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"Comparison of clinical efficacy and tolerability of Epidural 0.5% Levobupivacaine with 0.75% Ropivacaine in patients undergoing elective lower abdominal surgery"

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Abstract
The aim of the study is to compare the efficacy and tolerability of 0.5% Levobupivacaine and 0.75% Ropivacaine, in patients undergoing lower abdominal surgery.56 patients, ASA grade 1 and 2, were randomised to receive an epidural injection of study drug (17 ml 0.5% Levobupivacaine in group L and 17 ml of 0.75% Ropivacaine in group R. The objective of the study was to compare sensory, motor, haemodynamic and side effect profile of the 2 drugs. The mean time for onset of sensory block, maximum dermatome reached was faster and higher in R group. The time taken to attain maximum sensory level in two groups is similar. The Time for 2 segment regression and the duration for regression of sensory block to dermatomal level T_{10} were slower in group R. Total duration of analgesia in R group was 301.96, whereas in L group it was 319.09 min (p value 0.579). The time for complete reversal of sensory block was 345.54 in R group versus 418.93 min in L group (The p value <0.05).The onset of motor block, regression of motor block and duration of motor block were comparable in both the groups. The grade of motor block as per MBS score was significantly different in both groups. The time taken to attain the maximum motor blockade was 40.18 min in group R and 17.86 min in group L.(p value of 0.043). The mean duration of motor block in R group was146.25 ±48.58 min and in L group was 160.71 ±46.64 min. (p value >0.05). The MAP and HR were similar at different periods. Both study drugs produced effective epidural anaesthesia and were well tolerated in patients undergoing lower abdominal surgery.

Keywords: Epidural Anaesthesia, Levobupivacaine, Ropivacaine, Racemic mixture Bupivacaine Chirality, Isomers in Local anaesthesia drugs, Cardiotoxicity and Neurotoxicity in Local anaesthesia use

INTRODUCTION:

Local anesthetics inhibit the sodium channels on neural membranes that cause loss of conduction on neural structure. Elevated plasma levels of local anesthetics in central nerve system and cardiovascular system results in systemic toxicity when they are injected IV by mistake. They directly cause negative introphy, myocardial conduction abnormalities, and arrhythmias. Arrhythmogenic effects of toxic level of these drugs are related with repolarization of potassium, sodium, and calcium channels. Consequently, it results in slowing down of cardiac impulse conduction, widening of QRS complex, PR prolongation, atrioventricular block and fatal ventricular fibrillation or ventricular tachycardia. The search for newer and safer anaesthetic agents has always been one of the primary needs in anaesthesiology practice.[1]

The property of isomerism occurs when two or more compounds have the same molecular composition but with a different structure which often results in different properties. There are two types of isomerism stereoisomerism and structural isomersism[2]

Stereoisomerism has the same molecular formula and chemical structure, but the atoms are orientated in a different direction. There are two isomers (levo and dextro) each a mirror image of the other, called enantiomers. The R enantiomer rotates light to the right and the S enantiomer to the left. They have different properties like other isomers .The molecule of bupivacaine, has an asymmetric

carbon atom.(a chiral center). In the commercial presentation of this LA, there is a 50:50 proportion of Levobupivacaine, L (-) isomer, and dextro bupivacaine D (+) isomer. A racemic mixture is a preparation which contains both enantiomers.[3, 4] Severe CNS and CVS adverse reactions reported in the literature after inadvertent intravascular injection or intravenous regional anaesthesia have been linked to the R (+) isomer of bupivacaine. The levorotatory isomers have a safer pharmacological profile.[1]

