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Comparative Clinical Study Between Racemic Bupivacaine and Levobupivacaine in Supraclavicular Brachial Plexus Block

KEYWORDS: Bupivacaine, Levobupivacaine, Supraclavicular brachial plexus block.

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ABSTRACT *Background & Aims: Levobupivacaine, the pure s-enantiomer of bupivacaine is newer local anaesthetic with similar anaesthetic qualities of racemic but reduced toxic profile.*

We conducted the present study to evaluate and compare the differences in onset, duration and the quality of sensory and motor blockade of racemic bupivacaine versus levobupivacaine in supraclavicular brachial plexus block.

Methods: After clearance from institutional ethical committee, a double blind prospective randomized study carried out on 60 American Society of Anaesthesiologists (ASA) physical statuses I and II patients of either sex, aged 18 -60 years undergoing upper limb surgeries under supraclavicular block.

The patients were randomly assigned to either Group B: Bupivacaine 0.5% (0.4ml/kg) or Group L: Levobupivacaine 0.5% (o.4ml/kg) of 30 each, using a computer generated random number list.

We used Statistical Package of Social Science (SPSS) software, Analysis Of Variance (ANOVA) for comparing the age, weight, Chi- square for gender, ASA physical status and incidences of complication in either groups. Fisher test was applied for analysing the difference in onset, duration and quality of block.

Results: Onset of both sensory and motor block was found to be early with levobupivacaine with a statistically high significance. The duration of sensory, motor block and analgesia was prolonged with levobupivacaine. Complete failure or toxicity was reported in neither group.

Conclusions: Levobupivacaine is a newer, safer and longer acting local anaesthetic with rapid onset and block quality similar to the racemic bupivacaine. We recommend its use where prolonged duration of analgesia is considered.

INTRODUCTION:

Peripheral nerve block such as brachial plexus block is an indispensible technique commonly employed for upper limb surgeries.[1] Racemic bupivacaine is most commonly used local anaesthetic as it provides longer duration of action & favourable ratio of sensory to motor neural block.[1,2] However, the dextroenantiomer in the racemic mixture of bupivacaine results in cardiac & central nervous system toxicity.[3, 4, 5]. Levobupivacaine the s-enantiomer of bupivacaine is a recently introduced local anaesthetic that posess similar anaesthetic qualities as racemic bupivacaine.[6, 7, 8] In addition studies conducted on levobupivacaine reveal that this enantiomer has significantly less cardiac &central nervous system toxic effect than racemic bupivacaine.[9-12] Levobupivacaine has been shown to be safe &effective for central neuroaxial [13, 14]& brachial plexus block.[15-18] In brachial plexus block, where large volume of local anaesthetic are used, the use of levobupivacaine seems promising.[7, 15-18]

The primary outcomes to be studied were onset, duration &quality of sensory & motor blockade of two drugs. The secondary outcomes were to study & compare the toxicity & complication rate of both drugs.

METHODS:

After ethical committee approval & written informed consent, a double blind randomized prospective clinical study was carried out on 60 American society of anaesthesiologist (ASA) physical status I & II patients of either sex , aged 18- 60 yrs, undergoing upper limb surgeries under supraclavicular block. The sample size calculated was of 60 patients on the basis of previous studies. After power analysis, it was suggested that 28 patients in each group were sufficient to compare the primary outcomes of our study. We included 30 patients in each group considering the possibility of drop outs.

The patients were randomly assigned to either Group B: Bupivacaine 0.5% (0.4ml/kg) or Group L: Levobupivacaine 0.5% (o.4ml/kg) of 30 each, using a computer generated random number list.

