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"Comparison of Motor and Hemodynamic Profile of Epidural Levobupivacaine 0.5% And 0.5% Racemic Mixture Bupivacaine in Patients Coming For Elective below Umbilical Surgery"

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ABSTRACT:

This study was performed to compare the motor and hemodynamic profile of 0.5% racemic Bupivacaine and 0.5% Levobupivacaine, in patients undergoing below umblical surgery.surgery.
Methodology 56 patients, ASA grade 1 and 2, were randomised to receive an epidural injection of study drug (17 ml 0.5% racemic Bupivacaine in group R and 17 ml of 0.5% Levobupivacaine in group L. **(Group R VS Group L)** Even though, the onset of motor block was comparable in both the groups, Group L showed earlier onset of motor block at 5 min after zero time. (P value 0.002).The regression of motor block was faster in group L (p value 0.042).The time to obtain maximum level of motor blockade was found to be faster in Levobupivacaine group.(p value of 0.043).The number of patient obtaining MBS score of 3 was 62.5% in racemic Bupivacaine group and 37.5% in levobupivacaine group. The grade of motor block showed that, the levobupivacaine group had lesser grade than that of racemic group (p value of 0.016). The duration of motor block was similar in both the groups. The haemodynamic profile MAP, SpO_2 and HR were similar. **Conclusion:**Both 0.5% levobupivacaine and 0.5% bupivacaine produced effective epidural anaesthesia and their effects were clinically indistinguishable. Levobupivacaine produces less denser and shorter duration of motor block hence they can be used for labor analagesia, postop epidural analgesia and for ambulatory surgery.

KEY WORDS: Epidural Anaesthesia, Levobupivacaine, Racemic mixture Bupivacaine, Motor and Hemodynamic Profile, Isomers in Local anaesthesia drugs, Cardiotoxicity and Neurotoxicity in Local anaesthesia use.

1. INTRODUCTION

Over the past two decades, regional anaesthesia techniques have undergone significant modifications with the introduction of safer local anaesthetics. Bupivacaine, a commonly used local anesthetic, exists as a racemic mixture (50:50) of its two enantiomers: levobupivacaine (S-enantiomer) and dextrobupivacaine (R-enantiomer). Adverse reactions related to inadvertent intravascular injection or intravenous regional anesthesias have been associated with the R-enantiomer of bupivacaine, leading to increased mortality. To mitigate this risk, incremental low doses of local anaesthetics, test doses, and continuous infusions of low concentrations have been employed, particularly in obstetrics and postoperative pain relief. However, accidental intravascular injection remains a concern.[1,2] The levorotatory isomers were shown to have a safer pharmacological profile[3,4] with less cardiac and neurotoxic adverse effects.[5,6] The decreased toxicity of levobupivacaine is attributed to its faster protein binding rate.[7] Clinical trials have also reported the equivalent efficacy of levobupivacaine and the racemate [8-10] With equivalent clinical utility and an enhanced safety profile compared with bupivacaine, levobupivacaine could be an alternative to bupivacaine as a long-acting local anesthetic. In this study we have compared the motor and hemodynamic profile of levobupivacaine 0.5% and racemic mixture of bupivacaine 0.5 used for epidural anaesthesia in below umbilical surgery.

THE OBJECTIVES:

Primary Objectives:

1. Onset of motor block
2. Regression of motor block
3. Duration of motor block
4. Grade of Motor block as per MBS
5. Number of patients who achieved MBS of 3
6. Time to achieve Maximum Motor block as per MBS

Secondary Objectives:

1. Intraoperative hemodynamic profile

MATERIALS AND METHODS

After obtaining institutional ethical committee's approval and written informed consent, 56 patients belonging to both sexes, who were scheduled to undergo below umbilical surgery with epidural anaesthesia, were included.

Inclusion Criteria

1. Patient between 15 and 65 years of age
2. ASA grade 1 and 2
3. Patient with no history of allergy to amide local anaesthetics
4. No absolute or relative contraindication for regional anaesthesia.

Exclusion criteria

1. Patient younger than 15 years of age and more than 65 years of age.
2. Patient known to have hypersensitivity reaction to amide local anaesthetics
3. Patients with history of psychiatric disorders
4. ASA 3, 4 and 5.
5. Patients having absolute or relative contraindication for regional anesthesia

Patients were randomized into two groups group L and group R, by computer generated random numbers. The study was blinded (Patient and the anaesthesia provider were blinded of the groups.)

