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A COMPARATIVE STUDY OF 0.5% LEVOBUPIVACAINE AND 0.5% ROPIVACAINE IN SPINAL ANAESTHESIA FOR LOWER LIMB SURGERIES

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Keywords:

Subarachnoid block, levobupivacaine, ropivacaine, lower limb orthopaedic surgery, postoperative analgesia

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ABSTRACT

Background and aims: To search for a new amide local anaesthetic agent comparable with bupivacaine but with lower cardiotoxicity, we decided to do this prospective, double blind study with the aim of comparing the anaesthetic safety and the clinical efficacy of isobaric levobupivacaine 0.5% with that of isobaric ropivacaine 0.5% in spinal anaesthesia for lower limb surgeries. **Material and methods:** Seventy adult patients aged 18-65 years scheduled for various lower limb surgeries under spinal anaesthesia were randomly divided into two groups of 35 patients. Group S received levobupivacaine 15mg and Group R received ropivacaine 15mg. Patients were observed for onset, duration of sensory and motor blockade, post-operative analgesia using visual analogue scale, haemodynamic stability and complications if any. **Results:** In comparison, levobupivacaine provided significant earlier onset of sensory and motor block (9.09±1.63 and 8.54±1.36 minutes respectively) than ropivacaine (10.8±2.42 and 10.7±1.5minutes respectively). Duration of motor block and duration of analgesia was statistically longer with levobupivacaine (246±35.83 and 311.57±18.0 minutes respectively) as compared to ropivacaine (215.57±16.7 and 270.86±8.62 minutes respectively). Duration of sensory blockade and haemodynamics were comparable in both the groups ($P > 0.05$). **Conclusion:** In an equal dose (15 mg) levobupivacaine has a faster onset (sensory and motor block) and longer duration (motor block and analgesia) as compared to ropivacaine. This study suggests that ropivacaine may be suitable for short ambulatory surgical procedure. Levobupivacaine may be used as long acting local anaesthetic due to profound duration of motor blocks and analgesia.

INTRODUCTION

Local anaesthesia has been undergoing development for centuries and research continues to provide patients with anaesthetic agents that have superior safety and efficacy. Since 1965 bupivacaine was introduced in the market and was followed by reports of central nervous system (CNS) and cardiovascular system (CVS) toxicity. [1, 2] Identification of treatment resistant CVS toxicity leads to restrictions of its use.

Levobupivacaine the levorotatory isomer of bupivacaine is shown to have a safer pharmacological profile [3] with less cardiac and neurotoxic adverse effects as compared to bupivacaine. Several studies on human and animals support that faster protein binding rate of levobupivacaine reflects a decreased degree of toxicity, hence can be used as an alternative to racemic bupivacaine. Ropivacaine is a pure S(-) enantiomer, unlike bupivacaine, which is a racemate, developed for the purpose of reducing potential toxicity and improving relative sensory and motor block profiles. [4] Both levobupivacaine and ropivacaine have been studied for the spinal anaesthesia. Studies done with the use of ropivacaine for spinal anaesthesia reported that its shorter duration as compared with bupivacaine for this reason could offer anaesthesiologists a good option for ambulatory patients. Minimum effective local anaesthetic dose of levobupivacaine as recommended by an up- and-down sequential design study was 11.7 mg[5]. Hence we decided to conduct this prospective randomised, double blinded study with primary aim of comparing the safety and efficacy of equal dose 15 mg of isobaric levobupivacaine (0.5%) and isobaric ropivacaine (0.5%) for lower limb surgery with secondary aim of comparing the duration of postoperative analgesia.

MATERIALS AND METHODS

In the present study, after obtaining approval from Institutional Ethics Committee and informed written consent, seventy adult patients aged 18-65 years belonging to ASA Grade I-II, scheduled for lower limb surgeries under spinal anaesthesia were compared in a prospective, double blind and randomized manner. Patient's refusal, patients with CNS and CVS disorders, history of allergy to local anaesthetics, local site infection or injury/abrasion, patients on anticoagulant drugs or having blood dyscrasia with altered blood coagulation profile were excluded from our study. Patients were randomly divided into two groups: Group S received isobaric levobupivacaine 0.5%, 3ml (15mg); Group R received isobaric

ropivacaine 0.5%, 3ml (15mg). The randomization was done with sealed, opaque, sequentially numbered envelopes. In the operating room pulse rate, non invasive blood pressure (NIBP), respiratory rates, peripheral oxygen saturation (SpO2) were recorded before giving spinal anaesthesia. After securing intravenous (i.v) line infusion of 15ml/kg of ringer lactate solution was started. Patients were premedicated with inj. glycopyrrolate (0.04mg/kg), inj. ondansetron (0.08-0.1mg/kg) and inj. ranitidine (1.0mg/kg) i.v. Lumbar puncture was performed under all aseptic and antiseptic precautions with 23 gauge quincke spinal needle either in L2-L3 or L3-L4intervertebral space in the midline in sitting position. Correct needle placement was identified by free flow of cerebrospinal fluid and 3ml (15mg) of the study drug was injected over 10 seconds. Patients were immediately placed in supine position, time of injection was noted and the following parameters were evaluated.

