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COMPARISON OF EFFICACY AND TOLERABILITY OF EPIDURAL 0.5% LEVOBUPIVACAINE, 0.75% ROPIVACAINE, AND 0.5% RACEMIC MIXTURE BUPIVACAINE IN ELECTIVE LOWER ABDOMINAL AND LOWER LIMB SURGERIES: CHIRALITY IN LOCAL ANAESTHETICS.

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Abstract

Aim: This study evaluates the effectiveness and tolerability of three local anesthetics—0.5 percentage Levobupivacaine, 0.75 percentage Ropivacaine, and 0.5 percentage Racemic Bupivacaine Mixture—in abdominal and lower extremity surgeries." ASA grades 1 and 2 were randomly assigned to receive epidural injections of one of these anesthetic agents to 84 patients.

Objective: To evaluate sensory, motor, and hemodynamic effects and side effects of the three anesthetics.

Results: Initiation of sensory block proved to be faster in the Ropivacaine (R) group while compared to the Levobupivacaine (L) and Bupivacaine (B) groups ($p < 0.05$). The R group also reached a higher maximum dermatome level, reached maximum level of sensory at a faster rate, and had faster 2-segment deterioration and faster deterioration of sensory block to T10. Analgesia's total duration was 5.03 hours in group R, 3.714 hours in group B, and 5.32 hours in the L group ($p < 0.05$). Duration for the whole reversal of the sensory block was 5.75 hours in group R, 6.67 hours in group B, and 6.98 hours in group L ($p < 0.05$). Motor onset was similar, ($p > 0.05$), but time for maximum grade of motor blockade was longer, regression faster and duration shorter in ropivacaine group. The grade of the motor block according to the Modified Bromage Scale (MBS) score was significantly different, with mean scores of 2.86 ± 0.35 in R, 2.21 ± 0.87 in L, and 2.89 ± 0.41 in B ($p < 0.05$). The hemodynamic profiles (MAP, SpO_2, and HR) were similar across all groups.

Conclusion: All three anesthetics were effective in providing epidural anesthesia. Ropivacaine demonstrated superior efficiency with faster onset and longer duration of sensory block, while also producing a shorter motor block, making it particularly suitable for labor analgesia. Levobupivacaine and Ropivacaine were associated with less cardiovascular and neurotoxicity than Racemic Bupivacaine, making them preferable for extensive epidural and regional blocks.

Keywords: Epidural Anaesthesia, Levobupivacaine, Ropivacaine, Racemic Mixture Bupivacaine, Local Anaesthesia, Cardiotoxicity, Neurotoxicity.

1. INTRODUCTION

Neuraxial anesthesia, which includes spinal and epidural blocks, involves the targeted interruption of spinal nerve transmission to achieve sensory and motor paralysis during surgical interventions. Despite notable progress in the field, the risk of toxicity remains a significant concern in regional anesthesia. These techniques are frequently employed to deliver effective and localized pain relief for various surgical procedures, particularly

those involving the lower abdomen and extremities (Brau*et al*., 2000). By administering local anesthetics directly into the epidural or intrathecal space, neuraxial anesthesia affords several key benefits, including precise analgesia, diminished systemic adverse effects, and potentially expedited recovery when compared to general anesthesia (Uppal*et al*., 2020; Rawal, 2021; Rosenberg and Wu, 2012; Gadsden and Park, 2015).

The technique involves administering anesthetic agents close to the medulla spinalis, thereby interrupting neurite signals and ensuing in reversible sensory also with motor paralysis in the designated regions. This method facilitates effective pain control during and after surgical procedures while reducing the risks typically associated with systemic drug administration (Burm *et al*., 1994; Kopacz and Muir, 2014). However, neuraxial anesthesia presents its own set of challenges. Proper selection of local anesthetics and vigilant management of potential complications, such as toxicity and insufficient analgesia, are essential for ensuring the best possible outcomes.Local anesthetics employed in neuraxial blocks, including bupivacaine, ropivacaine, and levobupivacaine, differ in their pharmacological characteristics and safety profiles. The selection of these agents can significantly affect the efficacy, duration of analgesia, and risk of adverse effects (Chou *et al*., 2016; Casati and Baciarello, 2006; Casati and Putzu, 2005). As advancements in neuraxial anesthesia continue, ongoing research remains crucial for refining techniques, enhancing safety, and improving patient outcomes.Bupivacaine, a commonly utilized local anesthetic, is available as a racemic combination of its enantiomers, consisting of levobupivacaine (the S (−) isomer) and dextrobupivacaine (the R (+) isomer). (Lacassie and Columb, 2003; Cekmen *et al*., 2008; Cok *et al*., 2011). Fatal central nervous system (CNS) and adverse reactions of cardiovascular have been linked to the dextro form of bupivacaine following involuntary intravascular dose or venous regional anesthesia (McLeod andBleile, 2003; Wojcik*et al*., 2015; Hodgson *et al*., 1995).