Group R- Received 17 ml 0.5% Racemic Bupivacaine

Group L- Received 17 ml 0.5% Levobupivacaine
All the patients were visited on the pre-operative day and informed consent was obtained. The sequence of events in the theatre was explained.
After confirming adequate starvation, before induction of epidural anaesthesia, patient was preloaded with 500 ml of Ringer Lactate solution. After getting the patient on table, NIBP was attached. Continuous ECG monitoring and oxygen saturation were done.
Patient was put on left lateral decubitus position L3-L4 inter-spinous space was identified. Three ml of 2% lignocaine plain was used to infiltrate the skin and subcutaneous tissue. Epidural space was identified using 18G Tuohy needle, by loss of resistance to air technique. After confirming negative aspiration for blood or CSF, 3 ml of 2% Lignocaine 1 in 2, 00,000 adrenaline was used as test dose. Two minutes after the test dose, once subarachnoid or intravascular injection was excluded, the double blinded study drug was given.
Group R received 17 ml 0.5% racemic mixture Bupivacaine over 5 min period. (6ml 1 min wait, 6ml 1 min wait and 5ml)
Group L received 17 ml 0.5% Levobupivacaine over 5 min period. (6ml 1 min wait, 6ml 1 min wait and 5ml)
The end of injection of study drug is termed time zero for the purposes of subsequent assessment.
A 20 G catheter is advanced 5 cm into the epidural space and the needle was removed. The patient was made supine.
The patients PR, BP and SpO_2 were monitored. All the patients were put on face mask with O_2 at 4l/min flow. The surgical procedure was started 30 min after injecting study drug in to epidural space. A fall in MAP more than 20% was managed with 6mg Ephedrine. A fall in HR less than 50 bpm was managed with Atropine 0.6mg.
Onset of surgical sensory block was defined as time taken to achieve T10 dermatome level. After surgery is started, whenever it is deemed necessary 7ml more of study drug was given. (Double blinded). Whenever patient demanded for analgesia post operatively 100mg Tramadol diluted to 10ml with distilled water was injected epidurally, and time was noted.
Onset of motor block was defined as when patient has modified Bromage score of 2. Duration of motor block is defined as that time for which the modified score remains at least 2. Complete regression was defined as motor block with modified Bromage score of zero.
Modified Bromage scale scored as:
Zero, no paralysis, full flexion of hips, knees, and ankles;
One, inability to raise extended leg, able to move knees;
Two, inability to flex knees, able to flex ankles;
Or Three, inability to move any portion of the lower limb.
The Modified Bromage scale is a qualitative method of assessing motor block and might not reveal quantitative differences in motor block between the two drugs at the doses given.
All patients received Midazolam 0.05 mg/kg body weight for intra-operative sedation. All patients were allowed to breathe spontaneously throughout the surgical procedure In our study, patients in whom dural puncture was encountered were converted to GA and excluded from the study.

2. STATISTICAL METHOD APPLIED

Statistical analysis was done using SPSS version 29.0 Descriptive statistics was done by calculating mean, standard deviation, range and proportion appropriately. The inferential statistics (test of significance) was done using unpaired t-test and chi-square test.
p-value: it is the probability rate at 0.05 level of significance for corresponding degree

of freedom.
p>0.05 is not significant
p<0.05 is significant
p<0.01 is highly significant

3. RESULTS

The demographic profile in both group such as sex, age, educational qualification, ASA grading and BMI showed no significant difference.

MOTOR BLOCK

	Mean	SD	Median	Mode	P-value
Group L (Levobupivacaine)	0.89	0.49	1	1	0.002
Group R (Bupivacaine)	0.46	0.5	0	0	