Sensory blockade was assessed with the pinprick test. Motor blockage was assessed based on a modified Bromage scale (0= no paralysis, able to flex hips/knees/ankles; 1= able to move knees, unable to move extended legs; 2 = able to flex ankles, unable to flex knees; 3 = unable to move any part of lower limb). These tests were performed every 2 minutes until the start of surgery and maximum height of block attained was recorded 20 min after the spinal anaesthesia. All tests were performed by anaesthesiologist otherwise not involved in the study. The onset time of sensory or motor blockade was defined as the interval between intrathecal administration and time to achieve loss of sensation, or a modified Bromage score of 3, respectively. Intraoperatively vitals were monitored every 2 minutes for first 10 minutes and every 10 minutes till the end of surgery. Quality of intraoperative analgesia was graded as adequate (no sedation /analgesia required), inadequate (need of additional sedation/analgesia), failed (general anaesthesia required).If the block was inadequate, general anaesthesia was supplemented and the case was excluded from the statistics.

The duration of sensory and motor blockade were defined as the interval from intrathecal administration to the point of first two segment regression and the modified Bromage score zero respectively. 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 30 minutes after onset of surgery till the end of surgery and postoperatively. The duration of analgesia was defined as the time from intrathecal injection till the first demand for rescue analgesic when Visual analogue scale (VAS) was ≥ 4. Patient was given inj.Diclofenac sodium 75 mg i.m, as rescue analgesia.

Intraoperative complications and side-effects such bradycardia pulse < 60 per minute which was treated with inj. atropine sulphate 0.6 mg i.v, hypotension defined as >20% decrease in systolic BP from baseline BP (Treated with i.v. fluid, injection mephentermine 5mg i.v. bolus), nausea, vomiting, respiratory distress, irregular rhythm, shivering, pruritus, urinary retention etc. were noted and treated accordingly. parameters and side effect were observed at half an hour interval for two hours following surgery, then every hourly for next six hours then six hourly for the 24 hours after surgery.

All the observations will be recorded and all the results will be analyzed statistically using Microsoft Excel 2007. Sample size calculation was estimated based on a pilot study detecting a difference in duration of motor block after intrathecal administration of ropivacaine when compared to levobupivacaine. After allowing α error to be 0.5, power of study stands out to be 90%. Considering dropouts sample size was kept as 35 in each group.Qualitative data such as age, sex and maximum dermatome achieved were analyzed statistically using chi square test. Quantitative data were presented as mean ± standard deviation and statistically analyzed using the z test. P value < 0.05 was considered as significant.

RESULTS

In the present study 70 patients were randomly enrolled into the study. Table 1 shows demographic profile (age, weight, height and gender) and operative data. It shows that both the groups were comparable in their demographic profiles and duration of surgery. The distribution of types of surgery with number of patients in group S and group R were as shown in table 2. Table 3 shows characteristics of sensory and motor blockade in terms of onset and duration in both the groups. The mean time of onset of sensory and motor block was faster in levobupivacaine group (9.09±1.63 minutes and 8.54±1.36 minutes respectively) than ropivacaine group (10.8±2.42 minutes and 10.7±1.5minutes respectively). The mean duration of sensory blockade was comparable in group S (162.86±6.45 minutes) and in group R (161.29±5.05 minutes), However the mean duration of motor blockade was longer in group S (246 ±35.83minutes) than group R (215.57±16.7 minutes) which was statistically significant (*P*<0.05).The maximum sensory dermatome level attained in group S was T4 and in group R was T6, ranging from T4 -T12 and T6 –L1 respectively, with statistically significant difference as shown in figure 1.

Figure 2 shows changes in mean pulse rate (MPR) and mean arterial pressure (MAP) at different time interval. Patients were haemodynamically stable in both the groups.

The mean duration of analgesia was longer with levobupivacaine group 311.57±18.09 minutes compared to ropivacaine group 270.86±8.62 minutes, as shown in figure 3. One patient in group S developed nausea and vomiting, one patient in group S developed hypotension, and one patient in both the group S and R developed shivering. None of the patient developed dryness of mouth, sedation, respiratory depression, bradycardia and headache in both the groups.

