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Original Research Article

A COMPARATIVE STUDY OF INTRATHECAL LEVOBUPIVACAINE-FENTANYL AND BUPIVACAINE-FENTANYL FOR ORTHOPAEDIC LOWER LIMB SURGERY

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Abstract

Background: Orthopedic lower limb surgeries are one of the most common surgeries performed in India. These surgeries are preferably performed under regional anesthesia because of its unmatchable reliability, cost effectiveness, effective analgesia, muscle relaxation and prolonged postoperative analgesia. Bupivacaine is considered the gold standard long-acting local anesthesia for most loco regional procedures, Levobupivacaine is an attractive alternative to bupivacaine as it is less frequently associated with cardiovascular events. The present study was aim to compare the clinical and anesthetic property of intrathecal levobupivacaine and bupivacaine taking fentanyl as adjunct. **Materials and Methods:** Total 60 patients planned for the orthopaedic lower limb surgery were enrolled in the study and was randomly divided into two groups. Patients in group B (n=30) received the 3ml of hyperbaric 0.5% bupivacaine + 25 mcg of fentanyl whereas patients in group L (n=30) received 3ml of isobaric 0.5% levobupivacaine + 25 mcg of fentanyl. Motor blockade was assessed on a modified Bromage scale. Intraoperatively and postoperatively complications like fall in blood pressure, variation in heart rate were noted, treated and tabulated. **Result:** The mean age group in Group B is 38.67 ± 7.35 and in Group L is 35.23 ± 7.60 with a predominance of males in both groups. The mean time of onset to T8 level of sensory block in Group B is 5.23 ± 0.90 minutes and in Group L is 5.30 ± 1.09. The time to maximum sensory block in Group B 8.80 ± 1.30 minutes and in Group L is 8.20 ± 1.32 minutes. Time to maximum motor block i.e. Grade 3 motor blockade in Group B is 10.67 ± 1.35 minutes and in Group L is 10.20 ± 1.27 minutes. The time to VAS>4 in Group B is 228.83 ± 25.72 minutes and in Group L is 228.00 ± 25.78 minutes. The side effect that occurred was shivering. 4 patients in Group B and 3 patient Group L had shivering. Haemodynamic parameters were comparable between the two groups and remained within the physiological range. **Conclusion:** 0.5% isobaric levobupivacaine plus fentanyl produces similar block characteristics, similar hemodynamics and similar analgesia as 0.5% hyperbaric bupivacaine plus fentanyl. Thus, it is safe to say that we can use levobupivacaine in intrathecal bocks to produce a long duration of block with good analgesia and lower cardiotoxic profile.

INTRODUCTION

Orthopedic lower limb surgeries are one of the most common surgeries performed in India.[1] These surgeries are preferably performed under regional anesthesia as it is the most convenient anesthetic technique that offers many advantages. Regional anesthesia is used for such surgeries because of its unmatchable reliability, cost effectiveness, effective analgesia, muscle relaxation and prolonged postoperative analgesia.[2] Regional anesthesia has lot of advantages compared to general anesthesia for lower limb orthopedic surgeries.[3] Intrathecal anesthesia and epidural anesthesia are the most popular regional anesthesia techniques used for lower limb orthopedic surgeries.[4] Anesthesiologists in our country generally use the hyperbaric form of local anesthetics for spinal anesthesia now newer hyperbaric as well as isobaric local anesthetic drugs

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are available, with better pharmacokinetic property and similar block profile.[5]

Bupivacaine is considered the gold standard long-acting local anesthesia for most loco regional procedures, Levobupivacaine is an attractive alternative to bupivacaine.[6] Racemic bupivacaine is considered the long-acting local anesthetic of choice in several regional anesthetic procedures, especially for subarachnoid administration.[7] Levobupivacaine is the S-enantiomer of racemic bupivacaine. Clinical studies have shown that bupivacaine and levobupivacaine are equally effective, however, levobupivacaine has lower affinity for sodium channels in the heart and therefore it is less frequently associated with cardiovascular events.[8] Levobupivacaine is effective when administered as an epidural, spinal, peripheral nerve, ocular block, topical application or local infiltration. Levobupivacaine provides effective anesthesia and analgesia for a wide range of clinical populations and is a useful alternative to bupivacaine.[9] Both hyperbaric and isobaric local anesthetic drugs have their merits and demerits, mostly associated with the spread of drug and positioning of patient. Most orthopedic lower limb surgeries are conducted in supine position with minimal position change affecting the spread of drug.

