**Original article:**

**Comparative study of intrathecal Ropivacaine and Levobupivacaine in lower limb orthopaedic surgeries**

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**ABSTRACT:**

**Background and Objectives:**  Levobupivacaine and Ropivacaine are safer local anesthetics than bupivacaine when hemodynamic stability is considered. This study has been conducted to compare the efficacy of equianalgesic doses of isobaric levobupivacaine and ropivacaine in terms of sensory and motor blockade characteristics, effect on intraoperative haemodynamics, side effects when administered intrathecally.

**Methods:** A comparative study was conducted in 50 ASA grade I-II patients in age groups of 18-80 years undergoing lower limb orthopaedic surgeries. Patients were randomly divided into 2 groups of 25 each. Group R received 3 ml isobaric Ropivacaine 0.75 %( 22.5mg), whereas patients in Group L received 3 ml isobaric Levobupivacaine 0.5 %( 15mg) intrathecally. Patients were assessed for onset, duration of sensory and motor blockade, intraoperative hemodynamic parameters and side effects of these drugs.

**Results:** There was no difference in demographic data, onset of action and peak effect of sensory and motor block in both groups (p > 0.05). Duration of sensory and motor block and time to two segment regression were significantly longer in Group L than Group R. The difference between 2 groups for duration of motor block was statistically highly significant (p < 0.001). Deviation in intraoperative hemodynamic parameters showed no statistically significant difference. Incidence of side effects was low and difference was not statistically significant.

**Conclusion:** Based on present study we conclude that both levobupivacaine and ropivacaine are effective with stable hemodynamics without significant side effects when used intrathecally in equianalgesic doses. However, Ropivacaine has shorter duration of sensory and motor blockade than levobupivacaine. When 2 groups are compared, difference in duration of motor action is statistically and clinically significant.

**Keywords:** Isobaric**,** Levobupivacaine, Ropivacaine.

**INTRODUCTION:**

The ideal drug to be used intrathecally needs a good balance of sensory and motor block durations with minimal cardiovascular, neural, and other systemic adverse effects.Mechanism of action of all local anesthetics is via reversible inhibition of sodium ion influx in nerve fibers.

Lower limb surgeries may be performed under regional (spinal, epidural or peripheral nerve blocks) or general anesthesia. For intrathecally use, the most commonly used local anesthetic is racemic bupivacaine; which has low (1%) incidence of post operative complications.[1]However, it has been shown to have cardiotoxic effects more pronounced with R-isomer than S-isomer.[2]Introduction of levobupivacaine has been useful for offsetting this adverse effect. Ropivacaine is another local anesthetic agent which seems to be an attractive alternative to racemic bupivacaine.

Ropivacaine is produced as a pure ‘S’ enantiomer with lower lipid solubility, easier reversibility after inadvertent intravascular injection, significant reduction in central nervous system toxicity, lesser motor block and greater differentiation of sensory and motor block.Ropivacaine in an equipotency ratio of 1.5:1 to bupivacaine produces similar results with better preservation of motor function.[3]Shorter elimination half-life of Ropivacaine makes this local anesthetic more useful for short duration surgeries to get with painless and ambulatory patient in the postoperative period especially in lower abdominal and lower limb surgeries.[4]

Motor blockade of 0.75% ropivacaine is comparable to 0.5% bupivacaine and levobupivacaine. Increasing concentrations cause quicker onset, greater intensity, slower regression, and longer duration of motor blockade. [5, 6] Both of these agents are pure left isomers, and based on their three-dimensional structure; they have less toxicity to both the central nervous system and the heart.

Addition of dextrose to local anesthetics increases the density of injectate and provides earlier onset of motor and sensory block. When no dextrose is added, the solution becomes isobaric to cerebrospinal fluid which may limit the spread and produce longer duration of action.

This study was undertaken to compare and evaluate the efficacy of 3cc 0.5% isobaric levobupivacaine versus 3cc 0.75% isobaric ropivacaine for level, onset, duration of sensory and motor blockade of spinal anesthesia, haemodynamic changes and safety in American Society of Anesthesiologists (ASA) class 1 and II adult patients undergoing elective lower limb surgeries.

