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## ORIGINAL RESEARCH

# To Evaluate Efficacy and Safety of Isobaric Levobupivacaine Versus Hyperbaric Bupivacaine in Lower Limb Orthopaedic Surgeries

**Anjani Kumar Singh[1], Selvakumar Palaniappan[2], K. Selvaraju[3]**

[1]Assistant Professor, Department of Anaesthesia, School of Medical Sciences & Research, Sharda University, Greater Noida, UP, India

[2]Associate Professor, Department of Anaesthesia, Velammal Medical College Hospital and Research Institute, Madurai, Tamilnadu, India

[3]Associate Professor, Department of anaesthesia, Trichy SRM Medical College Hospital and Research Center, Trichy, Tamilnadu, India.

**ABSTRACT**

**Background: Neuraxial anaesthesia greatly expand the anaesthesiologist armamentarium in many cases providing alternative to general anaesthesia. Spinal anaesthesia is a popular technique for lower limb orthopaedic surgeries. Hyperbaric bupivacaine in 8% glucose is often used. Unintended intravascular injection of bupivacaine during regional anaesthesia may cause severe cardiovascular toxicity, including left ventricular depression,atrioventricular heart block,life threatnig ventricular tachycardia, fibrillation and sudden cardiac arrest which is difficult to resuscitate However levobupivacaine has similar efficacy but better safety profile than racemic bupivacaine.**

**Materials and Methods: This is prospective and cross-sectional study conducted at Department of Anesthesia, Tertiary care teaching hospital. Total 70 patients scheduled for elective lower limb surgeries, ASA physical status class I or II, were enrolled into this prospective randomized, double-blind study. Patients were randomly divided into two groups. For Group L (n = 35); 12.5 mg 0.5% (2.5 ml) levobupivacaine, for group B (n = 35); 12.5 mg 0.5% (2.5 ml) bupivacaine heavy administered intrathecally within 10 seconds.**

**Results: The mean age (Mean± SD) of patients was 40.43±9.74 years with range 22.00-56.00 years and the median age was 36.00 years in Group-B. In Group-L, the mean age (Mean ±SD) of patients was 40.83±9.74 years with range 22.00-67.00 years and the median age was 38.50 years. Mean duration of anaesthesia was 116.43± 24.63 minutes in Group B versus 112.33±26.52 minutes in Group L. Difference of mean Duration of Anaesthesia in two groups was not statistically significant (p=0.538). Mean duration of surgery was 95.32±9.43 minutes in Group L versus 96.53±9.43 minutes in Group B. Difference of mean Duration of Surgery in two groups was not statistically significant (p=0.464).**

**Conclusion: The results of this study indicate that levobupivacaine and racemic bupivacaine show equally effective potencies for spinal anesthesia. Bupivacaine group showed earlier onset of action but there is no significant difference between levobupivacaine and bupivacaine regarding the duration of sensory and motor blockade.**

**Keywords: Isobaric Levobupivacaine, Hyperbaric Bupivacaine, Spinal Anesthesia.**

**Corresponding Author:**Dr. Dr. K. Selvaraju, Associate Professor, Department of anaesthesia, Trichy SRM Medical College Hospital and Research Center, Trichy, Tamilnadu, India.

## INTRODUCTION

Spinal anaesthesia is a method used to induce anesthesia by blocking the cluster of spinal nerves. Direct injection of local anaesthetic in CSF for spinal anaesthesia required small dose and volume of local anaesthetic to achieve sensory and motor blockade. Local anaesthetic injected in CSF, interrupting the afferent transmission of painful stimuli and abolishing the efferent impulses responsible for skeletal muscle tone, provided excellent operating condition. So, it provides simple, effective and safe analgesia in the peri-operative period.[1]

Spinal anaesthesia is easy, inexpensive and preferable technique for lower limb orthopaedic surgery, as it provides effective sensory and motor block with rapid onset, attenuation of stress response and less thromboembolic episodes. Bupivacaine is most commonly used local anaesthetic agent for spinal anaesthesia. However the cases have been reported where unintended intravascular injection of bupivacaine during attempted neuraxial anaesthesia resulted in sudden cardiac arrest which was refractory to resuscitation.[2] This motivated researchers to investigate about mechanism of local anaesthetic toxicity and to develop alternative agents which have similar efficacy but better safety profile than bupivacaine. Scientists have taken the advantage of the fact that amide local anaesthetic have a chiral centre and can exist as S (-) optical isomer(levobupivacaine or ropivacaine) and dextro R (+) stereoisomers.[3]