Exclusion criteria were patient with physical status ASAIII-IV, history of allergy to local anaesthetic, central or peripheral neuropathies, coagulopahties, skin lesion at the site of blockade, upper limb surgeries requiring bone graft, liver, kidney, neurological disease & patient refusal. On arrival to operation theatre, patient's baseline pulse rate, blood pressure & electrocardiogram were recorded. A 20G intravenous line was established & infusion started with ringer lactate solution. Hemodynamic variables were measured on arrival to the OT & every 5 min thereafter till the end of surgery. The patient received ultrasound guided brachial plexus block through supraclavicular approach by an experienced anaesthesiologist other than the one doing intra/postoperative assessment. Both were blinded to the treatment groups. After negative aspiration, 0.4 ml/kg of the study drug was injected over 1 min with repeat aspiration every 5ml. Assessment of the resulting block & hemodynamic variable (Heart Rate - HR, Blood Pressure - BP, Saturation - SPO2, Electrocardiogram - ECG) were recorded as described below. After 30 mins, if the block turns out to be adequate, surgery was allowed to continue. Complete failure of the block was considered when none of the nerve segments were blocked (median, radial,

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ulnar & musculocutaneous nerve) & general anaesthesia was given to these patients. Patients with complete failure of the block or unsatisfactory block (inadequate analgesia, relaxation & pt. requiring either IV sedation or GA) were excluded from our study. Only satisfactory block (complete block of all nerve segments) was considered. Assessment was carried out at 2, 5, 10, 15, 20, 25, 30 minutes until 5hrs &hourly there after the block had completely worn off, with time 0 –min being the time of completion of injection. Sensory block was measured as loss of pinprick sensation using blunt end of 27G hypodermic needle. Dermatomes C5to T1 was assessed. Onset time was the time to first loss of pinprick sensation in any dermatome. Duration of sensory block was graded as Grade 0 - sharp pin felt, Grade 1- analgesia, dull sensation felt, Grade 2 - anaesthesia, no sensation felt. Motor block was recorded using a three point scale. Onset time was the time to first loss of motor power (i.e. grade 1). Duration of block was the time from onset to complete recovery. Motor block graded as Grade 0 - no paralysis, Grade 1 - difficulty in raising the shoulder & weakness of the hand and Grade 2 - inability to move the upper limb.

Overall assessment of the quality of the block was made on a three point scale as follows; Grade 0 - Complete failure, Grade 1 -Unsatisfactory block (inadequate analgesia, inadequate relaxation or patient requires general anaesthesia), Grade 2 – Satisfactory block.

For statistical analysis, complete failure & unsatisfactory block (gr. 0, 1) were considered together as failure & compared with success (satisfactory block).

Duration of the surgery was noted. Patients were assessed for duration of analgesia as per numeric rating scale (NRS) from 0 -10 (0- no pain & 10 – worst pain).The NRS was recorded postoperatively & every 60 min till the score of 5. The rescue analgesia was given in the form of injection diclofenac sodium (1.5mg/kg) intravenous in a drip at the numeric rating scale of 5 & time of administration was noted. Patient's hemodynamics was monitored throughout the intra &postoperative period (pulse, respiration, BP, ECG, SPO2). All patients were observed for any side effect & complication like CNS toxicity, cardiac arrhythmias, pneumothorax, hematoma & post block neuropathy in the intra & postoperative period.

The data was entered & analysed by computer Software Statistical Package of Social Science (SPSS version 15.0) for windows. Mean difference between the 2 groups regarding age and weight were calculated using Analysis of Variance (ANOVA). Chi-square test was used to analyse difference between gender, ASA physical status & incidence of complications. Unpaired t –test was applied for assessment of onset & duration of motor & sensory block. Fisher test was applied for assessment of quality of block. Results were considered significant if p <0.05 & highly significant if <0.001

RESULT-

Sixty patients fulfilling the inclusion criteria were randomly assigned to one of the two groups. Two patients from group L & three patients from group B were excluded from study as they had to be given general anaesthesia for inadequate block leaving with group L 28 & group B 27 patients. Both the groups were comparable (p value >0.001) in terms of age, gender, weight & physical status (Table 1). There was no significant difference between both the groups in heart rate & arterial pressure (fig 1&2) ECG & SPO2 were maintained throughout the surgery in both groups .

