Section: Anaesthesiology

Original Research Article

# COMPARISON OF HYPERBARIC LEVOBUPIVACAINE WITH BUPIVACAINE FOR LOWER LIMB SURGERIES CONDUCTED UNDER SPINAL ANAESTHESIA: A PROSPECTIVE, DOUBLE BLIND, RANDOMISED CONTROLLED STUDY

**Mahendra Kumar[1], Alka Lunia[2], Dilip Kumar[3], M. L. Sharda[4]**

[1]Assistant Professor, Department of Anaesthesiology, Government Medical College, Barmer, Rajasthan, India.
[2]Assistant Professor, Department of Anaesthesiology, Government Medical College, Barmer, Rajasthan, India.
[3]Senior Resident, Department of Anaesthesiology, Government Medical College, Barmer, Rajasthan, India.
[4]Professor and Head, Department of Anaesthesiology, Government Medical College, Barmer, Rajasthan, India.

*Received* : 30/12/2022
*Received in revised form* : 03/02/2023
*Accepted* : 18/02/2023

*Keywords:*
*Hyperbaric Bupivacaine, Hyperbaric Levobupivacaine, Orthopaedic surgeries.*

Corresponding Author:
**Dr. Alka Lunia**
Email: alkalunia17@gmail.com

DOI: 10.47009/jamp.2023.5.2.40

Source of Support: Nil,
Conflict of Interest: None declared

*Int J Acad Med Pharm*
2023; 5 (2); 193-197

## Abstract

**Background:** Background: Hyperbaric bupivacaine is a commonly used drug for spinal anaesthesia. Hyperbaric levobupivacaine(S-enantiomer of bupivacaine) has lower cardiac-neurotoxicity and variable sensorimotor properties as compared to bupivacaine. This study was conducted to compare the efficacy of both drugs in spinal anaesthesia for conducting lower limb surgeries. **Materials and Methods:** After informed written consent, sixty-six patients belonging to ASA physical status I-II were equally divided into two groups, with group L receiving 3 ml of 0.5% hyperbaric levobupivacaine and group B receiving 3 ml of 0.5 % hyperbaric bupivacaine. Statistical package R software was used for the analysis of data between the two groups. Categorical data were expressed as percentage/ proportion and continuous data as mean ± SD. The chi-square test was used for the comparison of categorical variables and the independent student's t-test was used for quantitative data analysis. **Result:** Demographical data were comparable in both groups. Onset [group L(6.05 ± 1.1), group B(5.35 ± 1.51),(p=.213)] and regression[group L(8.15 ± 1.88), group B(6.83 ± 2.97),(p=.388)] of sensory block was not found to be statistically significant. Similarly, the onset and offset time of the motor block were also not statistically significant. Duration of analgesia was also comparable in both groups(p=0.327). Time to first micturition was statistically significant in group L and group B(p=.001). **Conclusion:** Our study demonstrated that 0.5% hyperbaric levobupivacaine is equally effective as 0.5% hyperbaric bupivacaine for spinal anaesthesia in lower limb orthopaedic surgeries.

## INTRODUCTION

Lower limb orthopaedic surgeries, both traumatic and non-traumatic are commonly performed under spinal anaesthesia. Hyperbaric bupivacaine is the most commonly used drug for intrathecal administration. Its easy availability, low cost and absence of side effects like transient neurological symptoms lead to widespread use. But the association of bupivacaine with side effects like dense motor blockade for prolonged duration and difficulty in micturition led to the development of alternatives such as ropivacaine and levobupivacaine.[1] Ropivacaine has a slightly distinct pharmacokinetic profile which possesses two third sensory anaesthesia but only fifty per cent motor blockade when compared with bupivacaine in a similar dosage. This made ropivacaine less desirable for surgeries requiring muscle relaxation. Being a pure S- enantiomeric form, Levobupivacaine filled this lacuna with almost similar pharmacokinetic profile as bupivacaine but with lesser cardiac and neurotoxicity.[2]

Hyperbaric levobupivacaine has been studied to a lesser extent for lower limb orthopaedic surgeries. Hence, we conducted this study to compare the efficacy of hyperbaric levobupivacaine with bupivacaine in lower limb orthopaedic surgeries in terms of sensorimotor profile and analgesic properties.


