COMPARISON OF ISOBARIC LEVOBUPIVACaine 0.5% AND ISOBARIC ROPIVACaine 0.5% FOR SPINAL ANAESTHESIA IN LOWER LIMB SURGERIES

1,5,6 Dr. Gautam Singh, 2Dr. Vasanti Kelkar, 3Dr. Sanhita Kulkarni, 4Dr. Prabha Nayak, 5Dr Anshul Udiavar, 6Dr Tejas Warkari

1,4,5 M. D. Anaesthesia, Resident*, 2M. D. Anaesthesia, Associate Professor, 3M. D. Anaesthesia, Professor and Head,
Department of Anaesthesia, MGM’s Medical College, Aurangabad, Maharashtra, India.

*Corresponding Author: Dr. Gautam Singh
M. D. Anaesthesia, Resident, Department of Anaesthesia, MGM’s Medical College, Aurangabad, Maharashtra, India.

ABSTRACT
Background: Levobupivacaine and Ropivacaine are the two recently introduced alternatives to Bupivacaine in clinical practice. We compared the efficacy of intrathecally administered isobaric 0.5% levobupivacaine and isobaric 0.5% ropivacaine in lower limb surgeries in terms of characteristics of sensory and motor blockade and intra-operative haemodynamic stability. Study Design: Prospective, randomized double blind study was carried out in sixty American society of Anaesthesiologists grade 1 – 3 patients in age group of 18 to 65 years having height between 150 - 180 cm undergoing lower limb surgeries. Material and Methods: The patients were divided in 2 groups of 30 patients each. Group-A received 3 ml Isobaric 0.5% Levobupivacaine whereas Group-B received 3 ml Isobaric 0.5% Ropivacaine intrathecally. Onset and duration of sensory and motor blocks, maximum height of sensory block and intraoperative haemodynamic parameters (heart rate and mean blood pressure) were compared. Results: Patients in Levobupivacaine group showed faster onset and longer duration of sensory and motor blocks. The median level of sensory block attained was higher (T6) in Levobupivacaine group than Ropivacaine group (T8). Ropivacaine group showed higher incidence of bradycardia whereas incidence of hypotension was comparable in both the groups. Conclusion: Both isobaric 0.5% Levobupivacaine and isobaric 0.5% Ropivacaine are effective with good haemodynamic stability when used intrathecally. Levobupivacaine has faster and prolonged sensory and motor blockade compared to Ropivacaine. While Ropivacaine can be a better drug for day care surgeries, Levobupivacaine is better for surgeries of prolonged duration.

KEYWORDS: Isobaric, Levobupivacaine, Ropivacaine, Spinal anaesthesia.

INTRODUCTION
Bupivacaine, available as a racemic mixture of its enantiomers dextrobupivacaine and levoupivacaine, has been the gold standard for intrathecal use in spinal anaesthesia for many years. Levobupivacaine and Ropivacaine are the two recently introduced alternatives to Bupivacaine in clinical practice. Levobupivacaine is the pure s (-) enantiomer of racemic Bupivacaine. It produces equivalent sensory block but shorter duration of motor block than intrathecal Bupivacaine. It has a lower risk of cardiovascular toxicity than Bupivacaine in both animal and human studies. Because of its low affinity to cerebral tissue, Levobupivacaine causes less CNS depression than Bupivacaine does. Ropivacaine is another enantiomer with less cardiovascular toxicity than Bupivacaine. Ropivacaine produces equivalent sensory block but short duration of motor block than intrathecal Bupivacaine. Both these drugs are available as isobaric solution in India.

As both these drugs have been recently introduced in India, not much work has been done comparing their intrathecal use. Hence we decided to compare the efficacy of intrathecally administered isobaric 0.5% levobupivacaine and isobaric 0.5% ropivacaine in lower limb surgeries. Primary outcome of our study was comparison of characteristics of sensory and motor blockade and secondary outcome was comparison of intra-operative haemodynamic stability.