**MATERIAL AND METHODS :**

After getting written informed consent from the study subjects and approval by institutional ethics committee, this prospective randomized double blind comparative study was conducted between May 2, 2021 to Oct 2, 2021 at BV(DU) Medical College and Hospital, Sangli. The study subjects were between the age of 18-80 years, ASA status I and II. Patients who were ASA status III and IV, those with a history of bleeding disorders, those who were allergic to local anesthetics, patients on anticoagulants, those suffering from infection at the site of spinal needle insertion, those having spinal abnormalities like spina bifida, meningocele or those who refused to give consent were excluded.

In total, 50 adult patients scheduled to undergo elective surgery and satisfying all the inclusion criteria enrolled for the study were randomly divided into two groups (n=25 each) according to computer-generated random numbers using the sealed envelope technique, to receive either a spinal block with 3-ml 0.5% isobaric levobupivacaine (group L) or 3-ml 0.75% isobaric ropivacaine (group R). The drugs were used from prefilled syringe. The anesthesiologist administering spinal anesthesia was blinded to the drug administered.

Basic demographic characteristics like age, sex, weight and height were noted during preanesthesia check up.As per our institutional protocol, all patients received injection glycopyrrolate 0.2mg intravenously prior to regional anesthesia to prevent vasovagal event. Intravenous access was secured with 18 G cannula and Ringer's lactate was started at 2 ml/kg/hr as a preloading solution. Intraoperative intravenous fluids were given as per kg body weight and operative loss. Spinal anesthesia was given under aseptic precautions in sitting position.

Group R received22.5 mg of isobaric ropivacaine (3 cc of .75%) intrathecally. Group L received15 mg of isobaric levobupivacaine (3 cc of .5%) intrathecally.

Electrocardiogram (lead II), heart rate, noninvasive arterial blood pressure, pulse oximetry (SpO2), respiratory rate, peripheraltemperature were monitored throughout the surgery as per standard protocols.

Characteristics of sensory block were assessed as per Gromley and Hill scale by assessing the changes in perception ofpin prick sensation.Sensory blockade was assessed every 1 min for 5 min, every 5 min for 30 min and then every 30 min during postoperative period till return of sensations. Onset of sensory blockade (time interval from intrathecal injection to L1 level) in min, highest sensory level achieved, time to achieve highest sensory level and two segment regression time from highest sensory level were recorded.

**Gromley and Hill scale:**

 Normal sensation – grade 0

Blunted sensation – grade 1

No sensation – grade 2(Grade 2 was considered as onset of sensory block)

Characteristics motor block were assessed as per Modified Bromage scale. They were assessed every 1 min for 5 min, every 5 min for 30 min and then every 30 min till return of power in lower limbs. Time to achieve (grade 3) motor block, maximum motor block, duration of motor block were recorded.

**Modified Bromage scale:**

Grade 0 = no paralysis, able to flex hips/knees/ankles

Grade 1 = able to move knees, unable to raise extended legs

Grade 2 = able to flex ankles, unable to flex knees

Grade 3 = unable to move any part of the lower limb (Grade 3 was considered as complete motor block).

Intraoperative and postoperative monitoring of pain was assessed with the help of a linear Visual analogue scale using a 10 cm line where 0 denotes “no pain” and 10 denotes “worst possible pain”; every 15 min after onset of surgery till the end of surgery and return of pain perception.

Duration of sensory block was taken as the time from the onset of sensory block to the time when the patient was given first dose of analgesic for post-operative pain relief.

Duration of motor block was taken as the time from complete motor block to when the patient had the ability to flex knees i.e. grade 1 on Bromage scale.

Quality of block was graded as

Adequate - no sedation/analgesia required

Inadequate - need of additional analgesia

Failed - GA required.

Patients were monitored for various perioperative complications like bradycardia (defined as pulse rate less than 20% of pre procedure value or < 50 beats/min. It was treated with Inj Atropine 0.6mg iv.), hypotension (systolic blood pressure less than 20% of pre procedure value or < 80/60 mmHg was considered as hypotension and was treated with IV fluids, oxygen and inj. ephedrine 5 mg IV bolus.), respiratory depression (decrease in respiratory rate < 10 / min or SpO2 to less than 90% was defined as hypoxia and treated with supplemental oxygen if required). Incidence of nausea and vomiting and urinary retention was also noted.