Racemic bupivacaine used for Spinal anaesthesia is providing a fast onset and effective sensory and motor blockade. Bupivacaine is available as a racemic mixture of its enantiomers, (dextrobupivacaine and levobupivacaine). Levobupivacaine is an effective long-acting amide local anaesthetic produced as a pure enantiomer. The sensory block is similar to that produced by an equivalent dose of bupivacaine. However, the motor block provided is of slower onset, lesser intensity and of shorter duration.[4] Levobupivcaine is an L enantiomer of bupivacaine. When administered for caesarean section it has been shown to have motor blockade of lesser intensity when compared to bupivacaine. It is considered more potent than ropivacaine due to its greater lipid solubility.[5]

Initial studies of levobupivacaine are now appearing in literature confirming its comparable clinical efficacy with racemic bupivacaine in spinal anaesthesia when it was used for lower limb orthopaedic surgeries, cesarean section, transurethral resection of prostate, lower abdominal surgery.[5] In all these studies, preparation of both bupivacaine and levobupivacaine were isobaric. Hyperbaric preparations of local anaesthetic are preferred in spinal anaesthesia as they produce more predictable and reliable sensory and motor block, with faster onset than a plain solution as observed for bupivacaine, ropivacaine, and levobupivacaine.[6]

Hyperbaric bupivacaine in spinal anaesthesia is still a gold standard in our country; however, there is scarcity of data which show comparable efficacy of intrathecal isobaric levobupivacaine versus hyperbaric bupivacaine.[7] Therefore we designed this study to compare sensory- motor block characteristics, hemodynamic profile and adverse effects of equivalent doses (12.5mg) of isobaric levobupivacaine and hyperbaric bupivacaine in spinal anaesthesia for lower limb orthopaedic surgery. Our ultimate objective is if isobaric levobupivacaine is found clinically effective, it can become a better alternative to hyperbaric bupivacaine in spinal anaesthesia, because it has lower toxic effects on cardiovascular system.[7]

## MATERIALS & METHODS

This is prospective and cross-sectional study conducted at Department of Anesthesia in a tertiary care teaching Hospital. After informed consent were obtained, 70 patients scheduled

for elective lower limb surgeries, ASA physical status class I or II, were enrolled into this prospective, randomized, double-blind study.

Patients refusing regional anesthesia, having contraindications to spinal anesthesia, those meeting the pre-determined exclusion criteria excluded from the study.

Following application of routine monitors (noninvasive BP measurement, electrocardiography, and pulse oximetry) and insertion of a peripheral 18 G i.v cannula, a rapid infusion of Ringer lactate solution 10 ml/kg was administered. Baseline systolic BP and heart rate were calculated as the mean of the three recordings. Patients were placed in the sitting position. After disinfecting the skin and infiltrating with 2% lidocaine, lumbar puncture was performed at the L3-4 interspace using a 25-gauge Quincke point needle. Patients were randomly divided into two groups. For Group L (n = 35); 12.5 mg 0.5% (2.5 ml) levobupivacaine, for group B (n = 35); 12.5 mg 0.5% (2.5 ml) bupivacaine administered intrathecally within 10 seconds.

Subsequently, patients were turned to supine position. Oxygen 4 L/min was administered via a facial mask. The sensory level of spinal anesthesia was assessed bilaterally in the anterior axillary line by pinprick, using a short beveled 25 G needle, and was recorded at baseline prior to spinal injection, then every 3 minutes for the first 15 min after injection, and every five minutes for the next 25 min, and at 60, 90, 120, 180, 240, 300, 360, 420, 480 minutes. Permission to perform operation was given once a T4-T6 level had been achieved. Considering the time of intrathecal injection as time zero, the time to onset of sensory block, the time taken to reach maximum sensory block level, the time to regression of two dermatomes of the sensory block, the duration of the regression of the sensory block level to T12 from the maximum level were recorded.

The level of motor block was assessed with modified Bromage scale (0 = no paralysis, able to flex hips/knees/ankles; 1 = able to move knees, unable to raise extended legs; 2 = able to flex ankles, unable to flex knees; 3 = unable to move any part of the lower limp). The time to onset of motor block, the time to reach Bromage 3 and the time of complete disappearance were recorded. 0, 3 min intervals for first 15 min; 5 min intervals for up to 30 min; and then @ 60, 120, 180, 240, 300, 360, 420, 480 minutes.

The calculation of the required sample size was based on mean and standard deviation of complete regression of spinal block after anesthesia with bupivacaine and levobupivacaine reported in previous investigation (10, 11): 30 patients per group were required to detect a 20-min difference in time for complete regression of spinal anesthesia with an expected effect size to standard deviation ratio of 0.9 accepting a two-tailed $\infty$ error of 5% and a ß error of 20%. Shapiro-Wilks normality test was applied to see whether the data distribution was normal.