TABLE: 1 DEMOGRAPHIC PROFILE

Variable		Group L	Group R	P-value
Age (in years)	(Mean±SD)	37.6±11.43	38.29±12.24	0.8
Sex	(M:F)	28:7	25:10	0.40
Height (in cm)	(Mean±SD)	164.51±0.08	164.66±0.06	0.93
Duration of surgery (in mins)	(Mean±SD)	125.14±12.64	124.91±12.72	0.93
Quality of block	Adequate	35(100%)	34(97.1%)	
	Inadequate/Failed	0	1(2.9%)	

(Statistical analysis done with z test and for gender with chi square test. $p<0.05$ significant)

TABLE 2: SHOWS CHARACTERISTICS OF SENSORY AND MOTOR BLOCKADE

Characteristics of blockade	Group S (Mean±SD)	Group R (Mean±SD)	P-value	z value
Sensory Blockade				
Onset (in mins)	9.09±1.63	10.8±2.42	0.0005*	-3.4708
Maximum sensory dermatome level attained (Range)	T 4 (T 4 – T 8)	T 6 (T 6 – L 1)	<0.001*	-
Duration (in mins)	162.86±6.45	161.29±5.05	0.26	1.14
Motor Blockade				
Onset (in mins)	8.54±1.36	10.7±1.5	<0.001*	4.76
Duration (in mins)	246±35.83	215.57±16.7	<0.001*	4.55

TABLE 3: SHOWS TYPES OF SURGERIES PERFORMED

Type of surgery	Group S	Group R
Tibia nailing	9	11
Tibia plating	2	1
Tibial nail/plate removal	4	1
Tibia cortical screwing	4	1
Tibial Ex fix	4	2
metatarsal k wiring	1	2
Distal femur plating	3	2
Patellar tension band wiring	2	5
Fibular rush pin	1	2
Tibial Ender's nailing	0	2
Bimalleolar fracture tension band wiring	5	6
Total number of patients patients	35	35