MATERIAL AND METHODS
After approval of ethical committee, the study was conducted in department of Anaesthesia over a period of one year. The study included American society of Anaesthesiologists grade 1 – 3 patients in age group of 18 to 65 years having height between 150 - 180 cm undergoing lower limb surgeries. Patients with severe cardiac, renal or hepatic disorders and those allergic to local anaesthetic agents were excluded from the study.
Procedure was explained to the patient and written consent taken for participation in study. The patients were divided in 2 groups of 30 patients each. Group-A received 3 ml Isobaric 0.5% Levobupivacaine (Levomolan by Neon laboratories) whereas Group- B received 3 ml Isobaric 0.5% Ropivacaine (Ropin by Neon Laboratories). Random allocation of groups was done by sealed envelope method. Height of the patient was noted. Monitors were attached and baseline parameters like heart rate (HR), Mean blood pressure (MAP), Oxygen saturation (SPO2) and ECG were recorded. Preloading was done by infusion of 500ml ringer lactate over 20 minutes (min.). Spinal anaesthesia was administered in sitting position in L3-L4 interspace with 23G quinke needle under all aseptic precautions. One anaesthetist administered the drug intratheclally while another anaesthetist recorded the findings. Both patient and the observer anaesthetist were blind to the study drugs used making the study double blind. Sensory block was tested by pin prick in midaxillary line every 3 min till peak sensory level i.e. two consecutive reading at the same dermatomal level is achieved. Thereafter sensory block was tested every 20 min till the block regression to L1 level. The time from spinal injection (T-0) to time taken to achieve T10 level was taken as onset of sensory blockade. The time from T-0 to L1 regression was taken as total duration of sensory block. Motor block was tested every 5 min using Bromage scale till grade 2 motor block was achieved. Onset of motor block was taken as time from T-0 to obtaining a motor block of grade 2. Thereafter motor block was tested in post op period every 15 min till complete recovery (grade 0) and duration of motor block was noted. Surgery was allowed after achieving sensory block up to T10 and grade 2 motor block. Failure to achieve the required block in 20 min was considered as failure of block and General Anaesthesia was given. After spinal anaesthesia was administered, HR and MAP were recorded every 3 min for first 20 min. Thereafter it was taken every 10 min till regression of block to L1. Decrease in MAP by more than 25% of base line was taken as hypotension and treated with inj. mephentermine 0.6mg IV. Inj. Ondensetron 4 mg intravenously and Inj. Diclofenac 75 mg intramuscularly was given at the end of surgery.

**STATISTICAL ANALYSIS**

Before the study was carried out, a power analysis indicated that 23 patients per group would be required to detect a 10% difference in haemodynamic parameters. The α error was set at 0.05 and β error at 0.9. Thus a sample size of n=30 per group was considered for our study.

All data was presented as Mean ± SD (Standard Deviation). Demographic data was analyzed using Chi-square test and statistical significance in mean difference was done using student’s t test. All statistical analysis was made using SPSS 22 for Windows (Statistical Package for Social Science). P < 0.05 was regarded as statistically significant. P < 0.001 was taken as highly significant and P > 0.05 was regarded as non significant.

**RESULTS**

The two groups were comparable regarding age, height and surgical duration. (p < 0.05) Patients in group L showed faster onset of sensory block (4.10±1.67 mins) compared to group R (7.50±3.03 mins), the difference being statistically highly significant (p=0.000).