**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 hemodynamics parameters. The error was set at 0.05 and β error at 0.9. Thus sample size of n=25 per group was considered for our study. All qualitative data were analyzed using Chi Square test and quantitative data using Student’s t-test. All statistical analysis was made using SPSS version 10.0 for windows (Statistical Package for Social Science). All data was presented as Mean ± SD (Standard Deviation). P > 0.05 was regarded as nonsignificant, p < 0.05 was regarded as statistically significant and p < 0.01 was taken as highly significant.

**OBSERVATION AND RESULTS:**

**Table 1: Comparison of demographic variables**

|  |  |  |  |
| --- | --- | --- | --- |
| **Groups variables** | **Group L(n=25)****(Levobupivacaine)** | **Group R(n=25)****(Ropivacaine)** | **P value** |
| **Age(in years)** | 30.6±10.0 | 31.1±10.2 | >0.05 |
| **Sex -male** | 21(84%) | 20(80%) | >0.05 |
| **Sex -female** | 4(16%) | 5(20%) | >0.05 |
| **ASA grading -I** | 20(80%) | 21(84%) | >0.05 |
| **ASA grading -II** | 5(20%) | 416%) | >0.05 |
| **Weight(kgs)** | 63.8±6.7 | 65.5±6.6 | >0.05 |
| **Duration of surgery(in min)** | 82±21.03 | 84±18.26 | >0.05 |

Age,weight,duration of surgery - Expressed as mean+/-SD

The groups were comparable with respect to age, sex distribution, ASA physical status, weight and duration of surgery time.

**Table 2: Sensory blockade characteristics (in min)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Group L(n=25)****(Levobupivacaine)** | **Group R(n=25)****(Ropivacaine)** | **P value** |
| **Onset of sensory block(min)** | 3.2±1.5 | 3±1.2 | >0.05 |
| **Height of sensory block at 20mins[T10:T8:T6:T4]** | 6:10:11:3 | 4:12:12:2 | >0.05 |
| **Time to two segment regression(min)** | 60±7.15 | 47±4.14 | <0.001 |

Onset and time to two segment regression expressed as mean+/-SD

 Height of sensory block expressed as ratios of dermatomal levels

Onset of sensory block was 3.2 ± 1.5 min in Group L compared to 3 ± 1.2 min in Group R (p > 0.05). Height of sensory block at 20 min was comparable in both the groups. Time to two segment regression was slower in Group L (60 ± 7.15 min) compared to Group R (47 ± 4.14 min). This difference was statistically highly significant (p < 0.001).s

**Table 3: Motor blockade characteristics (in min)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter**  | **Group L(n=25)****(Levobupivacaine)** | **Group R(n=25)****(Ropivacaine)** | **P value** |
| **Onset of motor block(min)** | 3.6±1.8 | 3.3±1.2 | >0.05 |
| **Partial motor block(Modified Bromage grade 2)** | 6.6±2.2 | 6.4±1.34 | >0.05 |
| **Complete motor block(Modified Bromage grade 3)** | 9.3±3.1 | 9.2±1.9 | >0.05 |
| **Duration of motor block(min)** | 170±16.4 | 140±10.1 | <0.001 |

Expressed as mean+/-SD

The mean time for onset of motor block in Group L was 3.6 ± 1.8 min compared to 3.3 ± 1.2 min in Group R (p > 0.05). Both the groups were comparable in terms of achieving partial and complete motor block (p > 0.05). The mean duration of motor block was longer in Group L, 170 ± 16.4 min when compared to Group R which was 140 ± 10.1 min. This difference was statistically highly significant (p < 0.001).

**Table 4: Visual Analogue Score (VAS**)

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter**  | **Group L(n=25)****(Levobupivacaine)** | **Group R(n=25)****(Ropivacaine)** | **P value** |
| **At the onset of block(0 min)** | 6/10 | 6/10 | >0.05 |
| **15 min** | 0/10 | 0/10 | >0.05 |
| **30 min** | 0/10 | 0/10 | >0.05 |
| **45 min** | 0/10 | 0/10 | >0.05 |
| **60 min** | 0/10 | 0/10 | >0.05 |
| **90 min** | 0/10 | 0/10 | >0.05 |
| **120 min** | 1/10 | 1/10 | >0.05 |
| **150 min** | 1/10 | 3/10 | <0.05 |
| **180min** | 3/10 | 4/10 | >0.05 |
| **210min** | 5/10 | 6/10 | >0.05 |

Both the groups were comparable in terms of VAS score (p >0.05) till 120 min.VAS score is more in group R than group L at 150min which is statistically significant (<0.05).