Onset of sensory as well as motor block was faster in group L (sensory 6.13+0.34 min, motor 5.05+0.29 min) than in group B (sensory 7.59+1.43 min , motor 5.99+0.49min) with p value <0.001, making it statistically significant. Duration of sensory block was 1036.57+93.7 minutes in group L as compared with 871.48+174.33 minutes in group B and the difference was statistically significant (P<0.001). The duration of motor block was 1049.46+95.02 minutes in group L as compared with 902.37+181.46 minutes in group B. Again duration of motor block was significantly longer in group L, with P value<0.001(table 2). Duration of analgesia was also significantly prolonged in group L (1048.32+97.24minutes) as compared to group B (900.41+177.74minutes) with p value <0.0001(table 2).

We observed similar quality of the block in both the groups which was statistically comparable (table3). Grade 2 (complete paralysis) was the most grade reached. We did not encounter a single patient of complete failure of block in either group as all blocks were given with the aid of USG (table 3). There were 2 unsatisfactory blocks in group L & 3 in group B. General Anaesthesia was given in these cases & they were excluded from the study. The differences between two groups were comparable (table3). No complication or adverse effects observ ed.

DISCUSSION:

We studied & compared levobupivacaine & racemic bupivacaine in patient undergoing upper limb surgeries under supraclavicular block. From our study it can be elicited that levobupivacaine provides early onset & prolonged duration of sensory block & motor block while quality of block is similar to racemic bupivacaine.

Brachial plexus block is close to the ideal anaesthesia technique for upper limb surgeries, for patients as it provides good intraoperative anaesthesia & postoperative analgesia. [1] The quest for ideal local anaesthetic devoid of any toxicity is still on. Racemic bupivacaine is the most commonly used local anaesthetic agent for brachial plexus block.[2] However, the reports of fatalities through cardiovascular (CVS)[3] & central nervous system (CNS)[3, 12] toxic effects were noted after accidental intravascular administration racemic bupivacaine which were attributed to the dextro (R+) enatiomer.[3, 8] Thereafter levobupivacaine, the pure s-enantiomer of bupivacaine emerged as safer alternative with similar clinical profile as racemic one.[9, 10] Several studies have been demonstrated & explained the mechanism of toxicity of bupivacaine.[4, 5, 19-21]

Bupivacaine has been shown to have indirect depression of cardiac conduction (AV conduction, QRS complex) & contractility by blocking mainly inactivated state of sodium channels. [19-21] Studies demonstrate dextro (R+) enantiomer has 2.4 times higher affinity for cardiac sodium channels & dissociates from it slowly as compared to levo (S+) enantiomer.[20-21] The estimated mean(SD) fatal dose through arrhythmia after intravenous administration of levobupivacaine in sheep 277(51) mg, larger than racemic one 156 (31) mg.[20]

The convulsive dose in sheep for levobupivacaine 103 (18) mg, larger than bupivacaine 85 (11) mg.[4, 12] Levobupivacaine cause less rapid blockade of the cell firing in nucleus tractus solitaries(NTS)[4] which explains its lower CNS toxicity compared to racemic one. Also one more factor for difference in toxicity between two enantiomer can be explained on the basis of their pharmacokinetics. The protein binding of levo is >97% as against 95% in case of bupivacaine. That means <3% of levo is free in plasma to have action on other tissues causing undesired toxic effect. [10-12]

Numerous studies have been carried out to evaluate the efficiency of the levobupivacaine as anaesthetic agent in respect to onset time, duration & analgesic qualities in brachial plexus block. [15-18]

The results of our study are in concordance with the result of Cox & colleague who also found early onset & prolonged duration of sensory block & prolonged duration of analgesia in patient receiving levobupivacaine for supraclavicular brachial plexus block.[15] However, we differ from Cox et al in onset & duration of motor block. We found early onset & also prolonged duration of motor block in group L which although

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statistically significant may not be clinically significant.

Levobupivacaine has vasoconstrictor activity as demonstrated in Aps Reynolds study which could explain the prolonged duration of action. [22] However, this is just a postulation. The longer duration of sensory block with levobupivacaine provides prolonged postoperative analgesia. Nonetheless in surgeries where early return of motor activity is desired, it may not suit the demand.