Organic molecules, such as bupivacaine, frequently display chirality, resulting in distinct biological interactions depending on their three-dimensional configuration. Advances in technology have facilitated the synthesis of optically pure enantiomers, such as levobupivacaine and ropivacaine, which possess a safe profile of pharmacologicwith reduced effects of cardiac and neurotoxic compared to their racemic mixtures. Research indicates that these pure isomers, particularly the S(−) enantiomers, interact with proteins more rapidly and exhibit lower toxicity, owing to their unique interactions with ion channels (Pittman, 1993; Meyer and Williams, 2007; Wright and Harris, 2011; Schmidt and Fuchs, 2009; Cowan and Muir, 2012).

Chirality plays a pivotal role in the pharmacological properties of local anesthetics. The unique three-dimensional configurations of enantiomers lead to varied interactions with biological receptors, thereby affecting their efficacy and safety profiles. Pure S(−) enantiomers, such as levobupivacaine and ropivacaine, demonstrate diminished cardiotoxicity and neurotoxicity relative to their racemic counterparts. This is attributed to their selective binding and more rapid interactions with target proteins (Hohle and Mackenzie, 2006; Ropp and Hawkins, 2011).

Despite extensive research into the individual properties of levobupivacaine, ropivacaine, and racemic bupivacaine, scantiness of inclusivestudies comparing their efficacy and tolerability is found. This research seeks to fill this gap by systematically evaluating and comparing the clinical outcomes of 0.5 percent levobupivacaine, 0.75percentage ropivacaine, and 0.5percentage racemic bupivacaine in epidural anesthesia for surgeries involving the lower abdomen and lower limb. The objective is to provide a detailed comparison of their relative performance and safety profiles, which will inform clinical decision-making and optimize patient care. By addressing this comparative analysis, the study aims to bridge existing gaps in clinical practice and contribute to the refinement of anesthetic procedures.

2. Materials and Methods

2.1 Study Design and Ethics

The Scientific Appraisal Board approved this study and the Institutional Ethics Committee (IEC) of Saveetha Medical College (Approval Number: 009/06/2023/IEC/SMCH). Written consent was received from all applicants, ensuring voluntariness and confidentiality of data (Emanuel*et al*., 2000; World Medical Association, 2013).

2.2 Inclusion and Exclusion Criteria

2.2.1 Inclusion Criteria(Kopp and Bagnall, 2015)

1. Patients aged 15 to 65 years.
2. ASA physical status grades 1 and 2.
3. No history of allergy to amide local anesthetics.
4. For regional anesthesia, complete or controversy is not found.

2.2.2 Exclusion Criteria(Gan *et al*., 2008)

1. Patients younger than 15 years or older than 65 years.
2. Known hypersensitivity to amide local anesthetics.

3. Psychiatric disorders history.
4. ASA physical status grade 3, 4, or 5.
5. Absolute or relative contraindications for regional anesthesia.

2.2.3 Patient Enrolment

Patients Eighty-four in number for surgery of the lower abdomen and lower limb were enrolled after institutional ethical committee approval along with consent in written format. Random assignment given by computer-generated numbers was done and patients were divided into three groups. The study was conducted in a double-masked method (neither patients nor treatment providers were aware of the group assignments).

2.3 Group Assignments

- **Group R:** Seventeen millilitres of 0.75 percentage Ropivacaine.
- **Group L:** Seventeen millilitres of 0.5 percentage Levobupivacaine.
- **Group B:** Seventeen millilitres 0.5 percentage Racemic Bupivacaine.