ISSN (O): 2687-5365; ISSN (P): 2753-6556

## MATERIALS AND METHODS

After approval from Institution's ethics committee, and informed written consent from patients, Sixty six patients were included in this study with two groups of equal allocation ratio. Inclusion criteria of the study comprised of American society of anaesthesiology(ASA) physical status I–II patients, aged 18–65 yr, scheduled to have surgery of lower (fracture femur, fracture tibia, Knee arthroscopy, etc). Patients refusing spinal anaesthesia, with ASA physical status >II, respiratory diseases, cardiac disease, diabetes, or peripheral neuropathy, patients receiving long-term analgesic therapy, opioid abuse and allergy to drugs under study were excluded from the study.

Patients were randomly divided into two groups of 33 each using a computer-generated random number table and sealed opaque envelope techniques were used for blinding. Patients in group L received 3 ml 0.5% hyperbaric levobupivacaine for spinal anaesthesia while patients in group B received 3 ml 0.5% hyperbaric bupivacaine for the same. The patient and primary investigator were blinded to the drug injected. Drugs were provided by a third anaesthesiologist who was not part of the research. Standard ASA monitoring was used during the intraoperative period and consisted of non-invasive blood pressure, electrocardiogram and pulse oximetry. A wide bore cannula (18 G) was secured in the upper limb and the patient was preloaded with 8ml/kg of isotonic lactated ringer fluid. The patient was premedicated with 0.03 mg/kg Inj midazolam before administration of spinal anaesthesia. After disinfecting the skin and infiltrating with 2% lidocaine, spinal anaesthesia was performed at L2-L3/ L3-4 interspace using a 25-gauge Quicke's spinal needle with the patient placed in the sitting position. The local anaesthetic solution was injected at 0.2ml/sec after appreciation of intrathecal space with free flow of cerebrospinal fluid. The patient was immediately turned to a supine position and oxygen 4 L/min was administered via a face mask. Surgery was started after the achievement of the T10 sensory block.

The primary investigator recorded the onset of sensory and motor blockade every minute until the achievement of the maximum level. Surgery was allowed to start on achievement of the T10 level blockade. The onset and regression of sensory level, motor blockade and duration of analgesia were compared between both groups. The level of sensory block was evaluated by loss of pinprick sensation, whereas motor blockade was evaluated using a modified Bromage Scale by Breen et al.[3] Readiness to surgery was defined as the presence of adequate motor block (Bromage score 2) and loss of pinprick sensation at T10 on both sides assessed at mid-axillary line. Further assessment was performed half hourly until complete regression of spinal anaesthesia. Regression of sensory blockade was defined as regression up to T10 from the maximum level. Haemodynamic parameters were also recorded during the intraoperative period. Clinically relevant hypotension was defined as a decrease in systolic arterial blood pressure by 20% or more from baseline values, and it was initially treated with a rapid IV infusion of 200 mL lactated Ringer's solution; if this proved to be ineffective, an IV bolus of ephedrine (6 mg) was given. Clinically relevant bradycardia was defined as a heart rate lower than fifty beats per minute, and it was treated with 0.6 mg Inj atropine administered intravenously. 2 mcg/kg intravenous fentanyl was used as a rescue analgesic during the surgery. Spinal anaesthesia was considered to have failed if general anaesthesia was required even after the administration of the rescue analgesic. Duration of surgery, the requirement of vasopressor, fluid boluses, time of first micturition and requirement of bladder catheterisation were also required. Postoperative analgesia consisted of 100 mg tramadol on first postoperative day with inj paracetamol 1000 mg used as rescue analgesic. The need for rescue analgesia was also recorded for the first 24 hours in the postoperative ward.

The calculation of the required sample size was based on the mean and standard deviation of complete regression of spinal block after anaesthesia with bupivacaine and levobupivacaine in the study conducted by Vanna et al.[4] With a 5% alpha error and power of the study at 80%, 30 patients were required in each group to detect a 15 min difference in time for regression of spinal anaesthesia up to T10. Adjusting for a ten per cent dropout rate, 33 patients were recruited in each group.

Statistical analysis was performed using statistical package R software. Data distribution was evaluated with the Shapiro-Wilks test for normal distribution. Demographic data, onset and offset time of sensory and motor block and duration of analgesia were analyzed with unpaired student's t-test. Categorical variables were analysed using Pearson's chi-square test. Continuous variables are presented as mean ± sd or as median(range); categorical data are presented as percentage/ proportion. A p-value of 5% was considered significant.