In Cox et al study, one patient developed CVS &CNS toxicity after accidental intravascular administration; another complained of pleuritic chest pain. However, none of the patients in our study developed toxicity as we gave USG guided block as against in study by Cox et al who used peripheral nerve stimulator. We did not encounter complete failure of block again due to the aid of USG which is shown to improve success rate & also reduce complication.

In the study by Cline et al duration of analgesia with levobupivacaine was less (833 minutes as against 1048.32minutes in our study). This difference could be attributed to difference in the technique, as brachial plexus block in Cline et al study was given by transaxillary approach.[18] In our study, there was no significant difference between groups in respect to maximum grade or failure rate of the motor block similar to Cox et al.

The limitation of the present study is the small number of cases. Though our results tends to suggest that levobupivacaine is longer acting local anaesthetic with early onset and prolonged effect, to obtain a definite result , study with enrolment of larger number of patients is required. Moreover, we included only patients with ASA I & II physical status only, a study of high risk patients to justify the safety of levobupivacaine has to be carried out.

CONCLUSION:

Levobupivacaine is a long acting local anaesthetic with rapid onset & a clinical profile closely resembling bupivacaine so we recommend it in upper limb surgeries demanding prolonged duration of analgesia. Safe outcome from anaesthesia is an important goal for any anaesthesiologist so the reduced toxic potential of this drug should be considered for regional anaesthesia wherever larger volume is required.

TABEL1: Patient's characteristics

Parameters	Group B	Group L
Age (Years)	35.7± 10.81	35.21±9.92
Weight (kg)	60.52±5.2	61.36±5.2
Gender (M/F)	19/8	17/11
ASA (I/II)	22/5	23/5

Table 2: Sensory and Motor Block Onset Time, Block and Analgesia Duration

	Group B (Mean±SD)	Group L(Mean ± SD)	P Value
Onset time of sensory block (min)	7.59±1.43	6.13±0.34	0.001
Onset time of motor block(min)	5.99±0.49	5.05±0.29	0.001
Duration of sensory block(min)	871.48±174.33	1036.57±93.7	0.001
Duration of motor block(min)	902.37±181.46	1049.46±95.02	0.001
Duration of analgesia(min)	900.41±177.74	1048.32±97.24	0.001

Table 3: Quality of Block

Grade	Group B, N (%)	Group L, N (%)	P Value
Satisfactory block(2)	27(90%)	28(93.3%)	0.667
Unsatisfactory block(1)	3(10%)	2(6.7%)	0.996
Complete failure(0)	0	0	NS

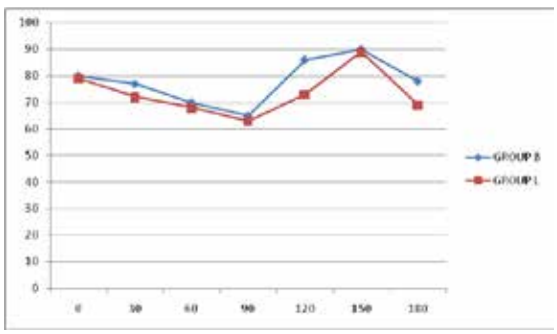

Figure 1: Comparison of pulse rate in both groups

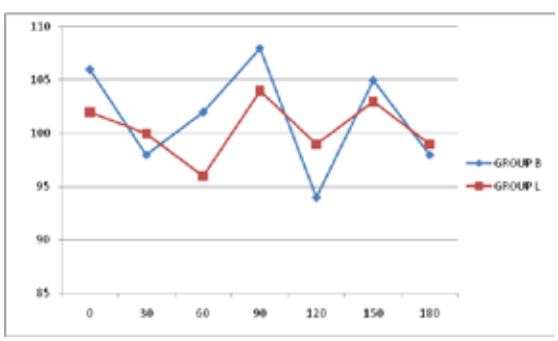

Figure 2: Comparison of mean arterial pressure

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