In the group L, 18 patients had maximum level of sensory block of T6 as compared to eight patients in Group R. No patient in Group-R had maximum sensory level of T4 compared to 5 patients in the group L; the difference is statistically highly significant. (p=0.000). (Figure 1)

The median level of sensory block attained was T6 (T4 – T10) in Levobupivacaine group and T8 (T6 – T10) in Ropivacaine group. The mean time for achieving maximum sensory level was 9.10±3.10 mins in group L vs. 12.23±6.15 min in group R. The difference was statistically significant (p=0.017). The mean duration of sensory block was longer (154.2±27.0 min) in Group-L group than 132.4±34.0 mins in Group-R (p=0.008). (Table 1)

The mean time taken for the onset of motor blockade was 3.70±2.32 mins in group L and 5.70±1.99 mins in group R. The difference is statistically highly significant (p=0.001). (Table 1)

Immediately after intrathecal injection, number of patients with grade 3 motor blockade were 10 (33.33%) compared with 2 (6.66%) in group R. This difference is statistically significant (p=0.0089). (Figure 2)

There was statistically highly significant difference (p=0.000) in duration of motor blockade in group L (169.3±18.2mins) compared to group R (138.0±31.6mins). (Table 1)

Two patients (6.67%) in group L and 9 patients (30%) in group R developed bradycardia. The difference was statistically significant (p=0.01928). The incidence of hypotension in both the groups was statistically comparable (Group L -20%, Group R – 13.33%, p=0.4902). (Table 2)
Table 1: Comparison of sensory and motor block parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group L (n = 30)</th>
<th>Group R (n = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of sensory block (Minutes) *</td>
<td>4.10 ± 1.67</td>
<td>7.50 ± 3.03</td>
<td>0.000 HS</td>
</tr>
<tr>
<td>Median level of sensory block †</td>
<td>T6 (T4 – T10)</td>
<td>T8 (T6-T10)</td>
<td>---</td>
</tr>
<tr>
<td>Time to achieve maximum Sensory Level (Minutes) *</td>
<td>9.10±3.10</td>
<td>12.23±6.15</td>
<td>0.017 S</td>
</tr>
<tr>
<td>Duration of Sensory Blockade (Minutes) *</td>
<td>154.2±27.0</td>
<td>132.4±34.0</td>
<td>0.008 S</td>
</tr>
<tr>
<td>Duration of motor block(minutes) *</td>
<td>3.70±2.32</td>
<td>5.70±1.99</td>
<td>0.001 HS</td>
</tr>
</tbody>
</table>

S = Significant, HS = Highly significant, * mean ± SD, † median (range)

Table 2: Incidence of complications.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Group L (n = 30)</th>
<th>Group R (n = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradycardia</td>
<td>2 (6.67%)</td>
<td>9 (30%)</td>
<td>0.01928 S</td>
</tr>
<tr>
<td>Hypotension</td>
<td>6 (20%)</td>
<td>4 (13.33%)</td>
<td>0.4902 NS</td>
</tr>
</tbody>
</table>

S = Significant, NS = Not significant.

Figure 1: Comparison of maximum level of sensory block attained.

Figure 2: Intensity of motor block immediately after intrathecal injection of study drugs.
DISCUSSION

It has been found that isobaric local anaesthetics are ideal for surgeries below T10 level of block and high volumes are required for surgeries above T10. In our study we selected patients posted for lower limb surgeries (mainly orthopaedic) requiring a blockade below T10. All the patients in our study were given spinal anaesthesia in sitting position considering patient comfort and a fact that level of sensory block after intrathecal administration of isobaric local anaesthetics is unaffected by the patient position.\(^6\)\(^7\) Levobupivacaine is claimed to be equipotent to racemic Bupivacaine and Ropivacaine is shown to be 2/3 times as potent as racemic Bupivacaine. According to a study conducted by Glaser et al\(^{[3]}\) using single shot spinal anaesthesia for hip replacement surgery, there was no significant difference in the minimum local anaesthetic dose of isobaric Levobupivacaine (11.7 mg) and that of Ropivacaine (12.8 mg) as assessed by the up and down method of Dixon. The mean (SD) total dose of Levobupivacaine required to complete surgery was 15.2 (4.0) mg and 15.5 (3.1) mg for Ropivacaine. Hence in our study, we used the dose 15 mg i.e. 3ml of 0.5% solution.