**Table 5: Comparison of means of heart rates(beats per min)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Time in minutes** | **Group L(n=25)bpm mean±SD** | **Group R(n=25)bpm****mean±SD** | **P value** |
| **Baseline** | 83.10±10.16 | 87.17±11.88 | >0.05 |
| **At the onset of block(0 min)** | 81.33±8.88 | 86.10±12.05 | >0.05 |
| **15 min** | 76.50±5.68 | 76.57±7.10 | >0.05 |
| **30 min** | 78.53±4.66 | 78.00±7.48 | >0.05 |
| **45 min** | 80.36±6.30 | 78.60 ±7.93 | >0.05 |
| **60 min** | 79.88 ±5.37 | 79.07 ±7.91 | >0.05 |
| **90 min** | 82.89 ±5.32 | 81.35 ±7.40 | >0.05 |
| **120 min** | 81.35 ±7.40 | 81.11 ±5.30 | >0.05 |
| **150 min**  | 81.50 ±2.84 | 83.20 ±5.40 | >0.05 |

Expressed as mean+/-SD

Mean baseline heart rate in group L was 83.1 ±10.16 beats per minute (bpm) and that in group R was 87.17 ±11.88 bpm, and they decreased to 71.6 ±9.37 (group L) and 72.4 ±11.14 bpm (group R) after the intrathecal injection 15min later, but the difference between two groups was not statistically significant (p>0.05). Heart rates in both the groups returned to baseline levels after 120 min.

**Table 6: Comparison of means of MAP (mm Hg)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Time in minutes** | **Group L(n=25)mean mm Hg** | **GroupR(n=25)mean mm Hg** | **P value** |
| **Baseline** | 94±9.68 | 97±10.25 | >0.05 |
| **At the onset of block(0 min)** | 94±8.56 | 95±9.71 | >0.05 |
| **15 min** | 86±6.75 | 85±6.14 | >0.05 |
| **30 min** | 90±6.70 | 88±7.57 | >0.05 |
| **45 min** | 90±7.86 | 89±6.53 | >0.05 |
| **60 min** | 92±8.19 | 91±8.58 | >0.05 |
| **90 min** | 95±9.72 | 93±8.69 | >0.05 |
| **120 min** | 94±8.46 | 93±7.82 | >0.05 |
| **150 min** | 96±9.62 | 94±9.73 | >0.05 |

 Expressed as mean +/- SD

The baseline MAP in group L was 94 mmHg and that in group R was 97 mmHg. MAP dropped in both the groups maximally at 15 min after giving the block. Later after 90 min of block the values of MAP returned to baseline in both the groups.The intergroup difference was not statistically significant (p >0.05).

Peripheral oxygen saturation (SpO2) evidenced by pulse oximetry, respiratory rate did not show significant variations in both the groups. There were no ST-T changes or rhythm changes observed on ECG in both the groups.

**Table 7: Comparison of side effects**

|  |  |  |  |
| --- | --- | --- | --- |
| **Side effect**  | **Group L****N (%)** | **Group R****N (%)** | **P value** |
| **Hypotension**  | 2(8) | 3(12) | >0.05 |
| **Bradycardia**  | 1(4) | 0(4) | >0.05 |
| **Nausea**  | 2(8) | 1(4) | >0.05 |
| **Vomiting**  | 0(0) | 0(0) | >0.05 |
| **Shivering**  | 1(4) | 1(4) | >0.05 |
| **Breathlessness**  | 0(0) | 0(0) | >0.05 |
| **Urinary retention** | 0(0) | 0(0) | >0.05 |

Peripheral temperature did drop by 1degree centigrade in both the groups after 15 min of sensory & motor block and remained low throughout the operative period. One patient each developed shivering which subsided within 5 min without any pharmacotherapy.

The incidence of side effects was low and not statistically significant in both the groups (p > 0.05).