P value: 0.002

P value ‹ 0.05 is significant

TABLE 1: MOTOR ONSET AT 5 MINUTES TIME INTERVAL

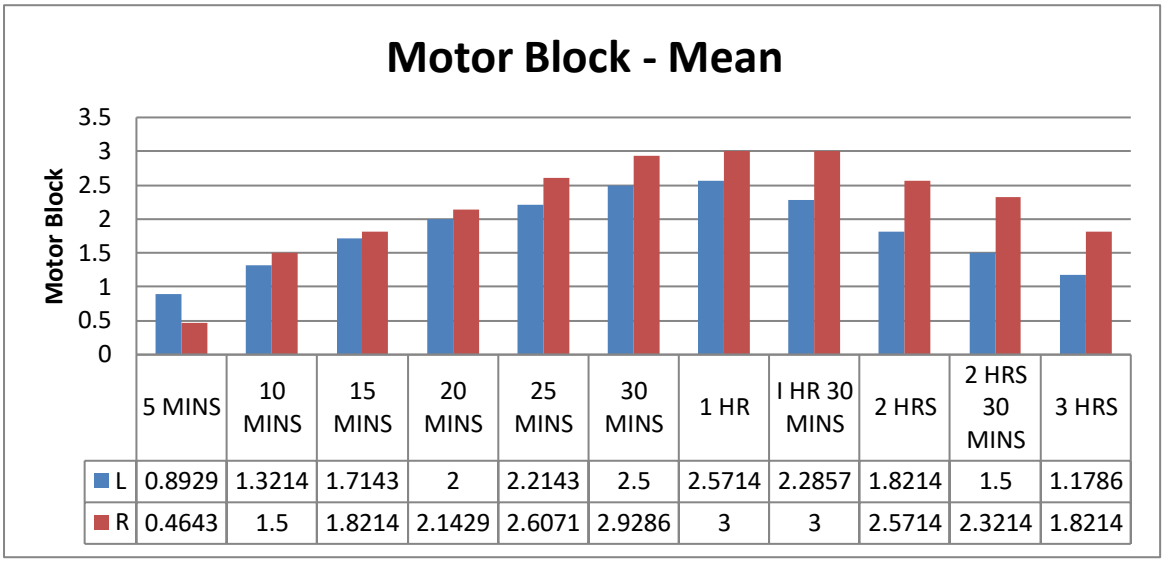
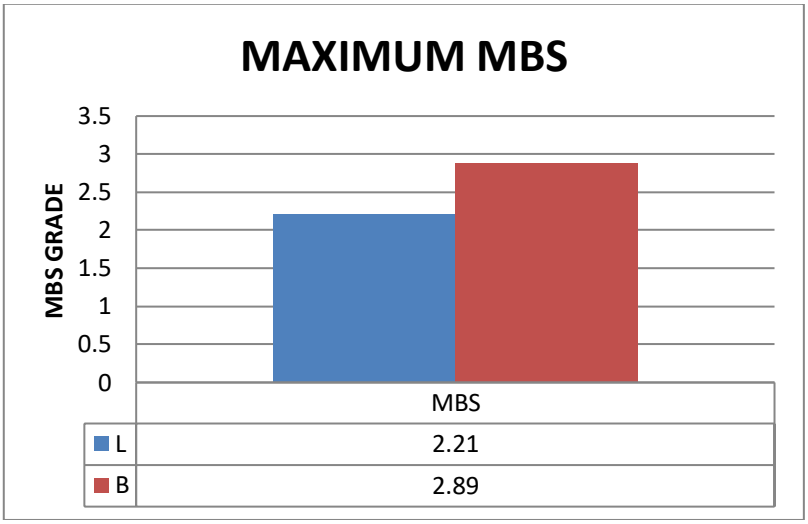


