Original Research Article

Comparative study to evaluate the clinical efficacy and safety of Isobaric Levobupivacaine Versus Hyperbaric Bupivacaine in lower limb orthopaedic surgeries

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Abstract

Introduction: Spinal anesthesia is a popular technique for lower limb orthopaedic surgeries. Hyperbaric bupivacaine in 8% glucose is often used. Clinically, this manifests as an unpredictable median sensory block height with a large inter-individual spread and is occasionally associated with block failure when the spinal block has not spread high enough for surgery. **Materials and Method**: This is prospective and cross-sectional study conducted at Department of Anesthesia, Tertiary care teaching Hospital over a period of 1 year. Total 60 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 = 30); 12.5 mg 0.5% (2.5 ml) levobupivacaine, for group B (n = 30); 12.5 mg 0.5% (2.5 ml) bupivacaine heavy administered intrathecally within some 10 seconds. **Results:** In both groups, there is a percentage decrease in SBP (mean preoperative SBP 127.93 ± 6.50 mmHg for Group B and 128.70 ± 5.40 mmHg for Group L) and DBP (mean preoperative DBP 78.83 ± 3.42 mmHg for Group B and 80.13 ± 3.05 mmHg for Group L) after 12 minutes of anesthesia (p=0.0157); and at 50, 55, 60, 65 min incidences of hypotension have more in Group B (p=0.0445, p=0.0365, p=0.0090, p=0.0202 respectively). Duration of surgery and duration of anaesthesia were also noted. Mean duration of surgery was 94.0667 ± 26.0714 minutes (range 20-130 min) in Group B versus 95.9667 ± 16.9349 minutes in Group L (range 45-120 min. Mean duration of anaesthesia was 104.6000 ± 24.4111 minutes in Group B (range 30-140 min) versus 101.4333 ± 26.4193minutes in Group L (range 25-130 min). No significant differences between the groups (p=0.6315). **Conclusions:** 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 blockades. Intrathecal administration resulted in higher incidences of bradycardia in bupivacaine group.

Keywords: Isobaric Levobupivacaine, Hyperbaric Bupivacaine, Spinal Anesthesia.

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Introduction

Spinal anesthesia is a popular technique for lower limb orthopaedic surgeries. Hyperbaric bupivacaine in 8% glucose is often used. Plain, or glucose-free, bupivacaine has been frequently referred to as "isobaric" in the literature, even after Blomqvist and Nilsson[1] demonstrated its hypobaricity. More recently, several studies have confirmed that plain bupivacaine is indeed hypobaric in comparison with human CSF[2]. Clinically, this manifests as an unpredictable median sensory block height with a large inter-individual spread and is occasionally associated with block failure when the spinal block has not spread high enough for surgery[3].

Although hyperbaric local anesthetic solutions have a remarkable record of safety, their use is not totally without risk[4]. To prevent unilateral or saddle blocks, patients should move from the lateral or sitting position rapidly and after mobilization of the patients, extension, or early return of the block may be seen. Hyperbaric solutions may cause sudden cardiac arrest after spinal anesthesia because of the extension of the sympathetic block[5]. The use of truly isobaric solutions may prove less sensitive to position issues.

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Hyperbaric solutions may cause hypotension or bradycardia after mobilization, isobaric solutions are favored with respect to their less sensitive to position issues properties[6].

Levobupivacaine is the pure S (-) enantiomer of racemic bupivacaine but is less toxic to the heart and CNS[7]. The plain levobupivacaine has been shown to be truly isobaric. Its use in this setting may there offer special advantages because this property may translate to a more predictable spread.

Spinal anesthesia has progressed greatly since 1885 and is used successfully in many different clinical situations. However, anatomy, choice of local anesthetic, physiologic effects of spinal anesthesia, patient positioning, and the approach to spinal anesthesia must all be considered. The patient should be educated about the possible side effects and complications that can occur from performing a spinal anesthetic to obtain informed consent before the procedure. If these factors are conducive for the patient to receive a spinal anesthetic, care must be taken to prevent complications. Learning how to perform spinal anesthesia is an invaluable skill that all anesthesiologists should have in their armamentarium.

Materials and method

This is prospective and cross-sectional study conducted at Department of Anesthesia in a tertiary care teaching Hospital over a period of 1 year. After institutional ethical approval and informed consent were obtained, 60 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 lactated Ringer's 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 = 30); 12.5 mg 0.5% (2.5 ml) levobupivacaine, for group B (n = 30); 12.5 mg 0.5% (2.5 ml) bupivacaine administered intrathecally within some 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 ∞ 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 20.0.1 and GraphPad Prism version 5. 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± s.d.) of patients was 36.4667 ± 9.6087 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± s.d.) of patients was 38.6667 ± 10.5056 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=0.4008)].

Table 1: Distribution of mean Age in two groups

		Number	Mean	SD	Minimum	Maximum	Median	p-value
AGE	Group-B	30	36.4667	9.6087	22.0000	56.0000	36.0000	0.4008
	Group-L	30	38.6667	10.5056	22.0000	67.0000	38.5000	

Table 2: Distribution of Sex in two groups

SEX	Group-B	Group-L	TOTAL
Female	8	12	20
Row %	40.0	60.0	100.0
Col %	26.7	40.0	33.3
Male	22	18	40
Row %	55.0	45.0	100.0
Col %	73.3	60.0	66.7
TOTAL	30	30	60
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0

Chi-square value: 1.2000; p-value: 0.27332

Association between Sex in two groups was not statistically significant (p=0.27332).