To improve the block characteristics of intrathecally administered low dose local anesthetics, addition of adjuvant is must.[10] Intrathecal opioids enhance sensory block without prolonging motor and sympathetic block like morphine, fentanyl, tramadol etc. Among them, Fentanyl has rapid onset of action, binds strongly to plasma proteins and potentiates the afferent sensory blockade thus facilitates reduction in the dose of local anesthetics.[2] Intrathecal opioids added to local anesthetics produce a well-documented synergistic effect, intensifying motor and sympathetic blockades, and enable successful anesthesia with the use of a low-dose local anesthetic which results in more stable hemodynamics.[11] There are several other adverse effects associated with the use of high volume of drugs, these side effects can be reduced with using low doses of local anesthetics. Adding adjuvants such as fentanyl potentiate the afferent sensory blockade and facilitate reductions in the dose of local anesthetics.[12]

Clinically, levobupivacaine is well tolerated in regional anesthesia techniques both after bolus administration and continuous infusion.[13] Reports of toxicity with levobupivacaine are scarce and occasional toxic symptoms are usually reversible with minimal treatment with no fatal outcome. Yet, levobupivacaine has not entirely replaced bupivacaine in clinical practice. Addition of opioids with hyperbaric bupivacaine is extensively researched, while studies for its addition with isobaric levobupivacaine and its block profile are still undergoing. With this view in mind, we planned this randomized double-blind study to compare these two local anesthetic drugs with opioid fentanyl as adjunct and assessed clinical and anesthetic property of the drug combination. The study comparative study of Intrathecal Levobupivacaine-Fentanyl and Bupivacaine-Fentanyl for orthopedic lower limb Surgery is designed for same.

MATERIALS AND METHODS

Study design: Present study was a double blind randomised controlled study in which 60 patients planned for orthopaedic lower limb surgery were enrolled. Total 60 patients were randomly divided into two groups. Patients in group B (n=30) received the 3ml of hyperbaric 0.5% bupivacaine + 25 mcg of fentanyl whereas patients in group L (n=30) received 3ml of isobaric 0.5% levobupivacaine + 25 mcg of fentanyl for spinal anaesthesia.

Methodology: Thirty minutes before the induction of spinal anaesthesia, we started the intravenous infusion of Ringer lactate 10ml/kg. In both groups, spinal anaesthesia was performed by one anaesthesiologist using the same technique with the patient in the sitting position using a midline approach at L3–L4 or L4–L5 with a 25-G Quincke's needle. After free flow of CSF observed, patients were administrated with levobupivacaine or bupivacaine taking fentanyl as adjunct at an injection interval of ≈30 s. Patients were moved to the supine position immediately after administration of the spinal blockade. The anaesthesiologist who performed spinal anaesthesia was blinded to the study groups. The study solutions used in the present study was prepared by another anaesthesiologist and used at room temperature (23°C).

Hemodynamic assessment: All patients underwent non-invasive monitoring of systolic blood pressure (SBP) and diastolic blood pressure (DBP), measurement of blood oxygen saturation (SpO2) using pulse oximetry, and electrocardiography for heart rate (HR). An observer recorded these parameters before spinal anaesthesia, every 1 min for 5 min after spinal anaesthesia, every 5 min thereafter for 20 min, and every 20 min until the end of surgery. Supplementary oxygen (4 lit/min) was given to all patients via a face mask.

Sensory and motor blockade: Blockade characteristics were assessed by testing for sensory and motor blockade. Sensory blockade was monitored with the pin-prick test at 1-min intervals for the first 5 min, then every 5 min for 20 min, until the end of surgery. Surgery was allowed if the upper dermatome level to the loss of pin-prick sensation was at least T8. The time to achieve sensory blockade of T8, maximum spread of sensory blockade, and time to L1 regression (as well as sensorial blockade levels at the beginning and end of surgery) was recorded. Motor blockade was assessed on a modified Bromage scale. Intraoperatively and postoperatively complications like fall in blood pressure, variation in heart rate were noted, treated and tabulated. Any other side-effects (e.g. shivering, respiratory depression, nausea, vomiting, pruritus

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etc.) was also be recorded. Rescue analgesic injection Diclofenac sodium was given, 75mg iv. in 100ml normal saline slowly over 20 minutes.