## RESULTS

Demographic data were comparable in both groups [Table 1]. The peak level achieved in both groups was T6. The onset time of sensory and motor block was comparable in both groups [Table 2]. Regression up to T10 was obtained earlier in group L (108.74 ± 29.45 min) but results were still statistically insignificant in both groups [Table 2]. The time of regression of motor block and time of first micturition was shorter in group L [Table 2]. No bladder catheterization was required in either of the groups. Haemodynamic parameters i.e. heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were comparable throughout


ISSN (O): 2687-5365; ISSN (P): 2753-6556

the intraoperative period [Figure 2]. No significant difference was observed in oxygen saturation and respiratory rate in both groups. Rapid intravascular volume expansion was required due to hypotension which was achieved with a similar volume of boluses in both groups [Table 3]. There was a significant difference observed in the requirement of bolus doses of ephedrine for the maintenance of haemodynamic stability, with group L requiring fewer doses [Table 3]. Bradycardia was observed in two patients in group L while three episodes were recorded in group B. Inadequate spinal block requiring rescue analgesic (fentanyl 2 mcg/kg) was required in three patients in group L as compared to group B. In group L and group B, no statistically significant difference was observed in the duration of surgery. On the first postoperative day, patients received almost 300 mg of Tramadol in both groups and postoperative pain relief was comparable in both groups.

**Table 1: Comparison of demographic profile between Group L and Group B**

| Variables | Group L(n=33) | Group B(n=33) | p value |
|---|---|---|---|
| Age(years) | 43.2 ± 14.7 | 46.7 ± 13.9 | 0.617 |
| Weight(kg) | 74.6 ± 15.3 | 78.4 ± 11.6 | 0.564 |
| Height(m) | 157 ± 17.2 | 151 ± 19.0 | 0.355 |
| Body mass Index (kg/ $m^2$) | 23. 2 ± 6.0 | 24.1 ± 6.3 | 0.403 |
| ASA PS(I/II) | 19/14 | 21/12 | 0.260 |

**Table 2: Comparison of block characteristic between group L and group B**

| Variables | Group L(n=33) | Group B(n=33) | p value |
|---|---|---|---|
| Onset of sensory block(min) | 6.05 ± 1.1 | 5.35 ± 1.51 | 0.213 |
| Onset of motor block(min) | 8.15 ± 1.88 | 6.83 ± 2.97 | 0.388 |
| Regression of sensory block upto T10 (min) | 108.74 ± 29.45 | 115.75 ± 31.04 | 0.563 |
| Regression of motor block(min) | 188.56 ± 24.76 | 203.31 ± 29.89 | 0.032 |
| Duration of analgesia (min) | 139.58 ± 30.35 | 148.5 ± 35.67 | 0.327 |
| Time to first micturition(min) | 198.65 ± 28.45 | 219.75 ± 25.98 | 0.001 |

**Table 3: Intraoperative vasopressor, fluid and analgesia requirement in Group L and Group B**

| Variables | Group L(n=33) | Group B(n=33) | p value |
|---|---|---|---|
| Doses of ephedrine | 1.0 ± 0.5 | 2.1 ± 0.7 | <0.001 |
| Fluid bolus(200 ml) | 2.3 ± 0.3 | 2.7 ± 0.7 | 0.345 |
| Rescue Analgesic | 3/33 | 1/33 | 0.100 |
| Tramadol consumption in first 24 hours(mg) | 300(200-300) | 300(200-300) | 1.00 |
| Duration of surgery | 65.80 ±10.90 | 68.70 ±9.80 | 0.258 |

**Table 4: Comparison of side effects between two groups**

| Side effects | Group L(n=33) | Group B(n=33) |
|---|---|---|
| Hypotension | 5 | 7 |
| Bradycardia | 2 | 3 |
| Nausea | 4 | 4 |
| Vomiting | 0 | 1 |
| Shivering | 9 | 8 |
| Urinary retention | 1 | 1 |