FIGURE 1: SHOWS MAXIMUM SENSORY DERMATOME LEVEL ATTAINED IN BOTH THE GROUPS

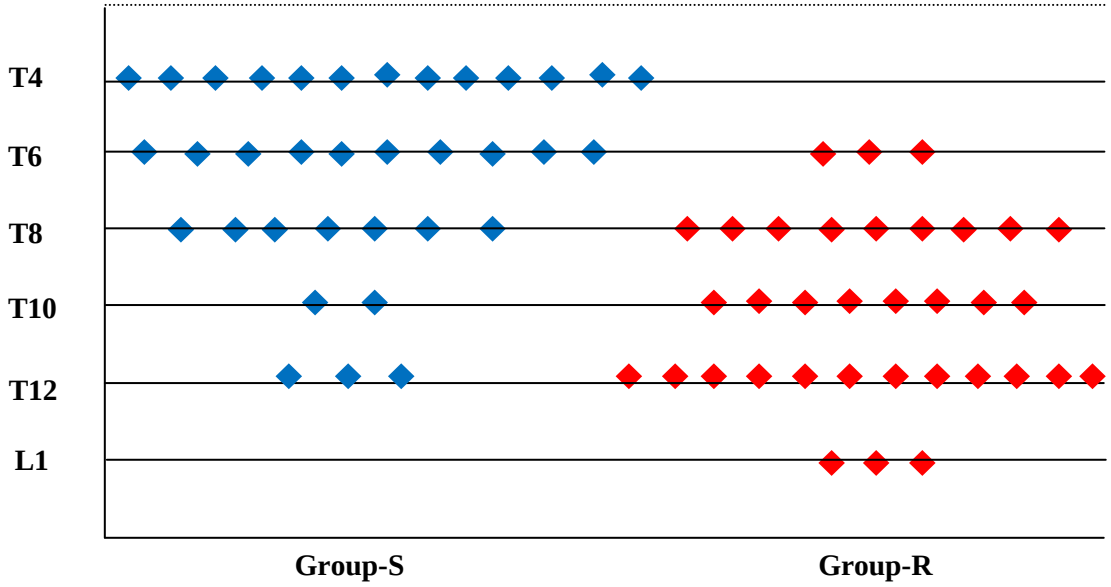
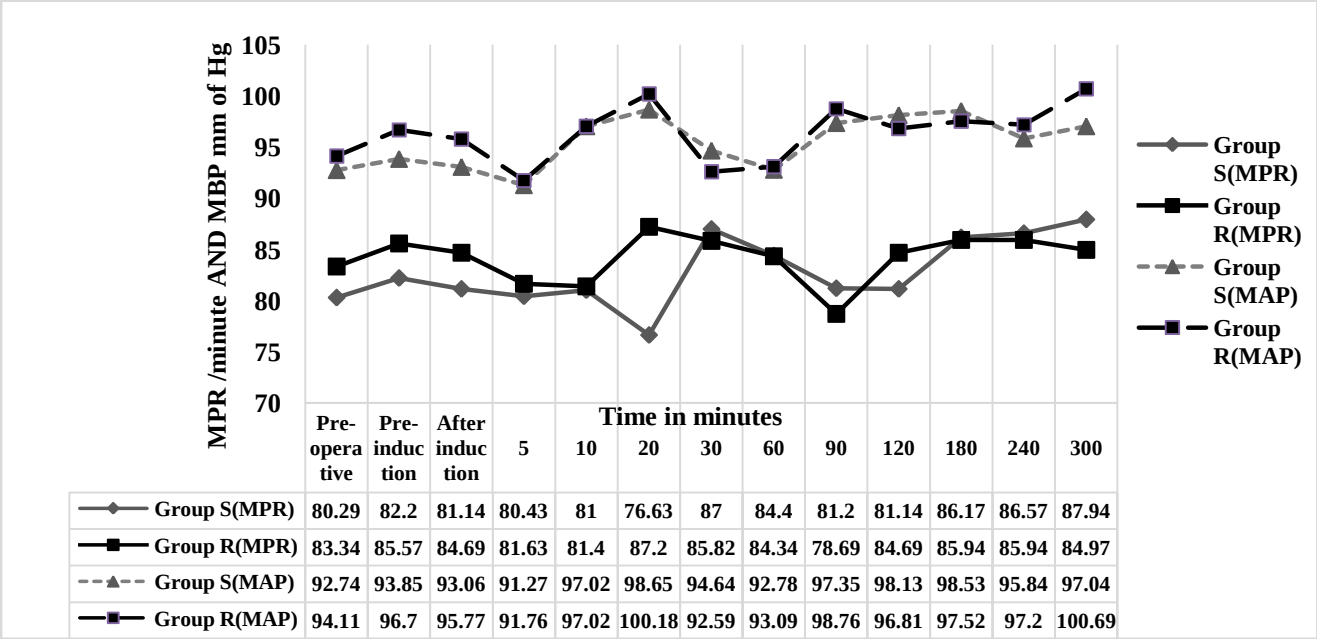
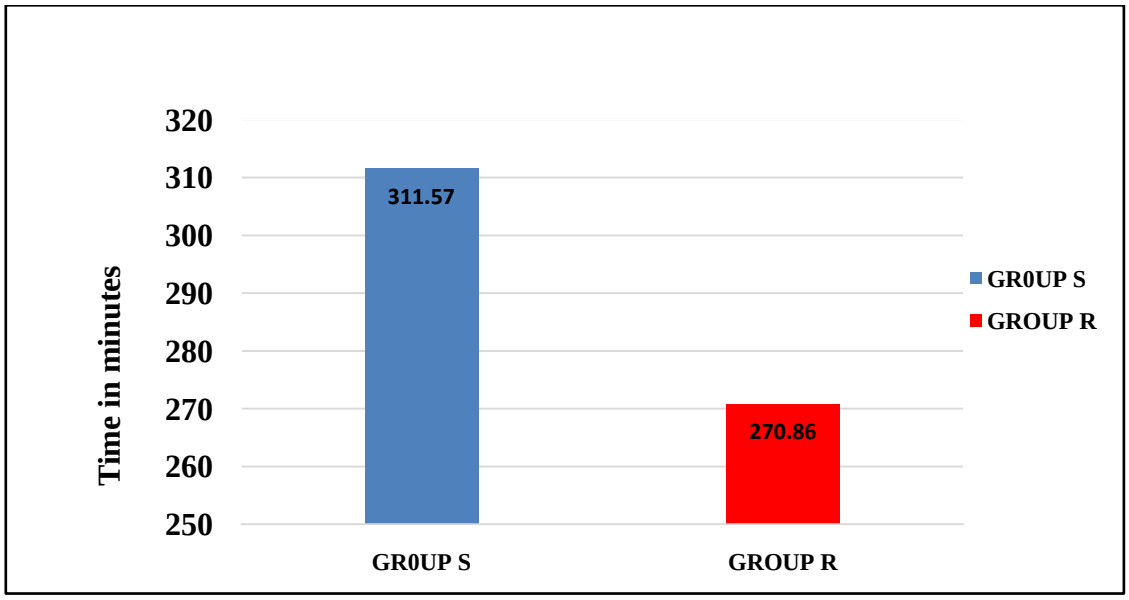