Statistical analysis: Data was analyzed using SPSS. Data was expressed as mean and standard deviation, number and percentages. The patient characteristics (nonparametric data) was analysed using the "Chi-square tests" and the inter group comparison of the parametric data was done using the "unpaired t-test." A p value<0.05 was taken statistically significant.

RESULTS

The mean age group in Group B is 38.67 ± 7.35 and in Group L is 35.23 ± 7.60. A predominance of males was observed in both B and L group (70% and 73.3% respectively). The mean body weight in Group B is 65.83 ± 7.24 kgs and Group L is 65.63 ± 6.56 kgs. The mean height in Group B is 170.27 ± 9.46 cm and Group L is 169.27 ± 8.74 cm. Majority of patients in both groups belong to the ASA Grade I [Table 1].

Table 1: Sociodemographic, anthropometric and clinical examination details of patients.

Variable	Domain	Group B	Group L	P Value
Age		38.67 ± 7.35	35.23 ± 7.60	0.080
Gender	Female	9 (30%)	8 (26.7%)	0.774
	Male	21 (70%)	22 (73.3%)	
Body weight		65.83 ± 7.24	65.63 ± 6.56	0.911
Height		170.27 ± 9.46	169.27 ± 8.74	0.672
ASA grade	Grade 1	21 (70%)	24 (80%)	0.371
	Grade 2	9 (30%)	6 (20%)	

The mean time of onset to T8 level of sensory block in Group B is 5.23 ± 0.90 minutes and in Group L is 5.30 ± 1.09. The time to maximum sensory block in Group B 8.80 ± 1.30 minutes and in Group L is 8.20 ± 1.32 minutes. The time to sensory regression to L1 level in Group B is 209.33 ± 16.07 minutes and in Group L is 211.00 ± 11.48 minutes. The time to onset to T8 level in Group B is 5.23 ± 0.90 minutes and in Group L is 5.30 ± 1.09 minutes. There is no statistically significant difference between the groups [Table 2].

Table 2: Time to reach sensory block.

Sensory block	Group B	Group L	P Value
Onset to T8 level (min)	5.23 ± 0.90	5.30 ± 1.09	0.797
Time to maximum sensory block	8.80 ± 1.30	8.20 ± 1.32	0.081
Sensory regression L1	209.33 ± 16.07	211.00 ± 11.48	0.646
Onset to T8 level (min)	5.23 ± 0.90	5.30 ± 1.09	0.797

10 patients in Group B and 7 patients in Group L attained highest level if sensory block at T6 level, while 20 patients in Group B and 23 patients in Group L attained highest level of sensory blockade at T8 level. 25 patients in Group B and 26 patients in Group L had L1 sensory level at the end of surgery, while 5 patients on Group B and 4 patients in Group L had T12 sensory level at the end of the surgery. There was no statistically significant difference between both the groups [Table 3].

Table 3: Levels of sensory block.

Levels of sensory block	Domain	Group B	Group L	P Value
Highest level of sensory block	T6	10 (33.3%)	7 (23.3%)	0.390
	T8	20 (66.7%)	23 (76.7%)	
Level of sensory block at the end of surgery	L1	25 (83.3%)	26 (86.7%)	1.000
	T12	5 (16.7%)	4 (13.3%)	

Time to maximum motor block i.e. Grade 3 motor blockade in Group B is 10.67 ± 1.35 minutes and in Group L is 10.20 ± 1.27 minutes. Time to motor regression to L1 level in Group B is 210.00 ± 18.52 minutes and in Group L is 210.50 ± 14.29 minutes. The time to VAS>4 in Group B is 228.83 ± 25.72 minutes and in Group L is 228.00 ± 25.78 minutes. The time to first analgesic request in Group B is 231.50 ± 25.97 minutes and in Group L is 230.67 ± 24.90 minutes. The total duration of surgery in both the groups was comparable. In Group B it was 193.00 ± 18.60 minutes and in Group L it was 191.67 ± 17.04 minutes. There was no statistically significant difference between the groups.

Table 4: Intraoperative and postoperative details.