PROCEDURE

On the pre-operative day, patients were briefed, and informed consent was obtained.
Prior to epidural anesthesia, treatment undergoers were administered a preload of 500 ml of Ringer's Lactate. Routine monitoring included heart rate (HR), electrocardiogram (ECG), oxygen saturation (SpO2), and non-invasive blood pressure (NIBP). Lying on the left side with the body's longitudinal axis perpendicular to the imaging table, the space of patient L3-L4 intervertebral is located.The skin and subcutaneous tissue were permeated with three milliliters of 2 percent lignocaine. Epidural space was accessed utilising an 18G needle (Tuohy) with the technique, of loss of resistance to air. Confirming the –ve aspiration for cerebrospinal fluid (CSF) or blood, a test dosage of 3 millilitersof 2 percent lignocaine along with 1 in 2 lakhs adrenaline was administered (Rapp and Eisenach, 2006; Cousins and Bridenbaugh, 1988). Two minutes post-test dose, the study drug was administered:

- **Group R:** 17 ml of 0.75% Ropivacaine, administered over 5 minutes (6 ml, wait 1 minute, 6 ml, wait 1 minute, 5 ml).
- **Group L:** 17 ml of 0.5% Levobupivacaine, administered over 5 minutes (6 ml, wait 1 minute, 6 ml, wait 1 minute, 5 ml).
- **Group B:** 17 ml of 0.5% Racemic Bupivacaine, administered over 5 minutes (6 ml, wait 1 minute, 6 ml, wait 1 minute, 5 ml).

The study at the dosage drug end was designated as time zero for succeeding assessments.

2.4 Epidural Catheterisation

The needle was removed after advancing the 20G catheter into the epidural space for 5cm. The supine position was used to place the patients. Continuous monitoring of PR, BP, and SpO_2 was performed. Patients were provided oxygen at 4 liters per minute through a face mask. Surgery commenced half an hour after administrating the drug taken for study. Hemodynamic instability, including a drop in MAP greater than 20% from baseline, was managed with 6 mg of Ephedrine. A decrease in HR below 50 bpm was managed with 0.6 mg of Atropine (Miller, 2009; Auroy *et al*., 1997).

Assessment

The sensory block was assessed utilising pinprick testing with a needle blunt one. Measured parameters included onset time of sensory block (period to achieve T10 dermatome), maximum level of the dermatome, time taken to attain the maximum level of sensory, regression to T10, 2-segment regression, the duration for first analgesia demand, and total recovery from the sensory block. Inadequate sensory block was managed by administering an additional 7 ml of the study drug during surgery.
Motor block was evaluated using the Modified Bromage Scale (MBS)

- **0:** No paralysis, of knees, ankles, and hips with full flexion.
- **1:** the presence of knee movement and not being able to raise the extended leg.
- **2:** presence of ankle movement and not able to move knees.
- **3:** not able to move the lower limb.

Motor block onset is defined as an MBS score of 2. Duration and complete regression of motor block (MBS score of 0) were recorded. For postoperative analgesia, 100 milligrams of Tramadol thinned in 10 milliliters of distilled water and administered epidurally as needed.

2.5 Statistical Analysis

With the use of the latest version of SPSS software, data were analysed. Descriptive statistics included range, mean, standard deviation, mean, and proportions. Illative statistics were performed using chi-square tests and unpaired t-tests. Comparisons among three groups were conducted using ANOVA. For general and high significance, the levels were set at p less than 0.05 and less than 0.01 respectively.

3. RESULTS AND DISCUSSION

This study assessed the efficiency and protection of Ropivacaine (R), Levobupivacaine (L), and Racemic Mixture Bupivacaine (B) in providing sensory and motor block for regional anesthesia. We aimed to compare these local anesthetics in terms of their demographic profiles, sensory and motor blockade characteristics, with overall hemodynamic stability. Analysis of the collected data was guided by established references in the field of anesthesiology, including the work of Choi *et al.*, 2003 who investigated the efficacy of local anesthetics in various surgical settings, and the comprehensive review by Chahar and Cummings III, 2012 on the comparative effects of different bupivacaine formulations. Our findings provide insights into the comparative performance of these anesthetics, contributing valuable information for clinical decision-making in regional anesthesia.

