ORIGINAL ARTICLE

A COMPARATIVE STUDY OF 0.5% LEVOBUPIVACAINE AND 0.5% RACEMIC BUPIVACAINE IN EPIDURAL ANAESTHESIA FOR LOWER LIMB SURGERIES

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ABSTRACT: AIMS AND OBJECTIVES: To compare the effect of 0.5% levobupivacaine and 0.5% racemic bupivacaine in epidural anaesthesia for lower limb surgeries **METHODS:** A prospective study was conducted with fifty ASA (American society of Anaesthesiologists) grade I and II patients undergoing elective lower-limb surgery under epidural anaesthesia. Exclusion criteria were patients with contraindication for epidural block or history of sensitivity to any studied drug. All patients gave their informed consent. Patients were randomly allocated to the following groups Group LB (n=25) received 20 ml of 0.5% levobupivacaine and Group B (n=25) received 20 ml of 0'5% bupivacaine. The onset, duration of sensory and motor block and side-effects were observed. **RESULTS:** The duration of sensory blockade were similar with Bupivacaine (326.4 ± 23.64 mins) and Levobupivacaine (335.2 ± 18.57 mins) with no statistically significant difference (p=0.1498). The duration of motor blockade were also similar with both Bupivacaine (229.6 ± 24.41) and levobupivacaine (218.4 ± 18.04) with no statistically significant differences (p=0.071). However patients allocated to receive Levobupivacaine showed a higher proportion of lack of motor blockade as determined by the modified Bromage scale and was statistically different (p=0.20). Bradycardia was seen in 2 patients in bupivacaine group and 1 patient in levobupivacaine group. Hypotension was observed in 5 patients of bupivacaine group and 3 patients of levobupivacaine group. **CONCLUSION:** Both drugs showed similar anaesthetic effects but a higher proportion of patients receiving levobupivacaine lacked motor blockade.
KEYWORDS: local anesthetics 0.5% levobupivacaine, 0.5% bupivacaine; lower limb surgeries, epidural anaesthesia.

INTRODUCTION: The use of epidural anaesthesia with local anaesthetics has increased with the development of epidural catheters for intra operative anaesthesia and also post-operative analgesia. Massive local anesthetics absorption although uncommon is a dreadful complication. Their toxic effects may be severe and of difficult reversal.

Currently, bupivacaine is the most common drug used for epidural anesthesia. Although it is generally well tolerated, it shows a cardiac toxicity significantly higher than other local anaesthetics, such as lidocaine. These toxic plasma concentrations of bupivacaine may have toxic manifestations such as seizures, hypotension, apnea and circulatory collapse 5-8 and may result in cardiac arrest and death[1] in case of accidental intravascular injection of the drug or due to rapid absorption into the blood stream.[2]

Bupivacaine is a racemic mixture consisting of equal amounts of the optic isomers levobupivacaine and dextrobupivacaine, also known as S(-) and R(+) enantiomers.[3] Based on demonstrations that racemic bupivacaine cardio toxicity is enantio-selective, that is, more pronounced with dextrobupivacaine, the R(+), levobupivacaine, was developed for clinical use as long lasting local anesthetic agent.[2] Levobupivacaine (LB) shows an extended duration of action, and is frequently used in surgery and obstetrics and postoperative pain management. Pharmacokinetically levobupivacaine has been compared to racemic bupivacaine alone and R+-bupivacaine alone in healthy volunteers after intravenous injection, epidural administration and brachial plexus block. At equal dosing, there are no differences in the pharmacokinetic parameters between these two agents.[1, 4] The duration of the analgesic effect is usually longer with B and LB than with other local anaesthetics; therefore, the need for additional injections of local anaesthesics is reduced. Likewise, they show a more favourable sensory-motor blockade ratio. Seizures were observed with lower doses of bupivacaine in pregnant ewes as compared to non-pregnant animals.[5] In human volunteers, levobupivacaine has shown lower negative inotropic effect as compared to bupivacaine. There were also less changes indicating CNS depression at EEG.[2] Another study has shown lower incidence of hypotension with levobupivacaine as compared to bupivacaine in pregnant patients anesthetized for cesarean section.

