg) was administered to the patient as rescue analgesia.

Complications
Complications such as hypotension, bradycardia, nausea, vomiting, urinary retention, headache, pruritus, and respiratory depression were observed.

RESULTS

In group I, mean heart rate (HR) at 5 min was 69.36±12.20 while it was 76.90±11.65 in group II which was statistically significant as $p<0.05$.

Mean arterial pressure (MAP) shows significant difference at 5, 10, 15 min as shown in above table. In group I, the incidence of hypotension was 44% while it was 8% in group II which was statically significant as $p<0.05$.

In group I, mean time to onset of sensory block was 2.72±0.08 min while it was 2.76±0.08 min in group II which was statistically nonsignificant as $p>0.05$. In group I, mean duration of sensory block

Table 1: Heart rate

Time interval (min)	n	Group I		Group II		t-test	p-value
		Mean	Standard deviation	Mean	Standard deviation		
0 min	50	79.98	11.95	79.84	11.47	0.060	0.952 (NS)
5 min	50	69.36	12.20	76.90	11.65	3.161	0.002 (S)
10 min	50	72.24	10.57	76.28	10.58	1.910	0.059 (NS)
15 min	50	75.02	9.17	77.12	8.64	1.179	0.241 (NS)
20 min	50	75.70	8.64	77.40	9.26	0.949	0.345 (NS)
25 min	50	76.36	9.01	78.10	8.76	0.979	0.330 (NS)
30 min	50	77.74	9.52	78.24	8.14	0.282	0.778 (NS)
45 min	50	78.48	10.26	79.22	8.61	0.391	0.697 (NS)
60 min	50	80.36	11.05	79.88	8.32	0.245	0.807 (NS)
75 min	50	79.76	9.88	80.64	7.92	0.491	0.624 (NS)
90 min	50	81.30	10.18	80.12	8.27	0.636	0.526 (NS)
105 min	50	80.70	9.93	80.42	7.46	0.159	0.874 (NS)
120 min	50	81.62	9.56	80.66	7.48	0.559	0.577 (NS)

Table 2: Mean arterial pressure

Time interval (min)	N	Group I		Group II		t-test	p-value
		Mean	Standard deviation	Mean	Standard deviation		
0 min	50	93.72	5.38	95.68	6.34	1.667	0.099 (NS)
5 min	50	76.81	9.22	88.60	9.21	6.400	0.001 (HS)
10 min	50	79.62	7.40	88.14	7.47	5.730	0.001 (HS)
15 min	50	85.07	4.93	89.18	5.85	3.804	0.001 (HS)
20 min	50	86.42	3.97	88.50	5.27	2.228	0.028 (S)
25 min	50	87.91	5.51	90.12	5.33	2.035	0.045 (S)
30 min	50	88.87	5.04	90.16	4.97	1.286	0.202 (NS)
45 min	50	89.79	5.09	90.78	5.15	0.971	0.334 (NS)
60 min	50	91.08	4.03	91.50	4.70	0.479	0.633 (NS)
75 min	50	91.45	3.87	91.76	4.92	0.346	0.730 (NS)
90 min	50	92.13	3.92	92.28	4.98	0.164	0.870 (NS)
105 min	50	92.49	3.88	92.12	4.06	0.462	0.645 (NS)
120 min	50	95.70	4.97	94.74	5.22	0.942	0.349 (NS)

Table 3: Sensory block characteristics (Min)

Sensory block	n	Group I		Group II		t-test	p-value
		Mean	Standard deviation	Mean	Standard deviation		
Onset of SB (min)	50	2.72	0.08	2.76	0.08	2.826	0.468 (NS)
Duration of sensory block (min)	50	247.90	24.12	311.18	15.57	15.588	0.001 (HS)

Table 4: Motor block characteristics (Min)

Motor block	n	Group I		Group II		t-test	p-value
		Mean	Standard deviation	Mean	Standard deviation		
Onset of motor block (min)	50	1.60	1.18	2.27	0.064	3.528	0.001 (HS)
Duration of motor block (min)	50	144.32	18.48	112.04	12.15	10.321	0.001 (HS)

was 247.90±24.12 min while it was 311.18±15.57 min in group II which was statistically highly significant as p<0.001.