3.1 Demographic Profile

- **Age**: The mean age is similar across all groups (Ropivacaine, Levobupivacaine, and Racemic Mixture Bupivacaine), with no statistically noteworthy variation (p-value more than 0.05). This suggests that age is not a confounding factor in the study.
- **Sex**: The distribution of sexes is comparable within the groups, with no noteworthy variation (p-value = 0.68), indicating that sex is evenly distributed and not biased towards any particular group.
- **BMI**: The Body Mass Index (BMI) is similar among the groups, with no statisticallynoteworthyvariations (p-value more than 0.05). This indicates that BMI is evenly distributed across the groups.
- **ASA Grade**: The ASA (American Society of Anesthesiologists) grade distribution is carried out in two grades of the patients in the first group the values seem to be 10, 19, and 20 and in the 2nd values seem to be 18, 8, 8 which are similar across the groups, with no statistically noteworthy variations (p-value more than 0.05). This implies that the physical status of patients, as classified by ASA, is consistent among the groups.
- **Education**: The educational qualifications of patients such as Illiterate, primary school, High school, HSC, and graduation in the three groups are similar (p-value > 0.05), indicating that educational level is evenly distributed and unlikely to impact the outcomes.

Table 1: Demographic Profileof Age, Sex and BMI in Different Groups

S. No	Parameters	Ropivacaine (R)	Levobupivacaine (L)	Racemic Mixture Bupivacaine (B)
1	Age	46.5 ± 16.68	44.68 ± 11.3	40.92 ± 12.75
2	Sex (Male)	20	17	11
	Sex (Female)	8	11	9
3	BMI	24.59 ± 4.96	26.52 ± 3.28	26.1 ± 0.54

Table 2: Educational qualification in different groups

S. No	Education	Ropivacaine (R)	Levobupivacaine (L)	Racemic Mixture Bupivacaine (B)

1	Illiterate	5	4	8
2	Primary School	1	6	3
3	High School	13	13	16
4	HSC	4	5	1
5	Graduation	5	0	0

Table 3: Types of Surgery

S. No	Surgery	Ropivacaine (R)	Levobupivacaine (L)	Racemic Mixture Bupivacaine (B)
1	Abdominal hernia repair	5	9	9
2	Ortho repair (ACL)	4	0	0
3	Inguinal Hernia	18	15	11
4	Colostomy Closure	1	0	0
5	TAH	0	2	3
6	Varicose Vein Repair	0	2	5

- **Type of Surgeries**: The different types of surgery performed they are Abdominal hernia repair, Ortho repair (ACL), Inguinal Hernia, Colostomy Closure, TAH, and Varicose Vein Repair. The types of surgeries performed across the categories are similar with no noteworthy differences (p-value more than 0.05). This suggests that the type of surgery is not a confounding factor in the results.

Efficacy study of racemic bupivacaine,ropivacaine, and levobupivacaine,in epidural anesthesia was made focusing on onset times, sensory block characteristics, and motor block profiles. Our findings suggest that ropivacaine has a meaningfully rapid onset of sensory block compared to levobupivacaine and bupivacaine, corroborating previous studies that have reported similar results (Cox*et al.*, 1998; Yang *et al*., 2007; Wang*et al*., 2010). Specifically, mean onset times for sensory block were 3.93 minutes for ropivacaine, 5.21 minutes for levobupivacaine, and 9.64 minutes for bupivacaine, indicating a faster onset with ropivacaine. These results align with the observations of Finucane *et al*., 1996 and Shalina Chandran *et al.*,2014 who found that ropivacaine produced faster onset times compared to bupivacaine.

3.2 Sensory Profile

Sensory Block at Different Time Periods: The sensory block levels at various times (0 to 180 minutes) show significant differences among the groups, with Ropivacaine and Levobupivacaine having lower values compared to Racemic Mixture Bupivacaine (p-values < 0.01). This suggests that Ropivacaine and Levobupivacaine may have a faster onset or more efficient sensory block compared to a Racemic Mixture of Bupivacaine.