Based on these data, this study aimed at comparing characteristics and possible complications of epidural block with bupivacaine or levobupivacaine in anesthesia for elective lower limb surgeries.

METHODOLOGY: This prospective, randomized clinical study was conducted at Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar for a period of 4 months from June 2013 to September 2013. Institutional Ethical committee approval was obtained for the study. Fifty patients scheduled for elective lower limb surgeries were randomly selected, and were divided in two groups of twenty five each i.e. Group LB and group B. The Inclusion criteria for patient selection were age group between 20-60 years, ASA grade I and II. Exclusion criteria were patients with spinal deformities, local skin sepsis, bleeding disorders, psychiatric illness, coma, head injury or intracranial lesions, or increased intracranial pressure.

Patients were screened for routine laboratory investigations like complete blood picture, complete urine examination, blood sugars, serum electrolytes, blood urea and serum creatinine. The procedure was explained to patients and written informed consent was taken from all the patients on the day of surgery.

On arrival in the operation theatre, a peripheral vein was cannulated with 18G intravenous catheter and 500 ml Ringer lactate was infused as preload for all the patients over a period of 15 minutes. Continuous monitoring of ECG, non-invasive arterial pressure and pulse-oximetry were started.

Pre-medication with ondansetron 0.08mg/kg intravenously and glycopyrrolate 0.02mg/kg intravenously was given. After thorough aseptic precautions, L2-L3 or L3-L4 Space was located and using a 18 G Huber point Tuohy needle epidural space identified with loss of resistance technique. Epidural catheter was threaded cranially and fixed. After aspiration to rule out subarachnoid or intravascular placement of the catheter, a test dose of 3 ml of 2% lignocaine

with adrenaline was injected through the catheter and finally the respective drugs were given to the respective groups.

The level of sensory block was tested by loss of response to pinprick. The time taken for the level of blockade to attain T_{10} was taken as onset of sensory block, the same was continued till the sensory block stopped ascending and taken as maximum level. The time of administration of the drug was considered the zero time to assess the duration of blockade.

After administration of the study or control drug and securing the catheter, the patient was placed in supine decubitus, staying in this position for the first 30 min. The metameric level of sensorial blockade was measured using the blunt edge of a needle every 3 mins up to 30 min of drug administration, and then every 30 min until the blockade disappeared. Motor blockade was measured by modified Bromage scale (0 = full movement, 1 = inability to rise extended leg but can bend knee, 2 = inability to bend knee can flex ankle, 3 = no movement) on both limbs every 5 minutes up to 30 minutes. Adverse events such as hypotension, bradycardia, nausea and vomiting and others were noted. Hypotension was defined as baseline systolic blood pressure decrease equal to or above 30%, and was treated with IV fluids and mephenteramine. Bradycardia was defined as HR below 60 bpm and was treated with atropine.

Haemodynamics like pulse rate, mean arterial pressure was recorded with Non-invasive blood pressure monitoring every 5 minutes for first half an hour then every 10 minutes thereafter.

STATISTICAL ANALYSIS: Data is presented as median (range), mean (Standard deviation) as appropriate. The data obtained were subjected to statistical computation with analysis variance t-test using statistical package Epi v2.3 open source and values for $P<0.01$ was considered as significant and $P<0.0001$ as highly significant.

RESULTS:

DEMOGRAPHIC DATA: In the present study, the demographic parameters (age, sex, and weight) were not significantly different.

PARAMETERS	GROUP B	GROUP LB	P VALUE
Age in years	37.64 ± 11.32	36.4 ± 11.56	0.7033
Sex (male)			
Weight in kgs			

Table1: Comparision of demographic profile of both groups

BASELINE CHARACTERISTICS: The baseline characteristics like heart rate, systolic and diastolic blood pressures are statistically not significantly different.