In group I, mean time to onset of motor block was 1.60±1.18 min while it was 2.27±0.064 min in group II which was statistically highly significant as p<0.001. In group I, mean duration of motor block was 144.32±18.48 min while it was 112.04±12.15 min in group II which was statistically highly significant as p<0.001.

DISCUSSION

Lower limb surgeries encompass a diverse array of orthopedic, vascular, and reconstructive procedures aimed at addressing a wide range of musculoskeletal and vascular pathologies affecting the lower extremities [13]. Lower limb surgeries aim to alleviate pain, correct deformities, restore joint function, and prevent or mitigate disability resulting from trauma, degenerative conditions, congenital anomalies, vascular disorders, and neoplastic diseases [14].

Our results were contrary to the study done by Gadkari *et al*. [15] on comparison of efficacy of intrathecal 0.5% isobaric levobupivacaine with fentanyl versus (LF) 0.5% isobaric bupivacaine with fentanyl (BF) for inguinal hernia repairand observed that the mean time for onset of sensory blockade was higher in case of Group LF (2.50±0.51 min) when compared to Group BF (1.67±0.37 min) and the difference was statistically significant (p<0.0001).

MAP shows significant difference at 5, 10, 15 min (Table 2) and the incidence of hypotension in group I was 44% while it was 8% in group II which was statistically significant as p<0.05. Our results were

Table 5: Complications

Complications	Group I (n=50)		Group II (n=50)		Chi-square	p-value
	Patients	Percentage	Patients	Percentage		
Nausea/Vomiting						
Yes	24	48	4	8	17.91	0.001 (HS)
No	26	52	46	92		
Hypotension						
Yes	22	44	4	8	7.78	0.005 (S)
No	28	56	46	92		
Bradycardia						
Yes	24	48	4	8	6.30	0.012 (S)
No	26	52	46	92		
Pruritus						
Yes	6	12	5	10	0.10	0.749 (NS)
No	44	88	45	90		
Urinary retention						
Yes	0	0	0	0	--	--
No	50	100	50	100		
Headache						
Yes	0	0	0	0	--	--
No	50	100	50	100		
Respiratory depression						
Yes	0	0	0	0	--	--
No	50	100	50	100		

similar to the study done by Goyal *et al*. [12] on spinal anesthesia with isobaric levobupivacaine with fentanyl and hyperbaric bupivacaine with fentanyl in elective cesarean sections and found that fall in systolic blood pressure and diastolic blood pressure as well as MAP in Group BF was noteworthy with about 6 patients requiring ephedrine to help the hemodynamics to be stable and the incidence of hypotension was 26.67% in group LF and 66.67% in group BF and concluded that hemodynamic stability was better with levobupivacaine when compared with hyperbaric bupivacaine. Our results were also similar to the study done by Erdil *et al*. [16] on the effects of intrathecal levobupivacaine and bupivacaine in the elderly. It was shown that in group bupivacaine, MAP values were significantly lower than in group levobupivacaine, starting from 10 min until 30 min after injection; p<0.05 compared to baseline. Moreover, the incidence of hypotension was 10% in levobupivacaine and 30% in bupivacaine group. Thus levobupivacaine is hemodynamically more stable.

Mean time to onset of sensory block in group I was 2.72±0.08 min while it was 2.76±0.08 min in group II which was statistically non-significant as p>0.05 (Table 3). Our results were similar to the study done by Duggal *et al*. [17] on comparison of intrathecal levobupivacaine with hyperbaric bupivacaine for elective caesarean section found that the mean time to onset of sensory block in group L was 3.87±0.73 min while it was 3.6±0.08 min in group B which on comparison was statistically non-significant. Also the mean time taken to reach maximum sensory level in group L was 8.13±1.71 min while it was 9.2±2.55 min in group B, which was statistically non-significant.

In our study, mean HR at 5 min in group I was 69.36±12.20 while it was 76.90±11.65 in group IIwhichwas statistically highly significant as p<0.002 (Table 1). In group I, the incidence of bradycardia was 48% while it was 8%in group II.Our results were similar to the study done by Goyal *et al*. [12] comparing spinal anesthesia with isobaric levobupivacaine with fentanyl and hyperbaric bupivacaine with fentanyl in elective cesarean sections and found the incidence of bradycardia to be 13.33% in LF group and 33.33% in BF group and the difference was statistically significant and concluding that levobupivacine has better hemodynamic stability. Our results were also similar to the study done by Kumar *et al*. [15] which compared the anesthetic potencies and hemodynamic changes of 0.5% isobaric levobupivacaine and 0.5% hyperbaric racemic bupivacaine for spinal anesthesia in lower abdominal and lower limb surgeries and found the incidence of bradycardia was 30% patients in group B as compared to 8% patients of group L and the difference was statistically significant. Thus levobupivacaine has better hemodynamic stability.