CHART 1: MOTOR BLOCK OVER TIME FROM 5 MINS TO 3 HOURS



P value: 0.016 P value › 0.05 is not significant

CHART 3: GRADE OF MOTOR BLOCK AS PER MBS

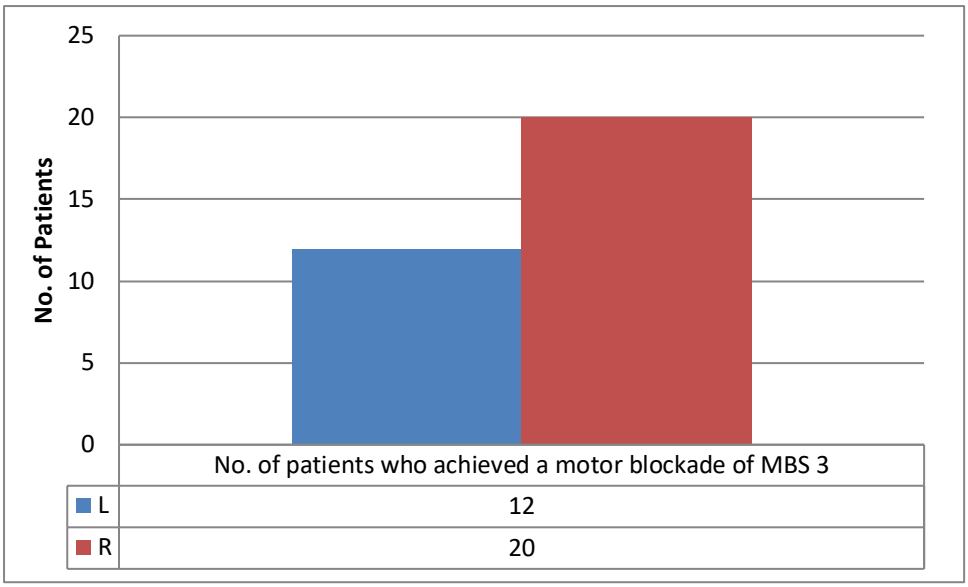
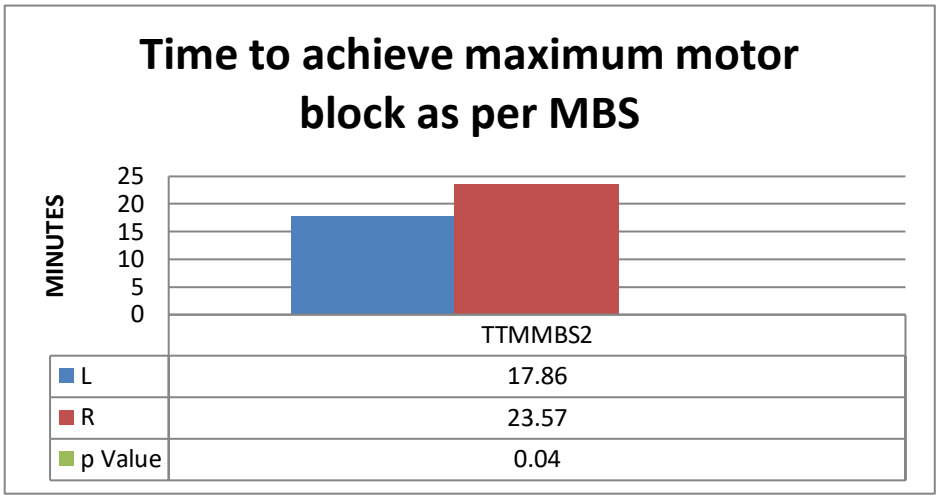
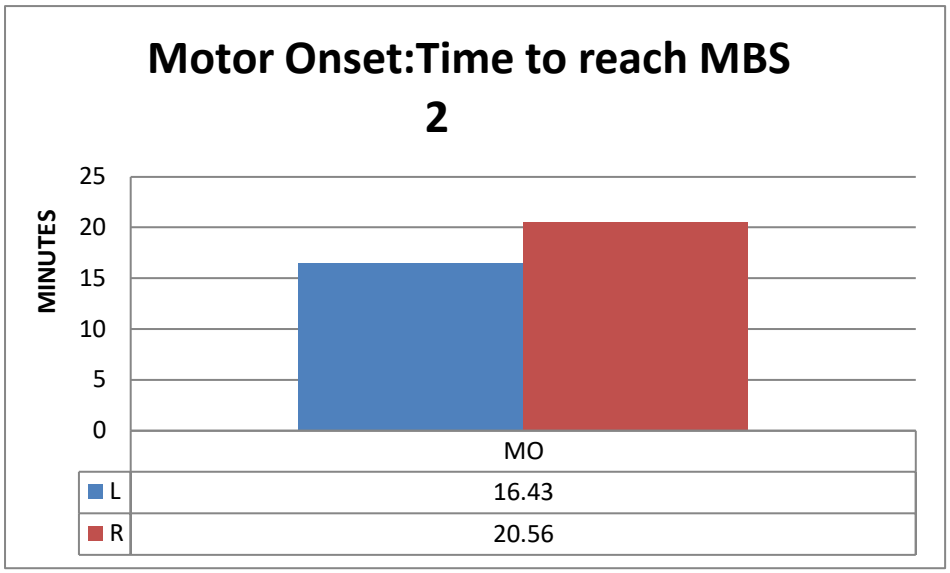


CHART: 4: NUMBER OF PATIENTS WHO ACHIEVED MBS OF 3
GROUP R: 62.5% GROUP L: 37.5%



P value 0.043 P value › 0.05 is not significant

CHART: 5 TIME TO ACHIEVE MAXIMUM MOTOR BLOCK AS PER MBS



P value: 0.069 P value › 0.05 is not significant

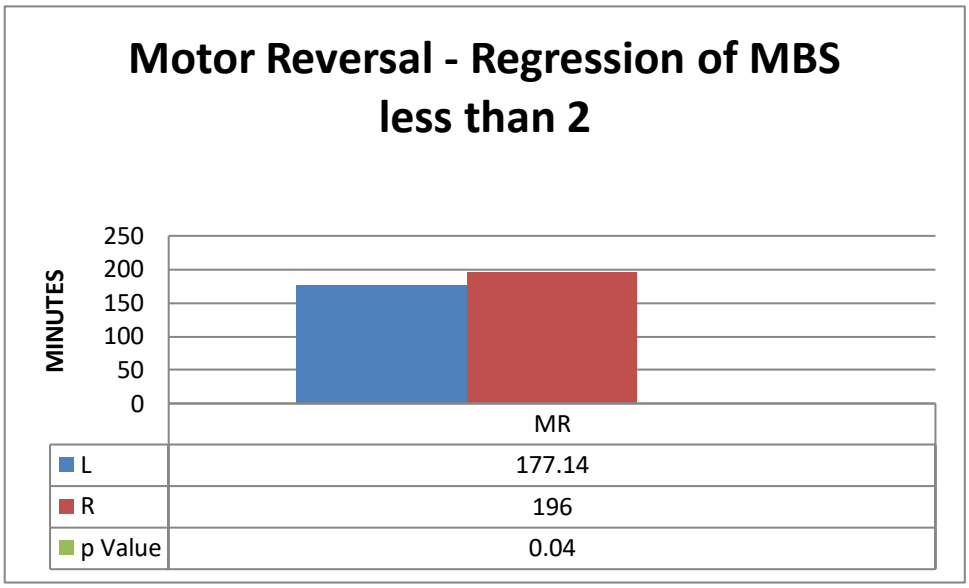
CHART 6: MOTOR ONSET – TIME TO REACH MBS 2