FIGURE 2: SHOWING COMPARISON OF INTRAOPERATIVE VITALS IN BOTH THE GROUPS



	Pre-operative	Pre-induction	After induction	5	10	20	30	60	90	120	180	240	300
	Time in minutes												
Group S(MPR)	80.29	82.2	81.14	80.43	81	76.63	87	84.4	81.2	81.14	86.17	86.57	87.94
Group R(MPR)	83.34	85.57	84.69	81.63	81.4	87.2	85.82	84.34	78.69	84.69	85.94	85.94	84.97
Group S(MAP)	92.74	93.85	93.06	91.27	97.02	98.65	94.64	92.78	97.35	98.13	98.53	95.84	97.04
Group R(MAP)	94.11	96.7	95.77	91.76	97.02	100.18	92.59	93.09	98.76	96.81	97.52	97.2	100.69

FIGURE 3: DURATION OF ANALGESIA



DISCUSSION

Spinal anaesthesia is a very old and popular anaesthetic technique, with a high success rate and a good safety profile. In order to further improve and understand safety issues as well as the clinical use of spinal anaesthesia, new local anaesthetics are being investigated for different applications. An important clinical consideration is the ability of local anaesthetics to cause a differential sensory and motor block. Bupivacaine, with its wide and unpredictable

latency of nerve block and enhanced neuro and cardio toxicity [6, 7] which need replacement with a drug of better anaesthetic and safety profile. In present study we have compared levobupivacaine, the pure S (-) enatiomer of racemic bupivacaine and ropivacaine, another enantiomer and showed both the agents at equal concentration of 0.5% were equally effective local anaesthetics when used for intrathecal administration.

Our study results shows that the mean onset time of sensory block (9.09min) and motor block(8.54min) were significantly faster in levobupivacaine compared to ropivacaine , which is comparable with the certain studies conducted by Mantouvalou M. et al [8], Glaser C et al[9] and Orhan G et al[10] . They have concluded that the onset was faster with levobupivacaine. Due to lesser lipid solubility, ropivacaine may penetrate the large myelinated A fibres more slowly than the more lipid soluble Levobupivacaine.[11] The study revealed that the duration of sensory block was comparable between both the groups. Other studies [8, 12] also reported that there were no statistically significant differences in the mean duration of sensory blockade between the levobupivacaine and ropivacaine groups. But studies [13, 14] which compared hyperbaric levobupivacaine and ropivacaine for orthopaedic and elective surgeries respectively found the shorter duration for resolution with ropivacaine, might be due to hyper baricity of the drug used. The mean duration of motor block was longer with levobupvacaine compared to ropivacaine. Studies have [8, 12, 15] found the blockade lasted significantly longer with levobupivacaine than with ropivacaine. The levobupivacaine have intrinsic vasoconstrictor property [4] and high lipid solubility of which is likely to penetrate the large myelinated motor fibres better compare to ropivacaine, which might be the reason for longer duration of motor blockade in levobupivacaine.

Quality of block was adequate in levobupivacaine group whereas only one patient in ropivacaine group had inadequate block but required only sedation. The duration of analgesia was longer with levobupivacaine compared to ropivacaine in our study. These results confirm that spinal ropivacaine is less potent than levobupivacaine. Another study done by malinovsky et al [11] suggested that the anaesthetic potency ratio between spinal ropivacaine and bupivacaine was 2:3,with lower anaesthetic potency achieved by 15 mg of spinal ropivacaine than by 10 mg of bupivacaine in patients undergoing endoscopic urological surgery. Study on different concentration of ropivacaine has shown that ropivacaine may be effective in providing intrathecal anaesthesia for patients undergoing lower limb surgery. [16]

We observed one patient in group S (2.9%) developed nausea and vomiting and hypotension. Shivering occurred in one patient in both the groups (2.9%). None of the patient reported dryness of mouth, sedation, respiratory depression, bradycardia and headache in both the group. SpO_2 remained stable throughout the observation period in both the groups.

In equal doses (15 mg) levobupivacaine has a faster onset (sensory and motor block) and longer duration (motor block and analgesia) as compared to ropivacaine. This study suggests that ropivacaine may be suitable for short ambulatory surgical procedure. Levobupivacaine may be used as long acting local anaesthetic due to profound duration of motor block and analgesia.

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