PARAMETERS	GROUP B	GROUP LB	P VALUE
heart rate in bpm	80.26 ± 6.42	76.48 ± 9.24	0.099
Systolic BP In mm of hg	110.42 ± 10.46	114.72 ± 12.24	0.1881
Diastolic BP In mm of hg	80.84 ± 8.26	84.24 ± 7.42	0.1323

Table 2: Comparison of baseline characteristics between the two groups

CHARACTERISTICS OF SENSORY BLOCKADE: The time taken for T10 sensory blockade with bupivacaine (11.32 ± 1.64) and levobupivacaine (12.16 ± 1.376) were not significantly different (p> 0.01). The maximum level of sensory blockade, the time taken for peak sensory blockade and the total duration of sensory blockade were not statistically different.

PARAMETERS	GROUP B	GROUP LB	P VALUE
Time taken for T10 blockade (in mins)	11.32 ± 1.64	12.16 ± 1.376	0.0556
Max. Level of sensory blockade (30 mins) T8 T6 T4	 9 (36%) 9 (36%) 7 (28%)	 5 (20%) 10(40%) 10(40%)	0.25
Time taken for peak sensory blockade (in mins)	24.60 ± 2.545	26.04 ± 2.78	0.062
Duration of sensory Blockade (in mins)	326.4± 23.64	335.2 ± 18.57	0.1498

Table 3: Comparison of sensory blockade between the two groups

CHARACTERISTICS OF MOTOR BLOCKADE: The duration of motor blockade were similar with both Bupivacaine (229.6 ± 24.41) and levobupivacaine (218.4 ± 18.04) with no statistically significant differences (p > 0.05). But the intensity of motor blockade as determined by modified bromage scale is statistically significant. Complete motor block was seen in 16% of bupivacaine group and only 4% of levobupivacaine group.

ADVERSE EFFECTS: Bradycardia was observed in 2 patients in bupivacaine group and 1 patient in levobupivacaine group which were statistically not significant. Hypotension was seen in 5 patients in bupivacaine group and 3 patients in levobupivacaine group which were statistically not significant. Nausea was observed in only 1 patient in levobupivacaine group.

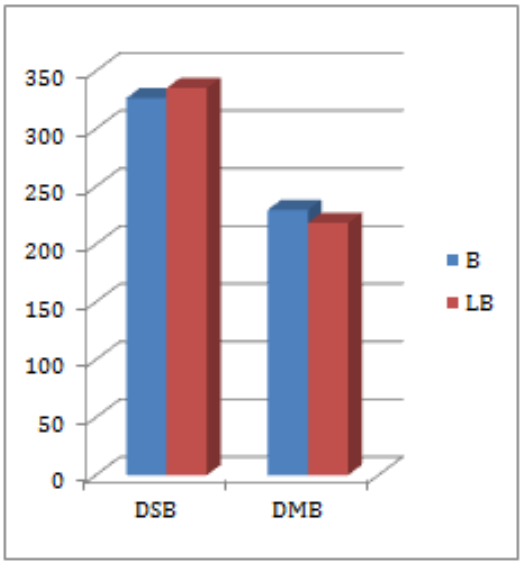
PARAMETERS	GROUP B	GROUP LB	P VALUE
Motor block at 30 mins (modified bromage) Degree 1 Degree 2 Degree 3	 6 (24%) 15(60%) 4 (16%)	 14(56%) 10 (40%) 1 (4%)	
Total duration of motor blockade	229.6 ± 24.41	218.4 ± 18.04	0.071

Table 4: comparison of motor blockade parameters between the two groups

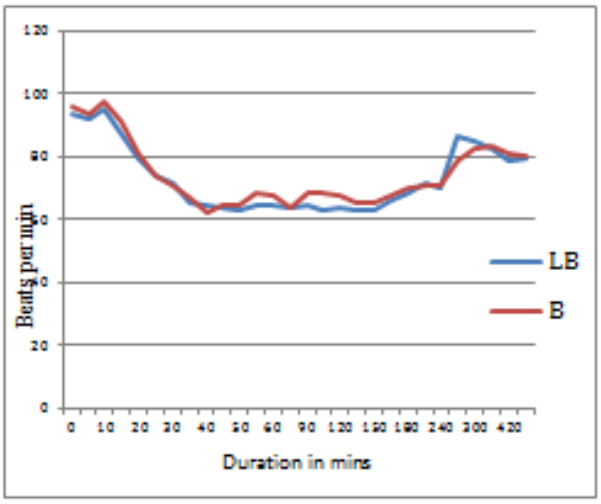
Side effects	Group B	Group LB
Bradycardia	2 (8%)	1 (4%)
Hypotension	5 (20%)	3 (12%)
Nausea and vomiting	–	1 (4%)