Table 4: Sensory Block at Different Time Periods From 0 to 180 Minutes

S. No	Sensory	Ropivacaine (R)	Levobupivacaine (L)	Racemic Mixture Bupivacaine (B)
1	5	7.07±2.58	11.07±1.06	11.07±1.15

2	10	5.71±1.78	9.64±1.09	10.14±1.53
3	15	5.21±1.57	8.29±1.69	8.64±1.81
4	20	4.86±1.38	7.29±1.74	7.29±1.74
5	25	4.79±1.37	6.57±1.31	6.14±1.32
6	30	4.79±1.37	6.07±1.01	5.64±1.22
7	60	4.79±0.99	6.21±1.13	5.57±1.26
8	90	4.86±1.00	7.07±1.58	6.07±1.58
9	120	5.57±1.47	8±1.96	7.07±1.84
10	150	6.79±2.13	9.07±1.67	8±1.88
11	180	7.71±2.91	10.14±1.53	8.86±1.75

3.3 Sensory Variables/Objectives

- **The onset of Sensory Block (TT10)**: The fastest onset was found in Ropivacaine (3.93 minutes), followed by Levobupivacaine (5.21 minutes), and Racemic Mixture Bupivacaine (9.64 minutes), with significant differences ($p < 0.01$).
- **Maximum Dermatome (MD)**: Ropivacaine reaches a lower maximum dermatome level compared to Levobupivacaine and a Racemic Mixture of Bupivacaine (p-value = 0.009).
- **Time to Maximum Sensory Level (TMD)**: Ropivacaine achieves ultimate sensory level faster (13.29 minutes) compared to Levobupivacaine (22.5 minutes) and Racemic Mixture Bupivacaine (25.7 minutes) ($p < 0.01$).

Table 5: Sensory Variables/Objectives

S. No	Sensory	Ropivacaine (R)	Levobupivacaine (L)	Racemic Mixture Bupivacaine (B)
1	TT10	3.93±2.90	8.21±3.65	9.64±4.89
2	MD	4.64±0.95	5.64±1.44	5.36±1.22
3	TMD	13.29±11.32	22.50±5	25.71±10.77
4	TR	157.50±50.08	113.57±31.99	130.71±45.61
5	TTR	220.71±50.47	170.36±49.70	187.5±39.68
6	TPA	301.96±86.59	319.29±60.11	222.86±38.66
7	TCR	354.54±77.35	418.93±78.52	400.71±36.71

- **Time for 2 Segment Regression (TR)**: Ropivacaine has a longer time for 2-segment regression (157.50 minutes) compared to Levobupivacaine (113.57 minutes) and Racemic Mixture Bupivacaine (130.7 minutes) (p-value = 0.001).
- **Duration for Regression to T10 (TTR)**: Ropivacaine has a longer duration for regression to T10 (220.71 minutes) compared to Levobupivacaine (170.36 minutes) and Racemic Mixture Bupivacaine (187.5 minutes) ($p < 0.05$).
- **Total Duration of Analgesia (TPA)**: Ropivacaine has a longer total duration of analgesia (301.96 minutes) compared to Levobupivacaine (319.09 minutes) and Racemic Mixture Bupivacaine (222.86 minutes) (p less than 0.05).
- **Time for Complete Reversal of Sensory Block (TCR)**: Ropivacaine has a shorter time for complete reversal (345.54 minutes) compared to Levobupivacaine (418.93 minutes) and Racemic Mixture Bupivacaine (440.71 minutes) (p-value = 0.00).

These results suggest that Ropivacaine generally provides a faster onset, shorter time to maximum sensory level, and quicker complete reversal compared to Levobupivacaine and Racemic Mixture Bupivacaine.The duration of sensory block and the maximum dermatome levels achieved were notably different among the three anesthetics. Our study found that ropivacaine had the shortest time to achieve the maximum sensory level and the longest time for sensory block regression, with significant differences observed compared to levobupivacaine and bupivacaine (Olofsen *et al.,* 2008). This is consistent with findings by Maheshwari *et al.,* 2016 who reported longer durations of sensory block with ropivacaine. The observed maximum dermatome levels reached (4.64 for ropivacaine, 5.64 for levobupivacaine, and 5.36 for bupivacaine) align with similar studies that noted differences in sensory levels between these anesthetics (Cox *et al*., 1998; Kopacz *et al*., 2000; Zaric *et al*., 1991; Murdoch *et al*., 2002; Needim *et al.*, 2008).