Onset of sensory block defined as time taken to achieve T10 level was 4.10±1.67 min in Group L whereas in the group R it was 7.50±3.03 min. This difference in the onset time was statistically highly significant. (p=0.000).

The values obtained for Group L in our study correlate well with that of Mehta et al\(^{[9]}\) (5.46±1.72 min), Das et al\(^{[9]}\) (4.2±1.99mins) and Helmi et al\(^{[10]}\) (4.8±2.2mins). In these studies the criteria for onset of sensory blockade was loss of pin prick sensation at T10 dermatomal level, similar to our study. The onset time observed by Fattorini et al\(^{[11]}\) (12±6 min) was slightly longer; the difference may be due to the use of lower dose (8 mg) of Levobupivacaine in their study. Glaser et al\(^{[3]}\) in their study using 3.5 ml of 0.5% Levobupivacaine found delayed onset of sensory block (11±6 min). However they did not define the exact dermatomal level for onset. Sultan et al\(^{[12]}\) reported the onset time of sensory block for Levobupivacaine as 6±3 mins which was higher compared to our study. The difference may be because of the use of lateral decubitus position while giving intrathecal injection. The values of onset time for sensory block in the group R in our study correlates with those obtained by Das et al\(^{[9]}\) (7.73±3.04 min) and Sultan et al\(^{[12]}\) (7±3min). Kallio et al\(^{[13]}\) found that median duration of analgesia at the level of T10 was 10 min. The higher values found in their study may be due to difference in concentration and volume of the drug used and method of statistical analysis. We used 3ml of 0.5% Ropivacaine whereas they used 2ml of 0.75% of Ropivacaine. For comparing the onset we used Mean ± SD as opposed to median values in their study.

In our study the maximum level of sensory blockade was T4 (n=5) in group L and T6 (n=8) in group R. Median level of sensory block was T6 (T4 – T10) in group L and T8 (T6 – T10) in group R. Our result correlates with study of Vellosillo et al\(^{[14]}\) where they found maximum level of sensory blockade for Levobupivacaine as T6 (T2-12). Vanna et al\(^{[15]}\) reported that maximum sensory level for Levobupivacaine achieved in their study was T9 (T4-T10) This difference may be because of less volume of drug (2.5 ml) used by Vanna et al\(^{[15]}\) whereas we have used 3ml of drug. Kallio et al\(^{[13]}\) in their study found maximum sensory level using Ropivacaine was T7 (T4-T12), results very similar to our study. The minimal difference may be because of different concentration of Ropivacaine. The mean time for achieving maximum sensory level in our study was 9.10±3.10 mins in group L vs. 12.23±6.15 min in group R. There was a statistically significant difference between the groups in the time taken for achieving maximum sensory level (p=0.017). These values in group L in our study were similar to those obtained by Glaser et al\(^{[3]}\) (8-10 min), Sultan et al\(^{[12]}\) reported 7±1.63 min as the time taken to reach maximum sensory level This variation may be due to their definition of maximum sensory level as T8. Vellosillo et al\(^{[14]}\) reported that maximum sensory blockade was achieved in 15mins which is markedly more than our results; this may be because of less drug volume taken in their study. Regarding 0.5% Ropivacaine, our results of time for maximum sensory level (12.23±6.15 mins) were higher than that observed by Kallio et al\(^{[13]}\) where median onset time was 30 mins. This higher value may be because they opted for lateral decubitus position for intrathecal injection. Das et al\(^{[3]}\) observed that time taken to achieve maximum sensory block was 7.73±3.04 mins which is comparatively lower than our study, but they did not mention the position of patient while giving intrathecal injection.

Duration of sensory blockade was defined as the time taken from completion of injection of drug till the regression of sensory level to L1.In our study the duration of sensory blockade was 154.2±27mins in group L compared to 132.4±34.0 mins in group R. The difference being statistically significant (p=0.008). Vellosillo et al\(^{[14]}\) found the same duration of sensory blockade (153mins) for Levobupivacaine as in our study. Vanna et al\(^{[15]}\) observed that the duration of sensory blockade for Ropivacaine was133mins which was similar to our study.