Table 3: Distribution of ASA in two groups

ASA	Group-B	Group-L	TOTAL
1	15	14	29
Row %	51.7	48.3	100.0
Col %	50.0	46.7	48.3
2	15	16	31
Row %	48.4	51.6	100.0
Col %	50.0	53.3	51.7

TOTAL	30	30	60
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0

Chi-square value: 0.0667; p-value: 0.796
Association between ASA in two groups was not statistically significant (p=0.7961).

Table 4: Distribution of mean DUR OF ANES in two groups

	Group	Number	Mean	SD	Minimum	Maximum	Median	p-value
DUR OF ANES	Group-B	30	104.6000	24.4111	30.0000	140.0000	110.0000	0.6315
	Group-L	30	101.4333	26.4193	25.0000	130.0000	111.0000	

Difference of mean Duration of Anesthesia in two groups was not statistically significant (p=0.6315).

Table 5: Distribution of mean DUR OF SURG in two groups

	Group	Number	Mean	SD	Minimum	Maximum	Median	p-value
DUR OF SURG	Group-B	30	94.0667	26.0714	20.0000	130.0000	102.0000	0.7390
	Group-L	30	95.9667	16.9349	45.0000	120.0000	95.0000	

Difference of mean DUR OF SURG in two groups was not statistically significant (p=0.7390).

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

HR	Group	Number	Mean	SD	p-value
HR 6hr	Group-B	30	86.8667	2.6747	0.4221
	Group-L	30	87.6333	4.4527	
HR 12hr	Group-B	30	87.8333	5.0315	0.6017
	Group-L	30	87.2000	4.2863	

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

SBP	Group	Number	Mean	SD	p-value
SBP6hr	Group-B	30	120.8333	6.9979	0.1565
	Group-L	30	123.1667	5.5029	
SBP12hr	Group-B	30	118.9333	8.5215	0.2624
	Group-L	30	121.1667	6.6493	

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

	Group	Number	Mean	SD	p-value
DBP6hr	Group-B	30	80.6667	1.5162	0.1411
	Group-L	30	79.8667	2.5152	
DBP12hr	Group-B	30	81.4000	1.4994	0.2122
	Group-L	30	80.9333	1.3629	

Table 9: Distribution of mean MAP at different time interval in two groups

	Group	Number	Mean	SD	p-value
MAP 6hr	Group-B	30	148.8111	3.4080	0.8506
	Group-L	30	148.9667	2.9444	
MAP 12hr	Group-B	30	144.7556	6.0426	0.0611
	Group-L	30	147.2333	3.7408	

Table 10: Distribution of mean SPO_2 at different time interval in two groups

	Group	Number	Mean	SD	p-value
SPO_2 6hr	Group-B	30	99.5667	.8976	0.8811
	Group-L	30	99.5333	.8193	
SPO_2 12hr	Group-B	30	99.9000	.3051	0.6936
	Group-L	30	99.8667	.3457	

Table 11: Distribution of mean OSB (T_{12}), in minutes, in two groups

	Group	Number	Mean	SD	Minimum	Maximum	Median	p-value
OSB(T12) (min)	Group-B	30	2.1667	.5254	1.1000	3.1000	2.1000	0.0001
	Group-L	30	2.8367	.7098	1.2000	4.2000	2.8500	

Table 12: Distribution of VAS 2nd hr in two groups

	GROUP		
VAS 2nd hr	**Group-B**	**Group-L**	**TOTAL**
0	25	22	47
Row %	53.2	46.8	100.0
Col %	83.3	73.3	78.3

1 Row % Col %	4 44.4 13.3	5 55.6 16.7	9 100.0 15.0
2 Row % Col %	1 50.0 3.3	1 50.0 3.3	2 100.0 3.3
3 Row % Col %	0 0.0 0.0	2 100.0 6.7	2 100.0 3.3
TOTAL Row % Col %	30 50.0 100.0	30 50.0 100.0	60 100.0 100.0

Chi-square value: 2.3026; p-value: 0.5120
Association between VAS 2nd hr in two groups was not statistically significant (p=0.5120).

Table 13: Distribution of VAS 6th hr in two groups

GROUP			
VAS 6th hr	**Group-B**	**Group-L**	**TOTAL**
0 Row % Col %	4 50.0 13.3	4 50.0 13.3	8 100.0 13.3
1 Row % Col %	9 69.2 30.0	4 30.8 13.3	13 100.0 21.7
2 Row % Col %	4 50.0 13.3	4 50.0 13.3	8 100.0 13.3
3 Row % Col %	5 50.0 16.7	5 50.0 16.7	10 100.0 16.7
4 Row % Col %	5 45.5 16.7	6 54.5 20.0	11 100.0 18.3
5 Row % Col %	3 30.0 10.0	7 70.0 23.3	10 100.0 16.7
TOTAL Row % Col %	30 50.0 100.0	30 50.0 100.0	60 100.0 100.0

Chi-square value: 3.6140; p-value: 0.6062
Association between VAS 6th hr in two groups was not statistically significant (p=0.6062).

Discussion

The present study demonstrates that levobupivacaine, the pure S (-)-enantiomer of racaemic 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 surgery.

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[10] and Fattorini *et al.* compared 3 ml[11] 0.5% isobaric bupivacaine with levobupivacaine, 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 anesthesia 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 one hand, there are also studies reporting that motor block develops and disappears faster when hyperbaric

solutions are used[14] on the other hand. 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 orthopedic surgery, they did not find severe hypotension and better cardiovascular stability was provided in the levobupivacaine group, Lovstad *et al*[15]. investigated minimum local anesthetic 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. Gunusen *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 anesthesia 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).

Conclusions

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 first 12 hrs, 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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