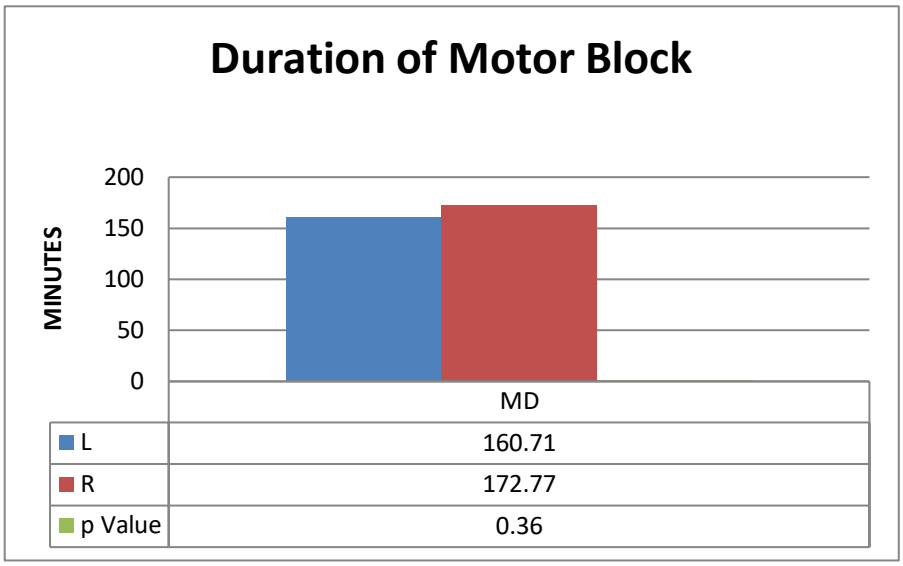
P value: 0.042 P value › 0.05 is not significant

CHART 7: MOTOR REVERSAL – REGRSSION OF MBS LESS THAN 2

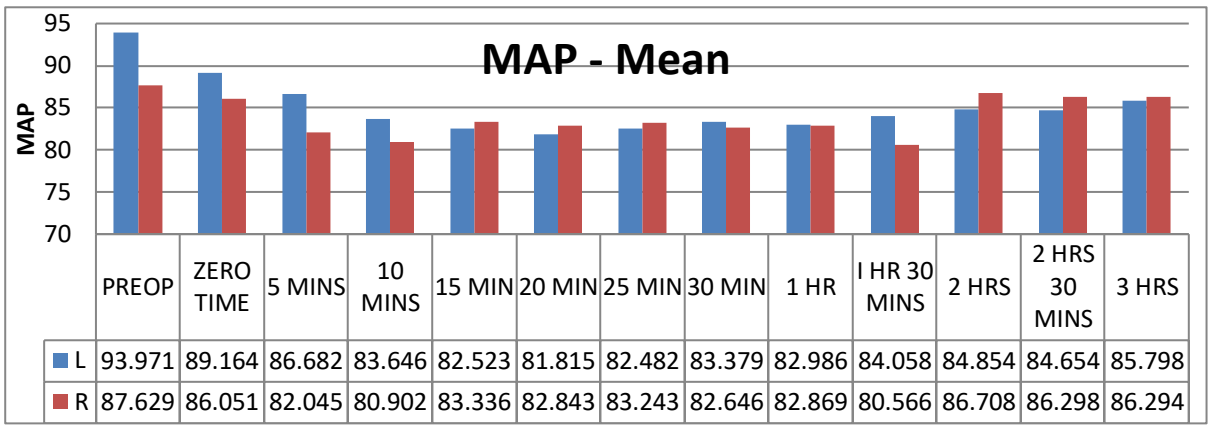
P value: 0.369 P value › 0.05 is not significant