**DISCUSSION:**

Spinal anesthesia is a safe and time-tested technique for administering anesthesia for lower abdominal and lower limb surgeries due to its rapid onset and effective sensory and motor blockade. Racemic mixture of hyperbaric bupivacaine (0.5%) is the most frequently used anesthetic agent.Plain bupivacaine is hypobaric when compared with cerebrospinal fluid (CSF). The addition of 8% glucose makes the solution hyperbaric and the resultant block becomes more predictable and safe. [1] To overcome its toxicity to the heart and CNS, S-enantiomers of bupivacaine namely levobupivacaine was introduced in practice. The decreased toxicity of levobupivacaine is attributed to its faster protein binding rate. [1]

Another amide local anesthetic agent Ropivacaine has been introduced for clinical use in 1990. It has a few properties that make it unique. Ropivacaine is less lipophilic than other local anesthetics, such as bupivacaine, and is less likely to penetrate large myelinated motor fibers. It, therefore, selectively acts on the nociceptive A, B, and C fibers over the AB (motor) fibers. Ropivacaine is also manufactured as a pure S (-) enantiomer which has significantly less cardiotoxicity and neurotoxicity. The claimed benefits of these moleculesare reduced cardiac toxicity on overdose and more specific effects on sensory rather than motor fibres. [2, 3]

It has been found that isobaric local anesthetics 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 orthopedic surgeries requiring a blockade below T10. All the patients in our study were given spinal anesthesia in sitting position considering patient comfort and a fact that level of sensory block after intrathecal administration of isobaric local anesthetics is unaffected by the patient position.[7] Levobupivacaine is claimed to be equipotent to racemic bupivacaine and ropivacaine is shown to be 2/3 times as potent as racemic bupivacaine.[8]

In our study, mean time for onset of sensory block was similar in both the groups which was in accordance with results observed by many researchers.[9-11] The lesser lipid solubility of Ropivacaine may cause this drug to penetrate the large myelinated A fibers more slowly than the levobupivacaine.[4]

The highest sensory level attained at 20 min after induction was similar in both the groups that was T4 level. Our study results were in accordance with that of ParpaglioniR et al. and Fasciolo A et al.[12,13]Vanna et al observed maximum sensory level for levobupivacaine was T8.[14] This may be because they used smaller volume of drug than our study.

In our study, the time to two segment regression of sensory block (60 ± 7.15 min) was longer in Group L than in Group R (47 ± 4.14 min). The difference was statistically highly significant (p < 0.001). Our results are in accordance with earlier studies. [8-11]Fasciolo et al[13] and Mehta A et al[8] found that the duration of sensory blockade for Levobupivacaine was 145 ± 28 min and 189.4 ± 42.9 min respectively and that for Ropivacaine was 122.47 ± 25.4 min and 144.32 ± 32.1 min respectively. The difference in results in these studies may be because of different parameters used for calculating duration.

The mean time for onset of motor block, time to achieve partial and complete motor block were similar in both the groups. The duration of motor block in Group L (170 ± 16.4 min) was longer than in Group R (140 ± 10.1 min). The difference was statistically highly significant (p < 0.001) Casati A et al[9] found that the duration of motor block in Levobupivacaine group was 210 ± 63 min while 166 ± 42 min in Ropivacaine group. Cappelleri G et al[10] also found that longer duration of motor block in Group L (148- 201 min) than in Group R (136-154 min). Earlier studies found that blockade lasted significantly longer with Levobupivacaine which might be attributable to a greater intrinsic vasoconstrictor potency of Levobupivacaine.[7,15]

In both the groups, intraoperative hemodynamics and side effects were comparable. In our study, only one patient developed bradycardia which was treated with 0.6 mg inj atropine IV in Group L. In Group L, 2 patients developed hypotension, 2 developed nausea,1 developed shivering while in Group R, 3 patients developed hypotension, 1 patient had nausea and one patient developed shivering.The incidence of side effects was negligible with both the study drugs, which is consistent with earlier studies. [8, 11]

**CONCLUSION:**

Based on present study we conclude that both levobupivacaine (0.5%) and ropivacaine (0.75%) are effective with stable hemodynamics without significant side effects when used intrathecally in equianalgesic doses. However, Ropivacaine has shorter duration of sensory and motor blockade than levobupivacaine. When 2 groups are compared, difference in duration of motor action is statistically and clinically significant.

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