Intraoperative and postoperative details	Group B	Group L	P Value
Time to maximum motor block (grade 3)	10.67 ± 1.35	10.20 ± 1.27	0.173
Motor block regression L1	210.00 ± 18.52	210.50 ± 14.29	0.907
Time to VAS>4	228.83 ± 25.72	228.00 ± 25.78	0.901
Time to first analgesic request	231.50 ± 25.97	230.67 ± 24.90	0.899
Total duration of surgery	193.00 ± 18.60	191.67 ± 17.04	0.773

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The incidence of side effects in both groups was less. The side effect that occurred was shivering. 4 patients in Group B and 3 patient Group L had shivering. There was no statistically significant difference between the groups. There is no statistically significant difference in the mean of heart rate of both the groups. Overall, there is no statistically significant difference in the mean heart rate between groups at various intervals. In both the groups there was decrease in systolic blood pressure 5 to 10 minutes after intrathecal administration of the drug, which is due to the decreased sympathetic activity and vasodilatation. After that the trend of systolic blood pressure is comparable in both the groups. In both the groups diastolic blood pressure is comparable. There is one statistically significant different value at 40 minutes (p value-0.046), otherwise there is no statistically significant difference between both the groups. The mean arterial pressure in both the groups at various time is comparable. There is one statistically significant value at 80 mins (p value-0.044), otherwise there is no statistically significant difference between both the groups [Figure 1].

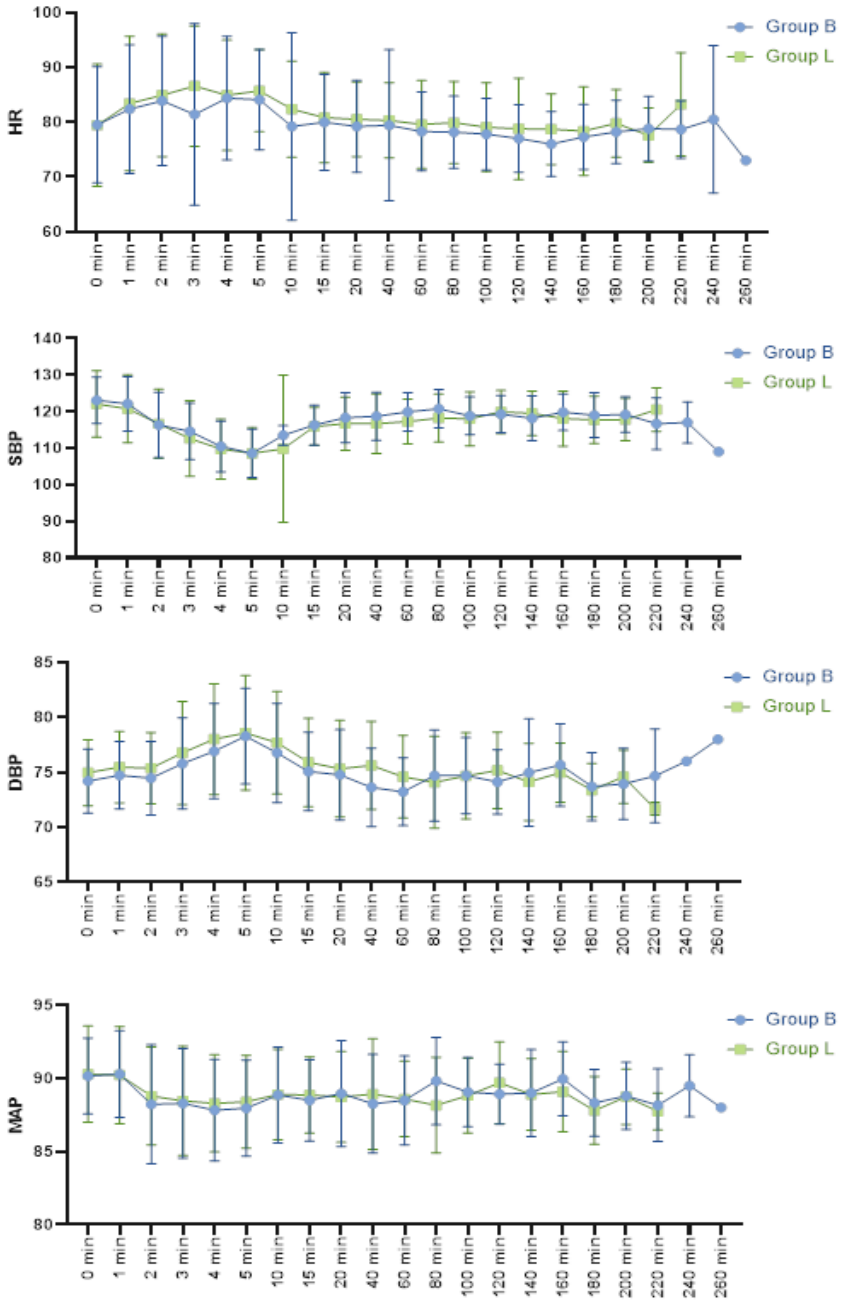

Figure 1: Intraoperative heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean atrial pressure (MAP).