CHART 8: DURATION OF MOTOR BLOCK





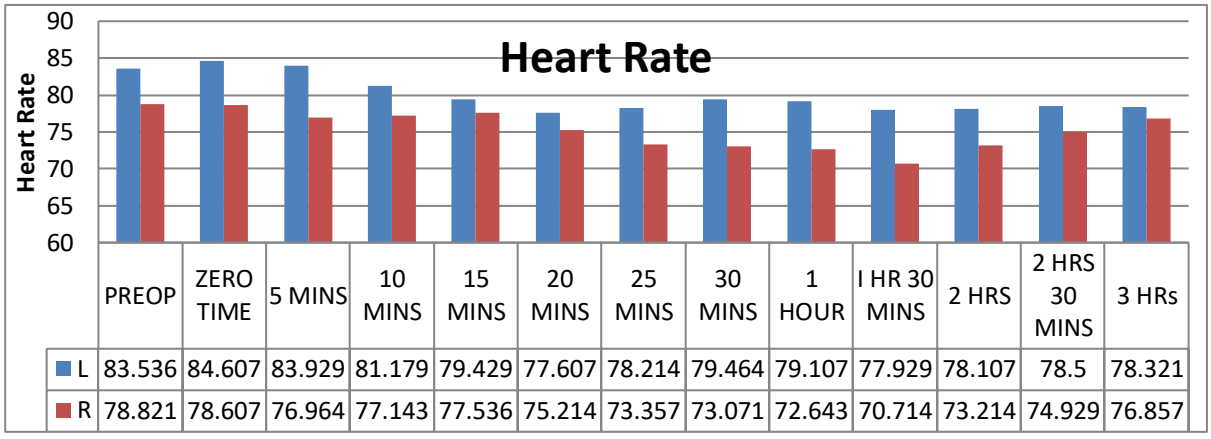
HAEMODYNAMIC PROFILE:



	PREOP	ZERO TIME	5 MINS	10 MINS	15 MIN	20 MIN	25 MIN	30 MIN	1 HR	I HR 30 MINS	2 HRS	2 HRS 30 MINS	3 HRS
L	93.971	89.164	86.682	83.646	82.523	81.815	82.482	83.379	82.986	84.058	84.854	84.654	85.798
R	87.629	86.051	82.045	80.902	83.336	82.843	83.243	82.646	82.869	80.566	86.708	86.298	86.294

P value › 0.05 is not significant

CHART 9: MAP OVER TIME FROM PREOP TO 3 HOURS

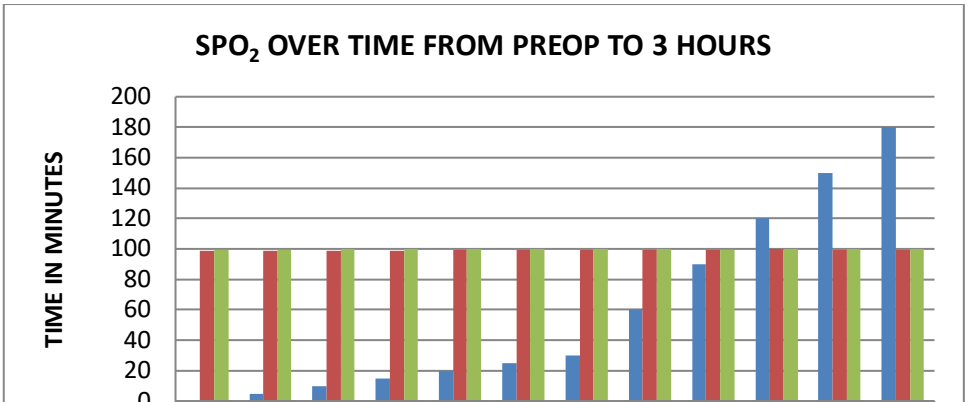


	PREOP	ZERO TIME	5 MINS	10 MINS	15 MINS	20 MINS	25 MINS	30 MINS	1 HOUR	I HR 30 MINS	2 HRS	2 HRS 30 MINS	3 HRs
L	83.536	84.607	83.929	81.179	79.429	77.607	78.214	79.464	79.107	77.929	78.107	78.5	78.321
R	78.821	78.607	76.964	77.143	77.536	75.214	73.357	73.071	72.643	70.714	73.214	74.929	76.857

P value › 0.05 is not significant

CHART 10: HEART RATE OVER TIME FROM PREOP TO 3 HOURS

CHART 11: SPO_2 OVER TIME FROM PREOP TO 3 HOURS



	1	2	3	4	5	6	7	8	9	10	11	12
TIME	0	5	10	15	20	25	30	60	90	120	150	180
L IN %	98.9	99	99.1	98.9	99.4	99.4	99.6	99.5	99.6	99.8	99.7	99.6
R IN %	99.5	99.7	99.8	99.8	99.8	99.8	99.8	99.9	99.6	99.9	99.9	100