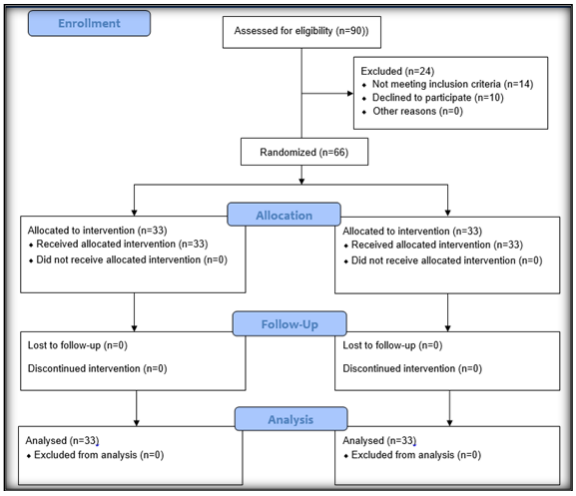


**Figure 1: CONSORT diagram of the study**

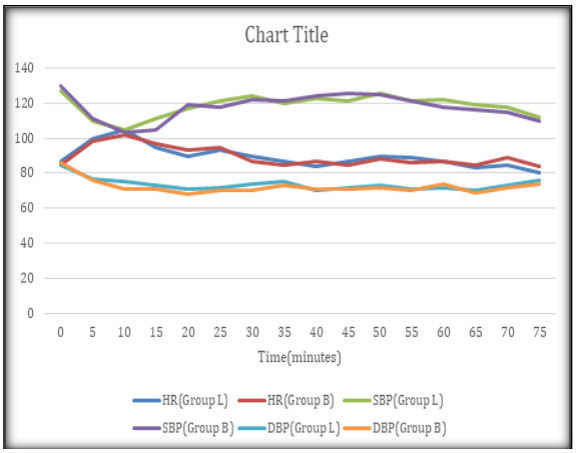


**Figure 2: Haemodynamic parameters of Group L and Group B**


ISSN (O): 2687-5365; ISSN (P): 2753-6556

## DISCUSSION

The present study demonstrates that hyperbaric 0.5% levobupivacaine is equipotent to bupivacaine when used for spinal anaesthesia in terms of onset and offset of sensorimotor properties and duration of analgesia. The side effect profile is also comparable in both groups. The only difference observed is that of difficulty in micturition in the postoperative period. Patients in group L were able to void urine earlier as compared to group B($p=0.001$). Haemodynamic changes in both groups were also comparable during all the periods of observation($p>0.05$). Fluid boluses required to correct hypotension were similar in both groups but the difference in requirement of vasopressor(ephedrine) was observed and found to be statistically significant($p<0.001$).

Bupivacaine has been widely used for spinal anaesthesia in infra-umbilical surgeries including orthopaedic surgeries of the lower limb. It provides profound analgesia and long-acting motor blockade but it is accompanied by a plethora of side effects such as hypotension, bradycardia and delayed micturition.[5] Though preloading and co-loading lower the incidence of autonomic(haemodynamic) complications but motor blockade is still largely unpredictable and that too without any prevention. Hence, various local anaesthetics with similar sensory profiles but devoid of side effects have been explored to replace bupivacaine.[1] Ropivacaine and levobupivacaine were analysed for the same but Ropivacaine was observed to have only two-thirds the sensory and half of the motor effect of bupivacaine. This limited its use in lower limb surgeries requiring muscle relaxation.[6] These limitations were not observed in levobupivacaine which is a pure S enantiomeric form of bupivacaine but this was limited by the absence of commercial hyperbaric preparation. With the availability of hyperbaric levobupivacaine, this gap has been largely filled.

The currently available data on levobupivacaine and racemic bupivacaine for epidural anaesthesia, brachial plexus blocks and local infiltration show a similar analgesic potency.[7] Lee et al. measured the effects of levobupivacaine in urological surgery patients and compared the efficacy of 2.6 ml of an isobaric 0.5% levobupivacaine with 0.5% bupivacaine and observed no significant differences in potency and side effects.[8] Glasser et al observed similar clinical effects, including sensory and motor block when comparing 0.5% levobupivacaine and bupivacaine.[9] Alley et al conducted a randomized, cross-over study in healthy volunteers to compare 0.25% hyperbaric levobupivacaine and bupivacaine for spinal anaesthesia and observed equivalent clinical efficacy in the dose range of the 4-12-mg.[10] In labour, Veracauteren et al used two ml of both drugs as the initial subarachnoid injection for combined spinal-epidural analgesia and found similar clinical effects with the exception that no motor block was observed in levobupivacaine group while one third patients in the bupivacaine group had grade 1 motor blockade.[11]

Goyal et al observed that levobupivacaine is not as potent as bupivacaine.[12] Similarly, Singh et al also claimed shorter duration of anaesthesia and motor blockade in the levobupivacaine group in their study.[13] This difference in observation can be attributed to isobaric nature of the preparation used by them whereas we used hyperbaric preparation which was found to be equally effective as hyperbaric bupivacaine. Similar findings were reiterated by Sethi et al in their study.[14] Comparison of isobaric preparation was a commonplace for intrathecal injection as hyperbaric preparations have to be made personally which limited the standardization of such preparations. Self-made preparations used in previous research had variable percentages of dextrose resulting in variable baricity and hence, the discrepancy in effects.[15] Also, the sterility of drugs could not be ensured for intrathecal injection, though no cases of infection were reported in any of the studies. Though individual trials have reported the benefits of hyperbaric solutions over isobaric solutions but similar results were not reflected in meta-analysis conducted by Sng et al due to lack of standard definitions in various trials.[16]

No adverse reaction or complication was observed in our study. But the incidence of side effects was comparable in both the groups. Similar observations have been made by previous researchers.[17]

The present study demonstrated that 0.5% hyperbaric levobupivacaine is equally effective as 0.5% hyperbaric bupivacaine for spinal anaesthesia in lower limb orthopaedic surgeries. The onset and offset time of the sensory and motor blocks, peak block height, duration of analgesia and hemodynamics properties are similar to bupivacaine. Further studies with hyperbaric levobupivacaine will be required to strengthen our findings.