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DISCUSSION

We carried out a study entitled "Comparative study of Intrathecal Levobupivacaine-Fentanyl and Bupivacaine-Fentanyl in Orthopedic lower limb surgeries". The study subjects comprised of patients planned for orthopaedic lower limb surgery and spinal anaesthesia. All the patients entering the study were subjected to a detailed pre-anaesthetic evaluation to rule out the presence of any significant co-morbidity.

Nerve blocking potency of levobupivacaine is similar to bupivacaine, it interferes with the opening of the sodium channel, which inhibits conduction of the action potential in nerves involved in sensory and motor activity and sympathetic activity.[14] The duration of action of levobupivacaine is dose dependent and it was found that 10 mg is the minimum dose for effective sensory and motor block in spinal anesthesia.[15] Kokki et al. demonstrated that the clinical characteristics of intrathecal levobupivacaine in young children are fairly similar to those obtained with racemic bupivacaine at the same dose.[16] Cardiovascular events and collapse can still occur with either bupivacaine or levobupivacaine with accidental intravascular injections, but the potential for cardiac toxicity is less with levobupivacaine than with bupivacaine.[14] Monica del-Rio-Vellosillo et al. compared 12.5mg of isobaric bupivacaine with isobaric levobupivacaine, both groups presented analogous hemodynamic parameters before and during surgery. However, there were statistically significant difference in sensory and motor block characteristics between the groups, time to sensory onset to T8 was found to be 5.5 (2–42) minutes in bupivacaine group and 9 (1–25) in levobupivacaine group. Sensory regression in study was 153 (20–312) minutes in bupivacaine group and 154 (52–317) minutes in levobupivacaine group.[6] This is comparable and correlates with our study. The longer duration in our study is due to addition of adjuvant opioid fentanyl which prolongs the duration of action of local anesthetic agent and potentiates the sensory and motor blockade. Sensory regression in minutes was measured and it was 153 (20–312) in levobupivacaine group and 154 (52–317) in bupivacaine group. However, the level of sensory regression was not specified by them. Results are similar to our study, with no significant difference between both the groups. Study found a difference between both the groups in term of total duration of analgesia.

Glaser et al. also compared isobaric solutions (3.5mL of 0.5% levobupivacaine; 3.5mL of 0.5% bupivacaine) in 80 patients undergoing elective hip replacements. They found that efficacy and block characteristics of isobaric form of both the drugs were comparable.[17] Herrera et al. also compared isobaric levobupivacaine and hyperbaric bupivacaine and found that there is no significant variation in systolic and diastolic blood pressure in the first half hour after administration of the drugs. They however did not assess the motor and sensory block characteristics. Time to maximum sensory blockade was compared in their study. The volume of drug used by them ranged from 1ml to >1.5ml and adjunct fentanyl ranged from 5µgm to 15 µgm as the patient age ranged 65 years or more.[8] Ayça Sultan Şahin et al. compared isobaric bupivacaine and isobaric levobupivacaine, there was no significant difference in the time to onset of motor and sensory block. Mobilization of the patients was also earlier in the levobupivacaine group. Study showed that the onset time to sensory blockade was 9±4 in bupivacaine group and 6±3 in levobupivacaine group. There was no significant difference between the groups. Authors showed that the time to two-segment regression of sensory blockade was earlier in levobupivacaine group than in the bupivacaine group. Similarly, they mentioned recovery time of sensory blockade in minute 266 ± 112 in bupivacaine group and 175 ± 57 in levobupivacaine group, and there is a statistically significant difference, but the level of regression is not defined. They had no significant difference in attaining the maximum motor blockade similar to our study.[9] In our study motor regression to L1 occurred at 210.00 ± 18.52 minutes in group B and 210.50 ± 14.29 minutes in group L, there is no statistically significant difference (0.907). However authors showed a significant difference between the groups, they used isobaric form of both drug without any adjuvant. They state that surgeon satisfaction was more in levobupivacaine group.