Mean duration of sensory block in group I was 247.90±24.12 min while it was 311.18±15.57 min in group II which was statistically highly significant as p<0.001 (Table 3). Our results were also similar to the study done by Goyal *et al*. [12] who compared isobaric levobupivacaine 10 mg with Fentanyl 25 mcg (LF) and hyperbaric bupivacaine 10 mg with Fentanyl 25 mcg (BF) in elective cesarean sections found that mean duration of sensory block in LF was 128.34±14.63 min while it was 112.46±19.32 min in group BF which was longer in BF group. In our study, mean duration of analgesia in group I was 222.14±18.03 min while it was 279.86±13.08 min in group B which was statistically highly significant as p<0.001. Our results were also similar to the study done by Hakan Erbay *et al*. [18] in the study of comparison of spinal anesthesia with low-dose hyperbaric levobupivacaine plus fentanyl (L) and low-dose hyperbaric bupivacaine plus fentanyl (B) for transurethral procedures found that the mean duration of analgesia in terms of first analgesic requirement time in group B was 305±50 min while it was 389±146 min in group L, which was statistically highly significant (p=0.004).

Mean time to onset of motor block in group I was 1.60±1.18 min while it was 2.27±0.064 min in group II which was statistically highly significant as p<0.01 (Table 4). The mean duration of motor block in group I was 144.32±18.48 min while it was 112.04±12.15 min in group II which was statistically highly significant as p<0.001. Our results were similar to the study done by Sathyanarayana *et al*. [19] shows Maximum motor block was more in Bromage 1 in the Levobupivacaine and LD group compared to Bupivacaine which had more intense block with more patients achieving Bromage score of 2 and 3 though the findings have not reached statistical significance. In our present study, the incidence of nausea in Group I was 48% and in group II it was 8% and vomiting in Group I was 52% and Group II was 92% and the results were found to be highly significant. The incidence of hypotension in group I was 44% and in group II it was 8%. Thus, the difference was found significant as p=0.005. The incidence of bradycardia in group I was 48% and in group II it was 8%. Thus, the difference was found statistically significant as p<0.05 (Table 5). Our results were similar to the study done by Goyal *et al*. [12] In addition, nausea was noticed more frequently with hyperbaric bupivacaine. Other side effects such as headache, backache, itching, vomiting, and shivering were almost similar in both the groups.

CONCLUSION

We concluded that in lower limb surgeries, combination of levobupivacaine and fentanyl decreases the incidence of adverse effects such as hypotension and bradycardia, provides a better hemodynamic stability and offers shorter block time thus minimizing the risk and providing early mobility. Therefore, the combination of levobupivacaine with fentanyl could be preferred combination for lower limb surgeries.