3.4 Motor Profile

- **Motor Block at Different Time Periods**: There are noteworthy variations in motor block levels among the categories. Ropivacaine and Levobupivacaine show different motor block profiles compared to the Racemic Mixture Bupivacaine, with notable differences in the mean MBS scores (p-value = 0.00).

Table 6: Motor Block at Different Time Periods From 0 to 180 Minutes

S. No	Sensory	Ropivacaine (R)	Levobupivacaine (L)	Racemic Mixture Bupivacaine (B)
1	5	0.68±0.94	0.89±0.49	0.46±0.50
2	10	1.18±1.02	1.32±0.54	1.14±0.44
3	15	1.57±0.92	1.71±0.89	1.82±0.61
4	20	2±0.66	2±0.90	2.04±0.74
5	25	2.25±0.70	2.11±0.87	2.54±0.74
6	30	2.36±0.73	2.18±0.86	2.68±0.72
7	60	2.50±0.79	2.25±0.84	2.71±0.71
8	90	2.46±0.69	2.14±0.89	2.61±0,73
9	120	2.36±0.67	1.82±0.72	2.43±0.87
10	150	1.82±1.09	1.5±0.63	2.25±0.96
11	180	1.29±1.32	1.18±0.67	1.82±0.86

- **3.5 Motor Variables/Objectives**
  - **Maximum MBS:** Ropivacaine (2.86) and racemic mixture bupivacaine(2.89) showed no difference but levobupivacaine (2.21) was less denser compared to ropivacaine and racemic mixture bupivacaine (p-value=0.00).
  - **Time to Maximum Motor Blockade (TTMBS2)**: Ropivacaine takes the longest to achieve maximum motor blockade (40.18 minutes) compared to Levobupivacaine (17.86 minutes) and Racemic Mixture Bupivacaine (23.57 minutes) (p-value = 0.04).
  - **Duration of Motor Blockade**: Motor blockade's duration is longest in the Racemic Mixture Bupivacaine group (172.78 minutes) compared to Ropivacaine (146.25 minutes) and Levobupivacaine (160.71 minutes) (p-value more than 0.05).

Table 7: Motor Variables/Objectives

S. No	Sensory	Ropivacaine (R)	Levobupivacaine (L)	Racemic Mixture Bupivacaine (B)
1	MO	24.64 ± 31.11	16.43±11.74	20.56±26.11
2	MR	170.54 ± 45.95	177.14±39	196±39.32

3	TTMBS2	146.25 ± 48.58	160.71±46.64	172.78±44.9
4	MAX MBS	2.86 ± 0.35	2.21±0.87	2.89±0.41
5	TTMMBS2	40.18 ± 40.99	17.86±10.83	23.57±9.11

These findings indicate that while Ropivacaine might lead to a longer duration to attain ultimate motor block, it may have a shorter overall duration of motor blockade compared to Racemic Mixture Bupivacaine.In terms of motor block, there was no statistically noteworthy difference in the onset of motor block among the categories. This coincides with the findings of Brockway *et al.*, 1991; Finucane *et al.*, 1996 which detected similar motor block onset times among different anesthetic agents (Crosby*et al*., 1998; Faccenda *et al*., 1996; Finucane*et al*., 1996;Wolff *et al*., 1995). But the motor block's duration was notably longer with bupivacaine while compared to ropivacaine and levobupivacaine. This supports the findings of studies that reported longer motor block durations with bupivacaine (Brockway*et al.*, 1991; Brown *et al.*, 1990). The greater occurrence of complete motor block (MBS 3) in bupivacaine's category further aligns with previous research suggesting that bupivacaine induces a denser motor block compared to ropivacaine (Gandhi *et al*., 2020; Kumar *et al.*, 2018; Kerkkamp *et al*., 1990; Peuto *et al*., 2003).

3.6 Use of IV Fluids, Ephedrine and Supplementation

- **IV Fluids, Ephedrine, and Supplementation**: The usage of intravenous fluids, ephedrine, and any additional supplements is similar across all groups, indicating that the need for these interventions does not significantly differ between the anesthetics used.