After concerning all these studies, we choose 2.5ml of either 0.5% levobupivacaine or 0.5% bupivacaine as our test drug for orthopedic lower limb surgeries. Since in our country and in our institution, we use hyperbaric form of bupivacaine, which is very popular as a long-acting local anesthetic drug for intrathecal blocks, therefore we compared block characteristics and hemodynamic parameter with hyperbaric bupivacaine and isobaric levobupivacaine and selected a dose of 25 micrograms as an adjunct with the study drug for our study. The demographic data i.e. age, gender, weight and height of the patient in both the groups are comparable. In our study onset of blockade to T8 level is 5.23 ± 0.90 minutes in group B and 5.30 ± 1.09 minutes in group L, there is no statistical difference between the groups (p value-0.797).

After comparing 3mL of 0.5% spinal bupivacaine and levobupivacaine for hip surgery, Fattorini et al. found that there were no significant differences in spinal blockade characteristics.[18] Kaya et al compared low dose hyperbaric and hypobaric levobupivacaine in unilateral spinal anesthesia, maximum sensory blockade was achieved till T10 level, and the duration of blockade was comparable in both the groups.[19] These finding correlates with our study. Maximum sensory blockade reached was equivalent, 15 minutes. This was due to lateral positioning of the patient after spinal anesthesia was given. Despite of the fact that one of our test drugs

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was isobaric and the other was hyperbaric, there was no difference in the highest level of sensory block attained. Sanansilp et al compared isobaric and hyperbaric levobupivacaine and found that 2 patients in isobaric group and 9 patients in hyperbaric group attained highest level of sensory block of T4. They found that the time to peak sensory block was 9 and 10 minutes in respective groups.[5]

Hemodynamic parameters including systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were comparable at all the time during surgery. There was a decrease in systolic blood pressure 5 to 10 minutes after giving spinal anesthesia, this could be due to the sympathetic blockade and vasodilatation. Adequate preloading before spinal anesthesia prevented events of hypotension and bradycardia. These findings have been supported by studies conducted by Herrera et al, Monica del-Rio-Vellosillo et al., Misirlioglu et al and Gautier et al.[6,8,11,20] A few statistically significant values observed randomly in each parameter is not consistent with and anesthetic or surgical event and can be due to patient-to-patient variation.

Ilkben Gunusen et al. different dose of levobupivacaine combined with fentanyl for elective cesarean sections, they found that patients hemodynamics were more stable in patients receiving levobupivacaine combined with fentanyl.[21] These findings correlate with our study, in our study patients had stable hemodynamics in the levobupivacaine group because we added fentanyl. Intrathecal opioid enhanced the block characteristics, had stable hemodynamics and decreased the dose of local anesthetic drug. Bengisun et al. compared post-operative pain after intraarticular infiltration of levobupivacaine and bupivacaine and found that there was no difference in both the groups in heart rate and mean arterial pressure. In the postoperative period, VAS scores at the 1st, 2nd, 4th, 8th, 12th, 24th, and 48th hat rest and during mobilization were significantly lower in levobupivacaine group and bupivacaine group compared with control group.[22]

The limitations of this study include the small number of patients, single centric nature of the study, and the absence of an adequate protocol for postoperative analgesia. Further studies should be done with longer postoperative follow-up periods, testing other doses, and comparison with other drugs.

CONCLUSION

From the present study it can be concluded that the anesthesia and analgesia was satisfactory in both the groups. The hemodynamic parameters: systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were comparable in both the groups. There was no statistically significant difference in the onset of sensory and motor blockade and maximum level of analgesia between levobupivacaine plus fentanyl group and bupivacaine plus fentanyl group. The duration of motor and sensory blockade and regression to L1 level was also similar with no statistically significant difference. The duration of analgesia is similar between both the groups with no statistically significant difference. Side effects reported in both the groups were found to be comparable. Hence it can be concluded by our study that 0.5% isobaric levobupivacaine plus fentanyl produces similar block characteristics, similar hemodynamics and similar analgesia as 0.5% hyperbaric bupivacaine plus fentanyl. Thus, it is safe to say that we can use levobupivacaine in intrathecal bocks to produce a long duration of block with good analgesia and lower cardiotoxic profile.

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