**Statistical Analysis:**

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 25th version. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Chi-square test or Fischer’s exact test compared unpaired proportions, as appropriate.

## RESULTS

The mean age (Mean ±SD) of patients was 40.43±9.74 years with range 22.00-56.00 years and the median age was 36.00 years in Group-B. In Group-L, the mean age (Mean ±SD) of patients was 40.83±9.74 years with range 22.00-67.00 years and the median age was 38.50 years. Difference of mean age in two groups was not statistically significant. Thus, age was matched in two groups. There was no statistically significant difference in age distribution between the groups. [Numerical variables between groups compared by t-test; (p=0.354)].

**Table 1: Distribution of mean Age in two groups**

| Group B(Mean ±SD) | Group L(Mean ±SD) | p-value |
|---|---|---|
| 40.43±9.24 | 40.83±9.74 | 0.354 |

**Table 2: Distribution of Gender in two groups**

| Gender | Group BN (Percentage) | Group LN (Percentage) | p-value |
|---|---|---|---|
| Male | 24 (68.5%) | 22 (62.8%) | 0.534 |
| Female | 11 (31.5%) | 13 (37.1%) | |
| Total | 35 (100%) | 35 (100%) | |

Chi-square value: 1.142; p-value: 0.534

Association between gender in two groups was not statistically significant (p=: 0.534).

**Table 3: Distribution of ASA in two groups**

| ASA | Group BN (Percentage) | Group LN (Percentage) | p-value |
|---|---|---|---|
| 1 | 19 (54.2%) | 18 (51.4%) | 0.635 |
| 2 | 16 (45.7%) | 17 (48.5%) | |
| Total | 35 (100%) | 35 (100%) | |

Chi-square value: 0.053; p-value: 0.635

Association between ASA in two groups was not statistically significant (p=0.635).

**Table 4: Distribution of mean Duration of anaesthesia and Surgery in two groups**

| Parameters | Group BMean ± SD | Group LMean ± SD | p-value |
|---|---|---|---|
| Duration of Anaesthesia(Minuets) | 116.43±24.63 | 112.33±26.52 | 0.538 |
| Duration of Surgery(Minuets) | 96.53±9.43 | 95.32±9.43 | 0.464 |

Mean duration of anaesthesia was 116.43± 24.63 minutes in Group B versus 112.33±26.52 minutes in Group L. Difference of mean Duration of Anaesthesia in two groups was not statistically significant (p=0.538). Mean duration of surgery was 96.53±9.43 minutes in Group B versus 95.32±9.43 minutes in Group L. Difference of mean Duration of Surgery in two groups was not statistically significant (p=0.464).

**Table 5: Distribution of mean HR at different time interval in two groups**

| | Group | Mean ±SD | p-value |
|---|---|---|---|
| HR at 30 min | Group-B | 87.46±3.65 | 0.535 |
| | Group-L | 88.62±2.47 | |
| HR at 60 min | Group-B | 88.73±2.37 | 0.375 |
| | Group-L | 88.48±3.75 | |

**Table 6: Distribution of mean SBP at different time interval in two groups**

| SBP | Group | Mean ±SD | p-value |
|---|---|---|---|
| SBP at 30 min | Group-B | 121.35±5.54 | 0.364 |
| | Group-L | 124.26±6.72 | |
| SBP at 60 | Group-B | 119.73±5.47 | 0.474 |
| | Group-L | 122.36±6.26 | |
| DBP 30 min | Group-B | 80.52±4.73 | 0.245 |
| | Group-L | 81.56±5.63 | |
| DBP at 60 min | Group-B | 82.63±4.78 | 0.465 |
| | Group-L | 81.36±5.74 | |

**Table 7: Distribution of mean MAP at different time interval in two groups**

| | Group | Mean ±SD | p-value |
|---|---|---|---|
| MAP at 30 min | Group-B | 94.01±7.74 | 0.736 |
| | Group-L | 96.52±6.43 | |
| MAP at 60 min | Group-B | 94.99±7.35 | 0.472 |
| | Group-L | 95.05±6.32 | |

**Table 8: Distribution of mean SPO2 at different time interval in two groups**

| | Group | Mean | p-value |
|---|---|---|---|
| $SPO_2$ at 30 min | Group-B | 99.35±3.43 | 0.453 |
| | Group-L | 99.46±4.24 | |
| $SPO_2$ at 60 min | Group-B | 99.37±3.63 | 0.742 |
| | Group-L | 99.83±3.36 | |