REFERENCES

1. Brull R, Macfarlane AJ, Chan VW. Spinal, epidural, and caudal anesthesia. In: Miller's Anesthesia. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015. p. 1684-720.
2. Rodgers A, Walker N, Schug S, McKee A, Kehlet H, Van Zundert A, *et al*. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: Results from overview of randomised trials. BMJ. 2000 Dec 16;321(7275):1493. doi: 10.1136/bmj.321.7275.1493, PMID: 11118174
3. Shafiei FT, McAllister RK, Lopez J. Bupivacaine. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2024 Jan.
4. Singh A, Gupta A, Datta PK, Pandey M. Intrathecal levobupivacaine versus bupivacaine for inguinal hernia surgery: A randomized controlled trial. Korean J Anesthesiol. 2018 Jun;71(3):220-5. doi: 10.4097/kja.d.18.27191, PMID: 29684982, PMCID: PMC5995016
5. Compagna R, Vigliotti G, Coretti G, Amato M, Aprea G, Puzziello A, *et al*. Comparative study between levobupivacaine and bupivacaine for hernia surgery in the elderly. BMC Surg. 2012;12(Suppl 1):S12. doi: 10.1186/1471-2482-12-S1-S12, PMID: 23173755
6. Fattorini F, Ricci Z, Rocco A, Romano R, Pascarella MA, Pinto G. Levobupivacaine versus racemic bupivacaine for spinal anaesthesia in orthopaedic major surgery. Minerva Anestesiol. 2006 Jul-Aug;72(7-8):637-44. PMID: 16865082
7. Bajwa SJ, Kaur J. Clinical profile of levobupivacaine in regional anesthesia: A systematic review. J Anaesthesiol Clin Pharmacol. 2013 Oct;29(4):530-9. doi: 10.4103/0970-9185.119172, PMID: 24249993, PMCID: PMC3819850
8. Gulec D, Karsli B, Ertugrul F, Bigat Z, Kayacan N. Intrathecal bupivacaine or levobupivacaine: Which should be used for elderly patients? J Int Med Res. 2014 Apr;42(2):376-85. doi: 10.1177/0300060513496737, PMID: 24595149
9. Akcaboy EY, Akcaboy ZN, Gogus N. Low dose levobupivacaine 0.5% with fentanyl in spinal anaesthesia for transurethral resection of prostate surgery. J Res Med Sci. 2011 Jan;16(1):68-73. PMID: 21448386, PMCID: PMC3063440
10. Chaudhary A, Bogra J, Singh PK, Saxena S, Chandra G, Verma R. Efficacy of spinal ropivacaine versus ropivacaine with fentanyl in transurethral resection operations. Saudi J Anaesth. 2014 Jan 1;8(1):88-91. doi: 10.4103/1658-354X.125951, PMID: 24665247
11. Girgin NK, Gurbet A, Turker G, Bulut T, Demir S, Kilic Nİ, *et al*. The combination of low-dose levobupivacaine and fentanyl for spinal anaesthesia in ambulatory inguinal herniorrhaphy. J Int Med Res. 2008 Dec;36(6):1287-92. doi: 10.1177/147323000803600616, PMID: 19094438
12. Goyal A, Shankaranarayan P, Ganapathi P. A randomized clinical study comparing spinal anesthesia with isobaric levobupivacaine with fentanyl and hyperbaric bupivacaine with fentanyl in elective Cesarean sections. Anesth Essays Res. 2015;9(1):57-62. doi: 10.4103/0259-1162.150169, PMID: 25886422
13. Kayir S, Kisa A. The evolution of the regional anesthesia: A holistic investigation of global outputs with bibliometric analysis between 1980-2019. Korean J Pain. 2021;34(1):82-93. doi: 10.3344/kjp.2021.34.1.82, PMID: 33380571
14. Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. Miller's Anesthesia 2 Volume Set: Expert Consult - Online and Print. 8th ed., Vol. 8. London, England: Churchill Livingstone; 2009. p. 1684-720.
15. Kumar Balasubramanian A, Pandian N, Rathnasabapathy B, Senthil E. A comparative study of the anesthetic potencies and hemodynamic changes of 0.5% isobaric levobupivacaine and 0.5% hyperbaric racemic bupivacaine for spinal anesthesia in lower abdominal and lower limb surgeries. Indian J Clin Anaesth.
16. Erdil F, Bulut S, Demirbilek S, Gedik E, Gulhas N, Ersoy MO. The effects of intrathecal levobupivacaine and bupivacaine in the elderly. Anaesthesia. 2009;64(9):942-6. doi: 10.1111/j.1365-2044.2009.05995.x, PMID: 19686477
17. Duggal R, Kapoor R, Moyal G. A comparison of intrathecal levobupivacaine with hyperbaric bupivacaine for elective Cesarean section: A prospective randomized double-blind study. J Obstet Anaesth Crit Care. 2015;5(2):78-83. doi: 10.4103/2249-4472.165135
18. Hakan Erbay R, Ermumcu O, Hanci V, Atalay H. A comparison of spinal anesthesia with low-dose hyperbaric levobupivacaine and hyperbaric bupivacaine for transurethral surgery: A randomized controlled trial. Minerva Anestesiol. 2010;76(12):992-1001. PMID: 21178911
19. Sathyanarayana LA, Heggeri VM, Simha PP, Narasimaiah S, Narasimaiah M, Subbarao BK. Comparison of epidural bupivacaine, levobupivacaine and dexmedetomidine in patients undergoing vascular surgery. J Clin Diagn Res. 2016;10(1):UC13-7. doi: 10.7860/JCDR/2016/17344.7079, PMID: 26894153