Table 5: comparison of adverse effects between the two groups

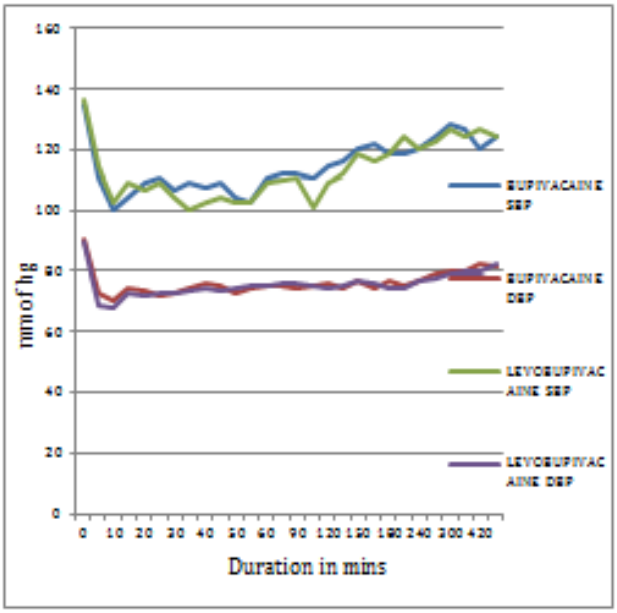
Comparison of duration of sensory and motor blockades between two groups



Comparison of systolic and diastolic blood pressure variations between two groups



Comparison of heart rate variability between the two groups



DISCUSSION: The present study was undertaken to compare the anaesthetic efficacy and the adverse effects of racemic bupivacaine and levobupivacaine.

The duration of sensory blockade was not significantly different with Bupivacaine (326.4 ± 23.64 mins) and Levobupivacaine (335.2 ± 18.57 mins) or LB group.

The duration of motor blockade were also similar with both Bupivacaine (229.6 ± 24.41) and levobupivacaine (218.4 ± 18.04) with no statistically significant differences ($p > 0.05$). However, the proportion of patients with motor blockade as determined by the modified Bromage

scale was statistically different. Patients allocated to receive Levobupivacaine showed a higher proportion of lack of motor blockade, although the duration of block is similar for both drugs. In 2000, Kopacz et al.,[4] in a randomized clinical trial, have evaluated 0.75% levobupivacaine and 0.75% bupivacaine for lower abdominal procedures. Motor block onset (Bromage 2 or 3) was longer for the levobupivacaine group and mean sensory block recovery time was 45 minutes longer for the levobupivacaine group.[3]

Lacassie et al. have shown that levobupivacaine is less potent as compared to bupivacaine (levobupivacaine / bupivacaine ratio 0.87).[6] A different study confirms these results, since there has been less intense motor block after epidural levobupivacaine and ropivacaine as compared to bupivacaine.

Bradycardia was seen in 2 patients in bupivacaine group and 1 patient in levobupivacaine group and was treated with inj. Atropine 0.6mg bolus. Hypotension was observed in 5 patients of bupivacaine group and 3 patients of levobupivacaine group and was treated with I.V. Fluids and Inj Mephentermine 6 mg bolus. In 1999, Bader et al. 0.5% racemic bupivacaine and 0.5% levobupivacaine in epidural blocks of patients submitted to elective cesarean section. They have observed similar effectiveness between drugs, with just a trend to faster blockade and higher incidence of hypotension in levobupivacaine group.

CONCLUSION: The present study demonstrated that Levobupivacaine, the pure S (-) enantiomer of racemic bupivacaine, is an effective local anaesthetic drug for epidural anaesthesia, is effective in surgery of the lower limbs and is comparable to racemic bupivacaine. The smaller rate of motor blockade and smaller duration of motor blockade show an interesting and potentially useful difference.

The study failed to demonstrate a better safety profile for Levobupivacaine compared to bupivacaine, although it is possible that significant differences could be obtained in larger sample size.

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