**Table 9: Distribution of mean OSB (T12), in minutes, in two groups**

| | Group | Mean | p-value |
|---|---|---|---|
| OSB(T12) (min) | Group-B | 2.03 ±0.32 | 0.0001 |
| | Group-L | 2.94±0.15 | |

## DISCUSSION

The present study demonstrates that levobupivacaine, the pure S (-)-enantiomer of racemic bupivacaine, is an effective local anesthetic for spinal applications. Onset time and duration of the sensory and motor blocks, peak block height, and hemodynamics are like those obtained with racemic bupivacaine. Ropivacaine is another enantiomer whose potency in intrathecal administration has been investigated. Wahedi et al.[8] reported that 0.5% spinal ropivacaine only achieved sufficient surgical anesthesia in 75% of cases, 30% being characterized by subtotal motor blockade. This result was since confirmed by Malinovsky et al.[9] who suggested an anesthetic ratio between spinal ropivacaine and bupivacaine of 2:3, with lower anesthetic potency achieved by 15 mg of spinal ropivacaine than by 10 mg of bupivacaine in patients undergoing endoscopic urological survgery.

In our study, sensory block levels required for surgeries were achieved in both groups, and it was observed that the hemodynamic stability with levobupivacaine was better maintained. In most of the studies where the same doses of levobupivacaine and bupivacaine were investigated, sensory and motor block characteristics were found to be similar. Glaser et al. compared 3.5 ml and Fattorini et al. compared 3 ml 0.5% isobaric bupivacaine with levobupivacaine,[10,11] and both reported that there was no significant difference in terms of maximum distribution, and durations of sensory and motor block.

We observed in our study that maximum sensory block level in levobupivacaine group was similar. Development of motor block was faster in bupivacaine than levobupivacaine group and lasted for similar duration. The results of our study are contradictory to those from the studies mentioned above. However, similar results have been also reported by Gautier et al.[12] during spinal anaesthesia for caesarean delivery. They compared the same doses of levobupivacaine and bupivacaine, and reported that while adequate anesthesia was maintained in the 97% of the patients in the bupivacaine group, this rate was 80% in the levobupivacaine group, and duration of motor block and analgesia was shorter in the levobupivacaine.

In our study also, sensory and motor block durations were found to be shorter in the levobupivacaine group. The effects of baricite on the block characteristics have been contradictory in literature: while some studies that report the difference in baricite does not affect block characteristics.[13] On the other hand, there are also studies reporting that motor block develops and disappears faster when hyperbaric solutions are used.[14] Therefore, we cannot ascribe the difference of sensory and motor block between the two groups in our study to the difference of baricite only.

In our study, the incidence of hypotension with bupivacaine was found to be 36.6%. The incidence of hypotension was significantly reduced to 16.6% in the doses we used in the levobupivacaine group. Fattorini et al.[11] reported that although they did not observe a significant difference in the sensory and motor block characteristics of levobupivacaine and bupivacaine among 60 patients who undergo major orthopaedic surgery, they did not find severe hypotension and better cardiovascular stability was provided in the levobupivacaine group, Lovstad et al.[15] investigated minimum local anaesthetic dose in caesarean sections, and they reported that in the levobupivacaine group, in which they administered similar doses with our study, the incidence of hypotension decreased significantly. Gunusehn et al.[16] have compared different doses of levobupivacaine-fentanyl combination in cesarean section and reported that 10 mg levobupivacaine with 10 μg fentanyl combination provides 100% effective anaesthesia but the incidence of hypotension was high. The higher hypotension rates reported by Gunusen et al. may be related to the difference in the definition of hypotension between the studies.[16]

The mechanism of this undesirable event remains uncertain; it may be related to lower cephalic diffusion of the local anesthetic and the consequent lower reduction of systemic vascular resistances. Levobupivacaine has been shown to result in greater vasoconstriction at all concentrations compared to racemic bupivacaine.[17] That would explain the lower incidence of hemodynamic effects compared to bupivacaine, which causes vasodilation (leading to arterial hypotension and bradycardia).

## CONCLUSION

In our study that subarachnoid administration of low-dose 0.5% levobupivacaine (mean volume of 2.5 mL) in patients undergoing lower limb surgeries was as safe as the administration of low-dose hyperbaric bupivacaine. Our results, especially regarding intra and postoperative events suggest that subarachnoid low-dose isobaric levobupivacaine was safer and should be used instead of hyperbaric bupivacaine in patients undergoing lower limb surgical procedures.

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