**Conflict of interest** Nil

## CONCLUSION

Our study demonstrated that 0.5% hyperbaric levobupivacaine is equally effective as 0.5% hyperbaric bupivacaine for spinal anaesthesia in lower limb orthopaedic surgeries.

## REFERENCES

1. Luduena FP, Bogado EF, Tullar BF. Optical isomers of mepivacaine and bupivacaine. Arch Int Pharmacodyn Ther. 1972;200:359-69.
2. Huang YE, Pryor ME, Mather LE, Veering BT. Cardiovascular and central nervous system effects of intravenous levobupivacaine and bupivacaine in sheep. Anesth Analg 1998;86:797-804.


ISSN (O): 2687-5365; ISSN (P): 2753-6556

3. Breen TW, Shapiro T, Glass B, Foster-Payne D, Oriol NE. Epidural anesthesia for labor in an ambulatory patient. Anesth Analg. 1993;77:919-24.
4. Vanna O, Chumsang L, Thongmee S. Levobupivacaine and bupivacaine in spinal anesthesia for transurethral endoscopic surgery. J Med Assoc Thai. 2006;89:1133-9.
5. Reiz S, Nath S. Cardiotoxicity of local anaesthetic agents. Br J Anaesth 1986;58:736-46.
6. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth. 2011;55:104-10.
7. Oraon P, Hembrom B, Kumar M, Ram B, Lakra L. Comparative Study between Intrathecal 0.5% Isobaric Levobupivacaine, 0.5% Isobaric Ropivacaine, and 0.5% Hyperbaric Bupivacaine in Elective Lower Segment Cesarean Section: A Randomized Clinical Study. Anesth Essays Res. 2022;16:238-243.
8. Lee YY, Muchhal K, Chan CK. Levobupivacaine versus racemic bupivacaine in spinal anaesthesia for urological surgery. Anaesth Intensive Care 2003;31:637-41.
9. Glasser C, Marhofer P, Zimpfer G, Heinz DJ, Sitzwohl C, Kapral S, et al. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. Anesth Anag 2002; 94: 194-8.
10. Alley AE, Kopacz DJ, McDonald SB, Liu SS. Hyperbaric spinal levobupivacaine: a comparison to racemic bupivacaine in volunteers. Anest Analg 2002; 94: 188-93.
11. Vercauteren MP, Hans G, De Decker K, Adriaensen HA. Levobupivacaine combined with sufentanil and epinephrine for intrathecal labor analgesia: a comparison with racemic bupivacaine. Anesth Analg 2001; 93: 996-1000.
12. Goyal A, Singi Y, Mallya P, Bhat G, P S. A Comparison Between Intrathecal Levobupivacaine and Bupivacaine for Quality and Safety During Infraumbilical Surgeries. Cureus. 2022;14:e30590.
13. Singh A, Gupta A, Datta PK, Pandey M. Intrathecal levobupivacaine versus bupivacaine for inguinal hernia surgery: a randomized controlled trial. Korean J Anesthesiol. 2018;71(3):220-225.
14. Sethi D. Randomised Control Trial Comparing Plain Levobupivacaine and Ropivacaine with Hyperbaric Bupivacaine in Caesarean Deliveries. Turk J Anaesthesiol Reanim. 2019;47:471-479.
15. McLeod GA. Density of spinal anesthetic solutions of bupivacaine, levobupivacaine, and ropivacaine with and without dextrose. Br J Anaesth 2004;92:547–51.
16. Sng BL, Siddiqui FJ, Leong WL, Assam PN, Chan ES, Tan KH, et al. Hyperbaric versus isobaric bupivacaine for spinal anaesthesia for caesarean section. Cochrane Database Syst Rev. 2016;9(9):CD005143.
17. Gristwood R, Bardsley H, Baker H, Dickens J. Reduced cardiotoxicity of levobupivacaine compared with racemic bupivacaine (Marcaine): new clinical evidence. Exp Opin Invest Drugs 1994; 3: 1209-12.


ISSN (O): 2687-5365; ISSN (P): 2753-6556