4. DISCUSSION

According to Buyse et al., the order of potency among local anaesthetics is as follows: bupivacaine> levobupivacaine>ropivacaine.[11] Levobupivacaine when calculate for base (as opposed to the hydrochloride salts used for bupivcaine and ropivacaine), contains approximately 13% more local anaesthetic that bupivacaine. The lower molecular weight of ropivacaine implies that there are 4% more molecules of ropivacaine compared to bupivacaine.[2] These differences have implications for comparisons, as the quantity (in milliliters) of local anaesthetics administered does not directly correlate with the dose of active anaesthetic. Thus, it is likely that levobupivacaine and ropivcaine may be slightly less potent. Analgesic efficacy primarily depends on concentration rather than the specific type of anaesthetic.[12] Bromage found that the total local anaesthetic dose, rather than the total volume determines the spread and quality of analgesia after epidural administration.[13] A low volume of a concentrated solution produces the most predictable extradural block, as proposed by Duggan et al.[14] Whiteside et al.,[15] demonstrated that low concentration/high volume patient controlled epidural analgesia(PCEA) is effective in treating postoperative pain and reducing drug dosed compared to low volume/high concentration. The concentration and dosing strategy play crucial roles in achieving optimal analgesia while minimizing side effects.

The mean grade of motor block at 5 min time interval of study in group L was 2.5 ± 1.23 and in group R was 3.25 ± 0.79, the p value being 0.018, which shows there was statistically significant difference. Levobupivacaine, an enantiomer of bupivacaine, exhibits intrinsic vasoconstrictive properties.[16] This may lead to reduced absorption of the local anaesthetic from the epidural space, potentially explaining its faster onset compared to racemic bupivacaine.

The time to reach MBS grade 2 (motor onset) was 16.42 min in group L and 20.55 min in group R, with p value 0.06 p, which shows there was no statistically significant difference. This corresponds to the results of the study done by Cox et al., [17] in the year 1998, and Bergamaschi F et al., [18] and Casati A et al.,[19] found that the onset of motor block was clinically longer in Bupivacaine group which is in concordance to our study. In a study by Cox et al., in the year 1998, while comparing levobupivacaine in two concentrations 0.5%

and 0.75% and racemic bupivacaine 0.5% in patients undergoing lower limb vascular surgery or arthroscopy, the onset of block and duration of motor block were similar with 0.5% preparations. Longer time of motor blocks in the 0.75% group indicates a dose response effect with the 0.5% and 0.75% concentrations of levobupivacaine.

Regression of Motor block to MBS grade 1 (Motor Reversal) was found to be 177.14 min in group L and 196.66 min in group R p value being 0.042 (statistically significant difference). Thus our study finds that the regression of motor block was quick in L group and hence this drug can be used for surgeries which require early ambulation and obstetric analgesia. Epidural analgesia is used for postoperative pain management, after major joint replacement. Achieving adequate pain relief with minimal motor block is a challenge.[20] Levobupivacaine is a long acting amide class of local anaesthetic commonly used in epidural infusions that provided effective analgesia with less motor blockade than racemic bupivacaine. By using, a smaller dose of levobupivacaine (eg. 0.125%) in combination with an opiod or nonopiod analgesic like clonidine, clinicians can achieve adequate pain control without excessive motor block.[21, 22]

Duration of motor block was similar in both the groups(p vale being 0.369 and mean values being 160.71 min in group L and 172.77 min in group R). This result corresponds to that of Cox et al., [17] in the year 1998; found out that the duration of motor blockade in Group L was 185 vs Group R 192 mins. In a study conducted by Kopacz et al., researchers compared 15 ml of 0.75% levobupivacaine and bupivacaine to assess their adequacy for major abdominal surgery. There was no significant difference in the speed on onset of motor block, the mean duration of motor block was 355±83 and 376±71 min for levobupivacaine and bupivacaine respectively[23]. In the year 2003, Faccenda et al., compared epidural injection of up to 25 ml of 0.5% levobupivacaine versus racemic bupivacaine for elective caesarean section. The duration of motor block provided by levobupivacaine lasted longer but was less deep than that produced by racemic bupivacaine.[24]

The grade of motor block as per MBS score was significantly different in both groups. (Mean 2.82±0.47in R vs2.17±0.86 in L)(p value:0.016) which is highly significant, implying the motor grade reached in group R is denser than in Group L. The time taken to attain the maximum motor blockade was 23.39±9.13 min in group R and 17.85±10.8 min in group L. This is statistically highly significant. (p value:0.043).The number patient achieving MBS 3 in motor block is 62.5% vs 37.5% in Group R and Group L respectively. This implies lesser grade motor block which wears off earlier than racemic bupivacaine is observed in this study. The addition of either 1:200,000 or 1:400,000 epinephrine to epidural levobupivacaine tended to increase the degree of motor blockade compared to equal dose of plain levobupivacaine, with no statistical significance.[25]

The new two S-enantiomer drugs, ropivacaine and levobupivacaine, have purportedly lesser motor block and toxicity relative to bupivacaine. The motor block minimal local analgesic concentration (MMLAC) studies have shown that ropivacaine and levobupivacaine are less potent than bupivacaine for motor blockade.[26] Among these factors, age, height and epidural catheter placement site seem to be most important.[13,27]. A high degree of variability in block height was reported with thoracic-sited catheter.[27-29] Nevertheless, as stated by Kehlet., et al[30], the best quality of postoperative analgesia is achieved by systemic analgesics combined with an epidural approach.