Das et al\(^{[9]}\) and Mehta et al\(^{[8]}\) found that the duration of sensory blockade for levobupivacaine was 145±28 mins and 189.4±42.9 min respectively and that for Ropivacaine was 122.47 ± 25.4 mins and 144.32 ± 32.1 mins respectively. The minimal difference in results in the studies may be because of different parameters used for calculating duration. Das et al 44 considered 2 segment regression from the maximum sensory block height as the duration of sensory blockade, whereas Mehta et al 38 considered time from the onset of sensory

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block to the time when the patient required first dose of analgesia.

Onset of motor blockade was defined as the time taken from the completion of injection of the study drug till the patient developed motor block of bromage scale 2. The mean time taken for the onset of motor blockade was 3.70±2.32 mins in group L and 5.70±1.99 mins in group R, the difference being statistically highly significant (p=0.001). Das et al[9] found that onset of motor block in Levobupivacaine group was 7.37±3.26 mins and 11.07±3.04 mins in Ropivacaine group which is longer than our study. Mehta et al 38 found onset of motor blockade as 5.46±1.73 mins for Levobupivacaine and 6.46±1.14 mins in Ropivacaine. Higher values in both these studies may be because they considered bromage grade 3 as onset of motor block while we considered grade 2 for onset. Vanna et al[13] observed earlier onset of motor block for levobupivacaine 7.5(3.2) mins than our study, may be due to less volume of drug used in their study. Our result for onset of motor block of group R correlates with study of Kaushik et al[16] (5.2±1.1mins).

Duration of motor blockade was taken as the time from the time of injection till complete motor recovery (Bromage scale 0). The duration of motor blockade in group L was 169.3±18.2min compared to 138.0±31.6mins in group R. The difference was statistically highly significant (p=0.000). Our values are similar to that observed by Das et al[9] (Group L159.6±29.54 min. and Group R 124.57±25.53min.) and Mehta et al[38] (Group L 172.76±38.9 min. and 128.24±29.1 min. in Group R). Vani et al[17] found that the duration of motor block for Levobupivacine (154.60) was more than Ropivacaine (90.90mins). Even though the conclusion is similar to our study, the actual duration of motor block of Ropivacine is less than our study. We could not find any explanation for this difference.

There was statistically significant difference in incidence of bradycardia (6.67% in group L and 30% in group R, p=0.01928). Most of the patients who developed bradycardia had baseline pulse rate around 70 and age above 60 years. Kuthiala et al[18] in their study concluded that the incidence of Ropivacaine- induced cardiovascular symptoms may be age related, incidence being higher in age group more than 60 years. A finding by Kallio et al[15] correlates with our study where 14 (47%) patients developed bradycardia in Ropivacaine group.

There was a marginal fall in blood pressure (mean) in both group L and groups R. Six patients in group L and 4 patients in group R needed a single dose of mephentermine 3 mg to treat hypotension. The difference in incidence of hypotension in both the groups was statistically not significant (p=0.4902). Mehta et al[8] observed hypotension in two (8%) patients in both the groups which is lower than our study.

CONCLUSION
Both isobaric 0.5% Levobupivacaine and isobaric 0.5% Ropivacaine are effective with good haemodynamic stability when used intrathecally. Levobupivacaine has faster and prolonged sensory and motor blockade compared to Ropivacaine. While Ropivacaine can be a better drug for day care surgeries, Levobupivacaine is better for surgeries of prolonged duration.

LIMITATION OF STUDY
As the study was carried out mostly in orthopaedic surgeries, we could not assess the quality of motor block in the intra operative period. Secondly, addition of bupivacaine group might have given a better idea about usefulness of these drugs as alternative to bupivacaine which we could not do due availability of limited number of patients.

REFERENCES