Table 8: Use of IV Fluid, Ephedrine, and Supplement

S. No	Sensory	Ropivacaine (R)	Levobupivacaine (L)	Racemic Mixture Bupivacaine (B)
1	IV Fluid	1.55±0.31	2.05±0.15	2.03±0.23
2	Ephedrine	10.8±5.02	6.00±0	6.86±2.26
3	Supplement	2±0	1.93±0.26	1.96±0.18

3.7 Hemodynamic Profile

- **Heart Rate**: No noteworthy differences in heart ratewere found among the categories at various intervals of time (p-values > 0.05), suggesting that the heart rate is stable and comparable across the different anesthetic groups.
- **Mean Arterial Pressure (MAP)**: There are some differences in MAP at specific time points, but overall, the values are comparable (p-value > 0.05).
- **Oxygen Saturation**: Oxygen saturation levels are similar across all groups (p-values > 0.05), indicating that oxygenation is maintained effectively regardless of the anesthetic used.

Figure 1: Heart Rate at Different Time Periods From 0 to 180 Minutes

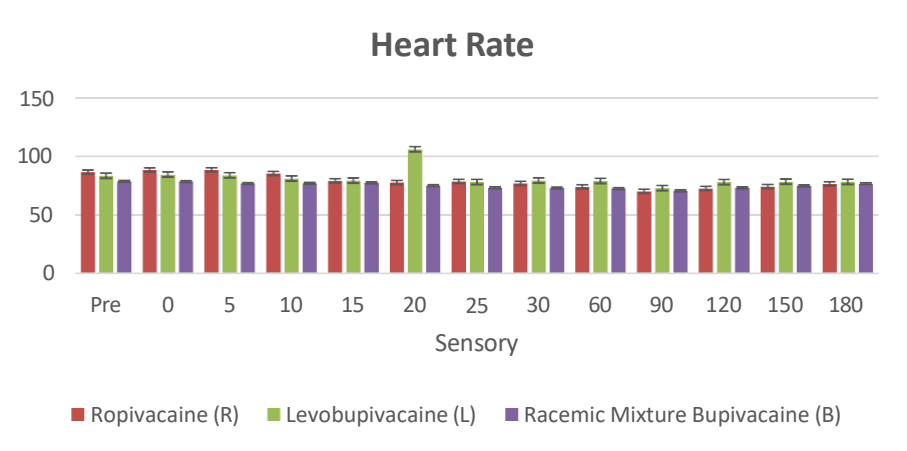


Figure 2: Mean Arterial Pressure (MAP)at Different Time Periods From 0 to 180 Minutes

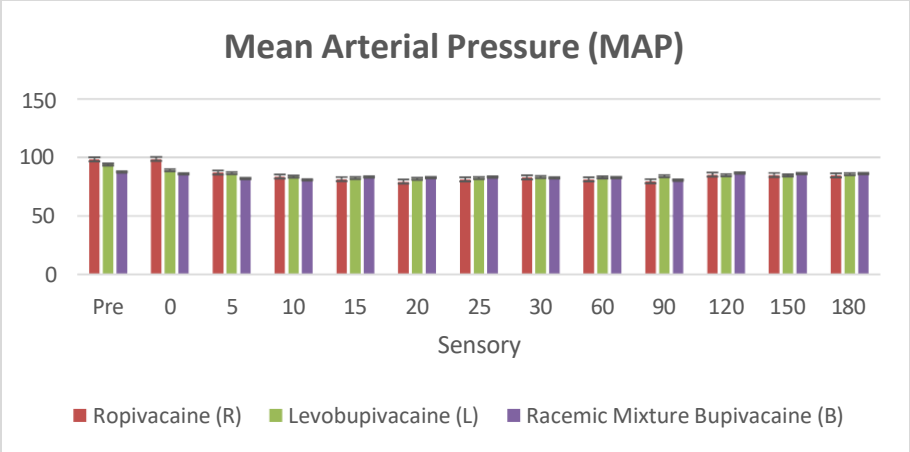
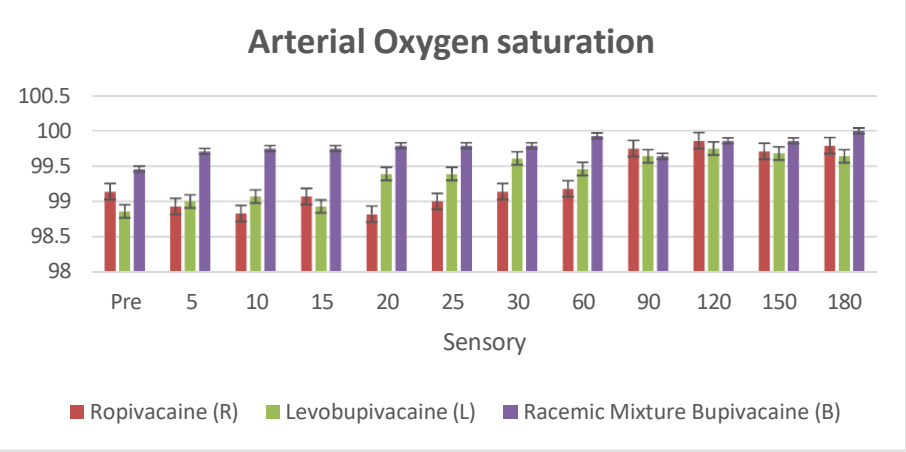