Casati et al., in the year 2003, compared epidural injection of 15 ml of 0.5% levobupivacaine, 0.5% ropivacaine or 0.5% bupivacaine in patients undergoing total hip replacement. He reported no differences in the sensory profile and motor profile among groups except that the

patients receiving 0.5% ropivacaine frequently had an inadequate motor blockade during surgery. In the same study, the authors also evaluated the quality of postoperative analgesia provided with a patient-controlled epidural infusion of 0.125% bupivacaine, 0.125% levobupivacaine or 0.2% ropivacaine. They reported adequate pain relief and sparing of motor function during the first postoperative period[19].

Murdoch et al., in the year 2002 studied the effects of different concentrations of levobupivacaine (0.0625, 0.125 and 0.25) for lumbar epidural analgesia (CEA) after orthopaedic surgery and reported a dose-dependent effect on quality of postoperative analgesia, and a morphine sparing effect with increasing concentrations of levobupivacaine. Moreover use of the highest concentration resulted in a more marked motor blockade, suggesting that if minimum impairment of motor function is required for early rehabilitation, the concentration should be kept as low as possible.[20]

However, when the 15 mg/ hr is given through a thoracic epidural catheter, Darnedde et al., in the year 2002 reported that large-concentration/small-volume (3 ml/h of 0.5% levobupivacaine) provided an equal quality of postoperative analgesia as the small-concentration/ large-volume (10 ml/h of 0.15% levobupivacaine) infusion, and induced less motor blockade and fewer hemodynamic repercussions.[31-34]

There were no clinically significant differences in the total amount of IV fluids infused, ephedrine used and rescue analgesics given intraoperatively among both the groups.

Hemodynamic profile:

The heart rate and MAP of the patients in both the groups were comparable intra operatively with no clinical or statistically significant differences. The incidence of hypotension was studied by Bergamaschi et al., in the year 2005, found it similar (Group L 66.7% vs 43.5%in Group R) when either Levobupivacaine or Bupivacaine was used for epidural anaesthesia.[18] Kopacz et al., in the year 2000, found out that the incidence of hypotension occurred in 82% of patients in Group L and 61% in Group R.[23]

In their study, Kopacz et al.,(2001) observed that in the Levobupivacaine group, tachycardia occurred in 3% of cases, while hypotension occurred in 10%.[25] These hemodynamic effects are expected due to sympathetic blockade accompanying epidural anaesthesia. The complexity of hemodynamic effects arises from factors such as the volume, type and concentration of the local anaesthetic, the level of blockade and the inclusion of vasoconstrictors. Interestingly adding epinephrine to epidural local anaesthetics tends to increase heart rate and decrease blood pressure more than plain epidural local anaesthetics. In another study by Dernedde et al., reducing the adjunct, epinephrine concentrations from 5.0 to 2.5 µg / ml resulted in decrease in hypotension but there was no statistically significance (p value 0.08)[33-34]

Group	Motor onset(min)	Mean of Maximum MBS GRADE	Time for maximum MBS Grade in(min)	Time for motor block to MBS 1(min)	Duration of motor block(min)	No of Patients with MBS Grade 3in %
L (Levobuivacaine)	16.42 ± 11.74	2.21±0.87	17.85±10.8	177.14±39.00	160±46.64	50%
R (Racemic Bupivacaine)	20.55 ± 26.17	2.89±0.41	23.39±9.13	196.66±39.32	172.77±44.90	85.71 %

SUMMARY:

5. CONCLUSION

Both 0.5% levobupivacaine and 0.5% bupivacaine produced effective epidural anaesthesia and their effects were clinically indistinguishable. Levobupivacaine causes less cardio and neurotoxicity when compared to racemic mixture buivacaine, hence they can be widely used in epidural and regional block techniques where large volume of drug is used. Levobupivacaine produces less dense and lesser duration of motor block hence they can be used for labor analagesia. In labor analgesia, ropivacaine has been widely used in practise. The use of levobupivacaine 0.5% via a lumbar epidural catheter produced a excellent postoperative analgesia without rehabilitation limiting lower extremity motor blockade. The combination of a potentially enhanced toxicity/safety profile and similar efficacy of the single-isomer local anesthetic levobupivacaine, as compared with racemic bupivacaine, indicates that levobupivacaine may be a useful analgesic for postoperative epidural neural blockade as CEA and PCEA. [21, 33, 34]

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Ethical Statements:
The study was approved by the ethical committee of Saveetha institute of medical and technological science (S.I.M.A.T.S) with number: 009/06/2023/IEC/SMCH.

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Conflict of Interest:
None

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