Figure 3:
Arterial Oxygen saturation at Different Time Periods From 0 to 180 Minutes



Our study found no significant differences in hemodynamic parameters (MAP and HR) among the three groups, which suggests that all three anesthetics are well-tolerated in terms of hemodynamic stability. This agrees with the conclusions of Senard *et al*., 2004 who detected no changes in parameters of hemodynamics between levobupivacaine and ropivacaine. The incidence of hypotension, though present, was managed effectively with

fluids and vasopressors, in line with observations by Sinnott and Stricharts, 2003; Bergamaschi *et al.,* 2005 and Kopacz *et al.*,2000 who noted similar rates of hypotension among these agents.

Regarding complications, hypotension was the primary adverse effect encountered, with no significant difference in incidence across the three anesthetics. This is consistent with other studies that reported similar rates of hypotension with bupivacaine and its alternatives (Shah *et al.,* 2017; Griffin and Reynolds, 1995; Finucane*et al.,* 1996; Kutiyala and Chaudhary, 2011). Notably, our study did not find significant occurrences of nausea, vomiting, or bradycardia, aligning with the results of Katz *et al*., 1990; Katz *et al*., 1993; Thompson *et al*., 1989 who also observed low rates of these complications.

4. CONCLUSION

The study concludes that an equipotent dose of 0.5 percentage levobupivacaine, 0.75percentage ropivacaine, and 0.5percentage racemic mixture of bupivacaine produces clinically indistinguishable, well-permitted, and efficient extradural anesthesia for those undergoing surgery in lower limb and abdomen. Toxic effects of left isomers are less on the CNS and on the circulatory system and can be used in epidural or peripheral nerve block.[2] Further studies and research should be carried out to find a drug with more protein binding (protein binding not altered by other drugs-drug interaction), should have decreased affinity and faster release from cardiac sodium channel once gets attached to it(preventing dreaded, difficult to reverse/ resuscitate cardiac toxicity of Bupivacaine group of Local Anaesthesia drugs).In summary, our study reinforces the clinical advantages of ropivacaine over levobupivacaine and bupivacaine, particularly with regard to faster onset of sensory block along with shorter motor block duration. However, bupivacaine continues to demonstrate longer-lasting sensory and motor blocks. The stability of hemodynamics and low incidence of severe adverse effects across all three anesthetics suggest their relative safety in clinical practice. Continuing the research could explore additional avenues or delve deeper into the implications of findings in diverse surgical settings besides patient populations.

The accepted safe plasma levels are approximately 1-2 µg/ml for racemic bupivacaine, 1.74±2.7 µg/ml for levobupivacaine, and 1.24±6.0 µg/ml for ropivacaine. To establish safe dosing for these anesthetics, further pharmacokinetic (PK) and pharmacodynamic (PD) studies are necessary, focusing on their plasma concentration and physiological models, especially in the context of spinal anesthesia (SAB), epidural anesthesia, and peripheral nerve blocks. Advances in cryo-electron microscopy (cryo-EM) could significantly enhance our understanding of NaV channel structures, potentially enabling the development of more targeted drug delivery systems that avoid cardiac NaV channels through nanotechnology. Additionally, genetic testing of CYP450 1A and 3A liver enzymes may assist in identifying individuals with varying metabolic rates, thereby improving the prediction and management of potential side effects.

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