Ropivacaine is a aminoamide long acting LA. It is the monohydrate of the hydrochloride salt of 1-propyl- 2',6'–pipecoloxydide. It is prepared as a pure S enantiomer. It belongs to pipecoloxydides group of LA drugs.. It is having a propyl group on the piperidine nitrogen atom in contrast to butyl group in bupivacaine.[5] The decreased toxicity of Ropivacaine is due to its faster protein binding rate. [6] The pure S (−) enantiomers of bupivacaine, i.e., levobupivacaine and ropivacaine were thus introduced into the clinical anaesthesia practice. In this study we have made an attempt compare the efficacy of levobupivacaine 0.5% and Ropivacaine 0.75% for epidural anaesthesia for lower abdominal and lower limb surgeries. The equipotent dose of 0.5% Levobupivacaine is 0.75% Ropivacaine because of the reduced lipophilic property of ropivcaine. The lipid solubility of levobupivacaine is 30 whereas that of ropivacaine is 2.8.

Studies, using an 'up-down-sequential allocation method to determine the minimal local anaesthetic concentration(MLAC) for pain relief during labour, pointed out that ropivacaine may be less potent than bupivacaine.[7,8] Using the same method, it was found that the minimal local anaesthetic concentration to produce motor block(MMLAC) was significantly higher for ropivacaine (0.497%) than for bupivacaine (0.326%).[9] The clinical relevance of this method has been questioned because it compares the potency at the ED50[10,11] Again measurements are made at one point of the dose-response curve, which does not provide information about the shape or slope of the Dose response curve. Therefore, no prediction can be made at the ED95, which is more of clinical importance.

The dosage of 0.75% ropivacaine and 0.5 % levobupivacaine is 2 per kg body wt.(for a 50 kg patient the toxic dose is about 150 mg and 100 mg respectively) The total volume used in our study in both the group is 17 ml(L=85 mg and R=127.50 mg). Hence in both the groups 17 ml was selected as the volume of the study **drug other** than the test dose.

AIM AND OBJECTIVES

AIM

To compare, the clinical efficacy and tolerability of Epidural 0.5% Levobupivacaine and 0.5% Bupivacaine in patients undergoing elective lower abdominal surgery.

OBJECTIVES

Primary Objectives

1. Sensory onset at T10 level
2. Maximum sensory level achieved(dermatome)
3. Time taken to achieve maximum sensory block
4. Time to two segment regression
5. Time to regress to T10 level
6. Time taken by the patient for demanding analgesia post operatively
7. Onset of motor block
8. Regression of motor block
9. Duration of motor block

Secondary Objectives:

1. Intraoperative haemodynamic profile
2. Adverse effects like nausea, vomiting, shivering and, headache.

MATERIAL AND METHODS

After obtaining Institutional scientific review board and ethical committee's approval (Number: 009/06/2023/IEC/SMCH) and written informed consent, 56 patients belonging to both sex, who were scheduled to undergo lower abdominal 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 5
5. Patients having absolute or relative contraindication for regional anaesthesia

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

Group R- Received 17 ml 0.75% Ropivacaine

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 using pulse oximeter were done.

Patient was put on left lateral decubitus position L3 L4 inter spinous space was identified. 3 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 1in 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 0.75% Ropivacaine 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. Level of sensory analgesia was measured by using pin prick with blunt end of needle. Onset of sensory block was defined as time taken to achieve T10 dermatomal level. Maximum dermatomal level achieved and the time taken to reach the level was recorded. Time to two segment regression was also noted..After 30 min 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.[12]

Onset of motor block was defined as when patient has modified Bromage score of 2. Duration of motor block is defined as time for which the modified score remains at least 2. Complete regression was defined as motor block with modified Bromage score of zero.[12]
Modified Bromage scale[12] 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.

All patients received Midazolam 0.05 mg/kg body weight for intraoperative sedation. All patients were allowed to breathe spontaneously throughout the surgical procedure. Patients who were found to have inadequate sensory block and in whom dural puncture was encountered were converted to GA and excluded from the study.

Statistical Method Applied:
Statistical analysis was done using latest SPSS version. 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 two-way repeated measure ANOVA and chi-square test.
P-value: it is the probability rate at 0.05 level of significance for corresponding degree of freedom.

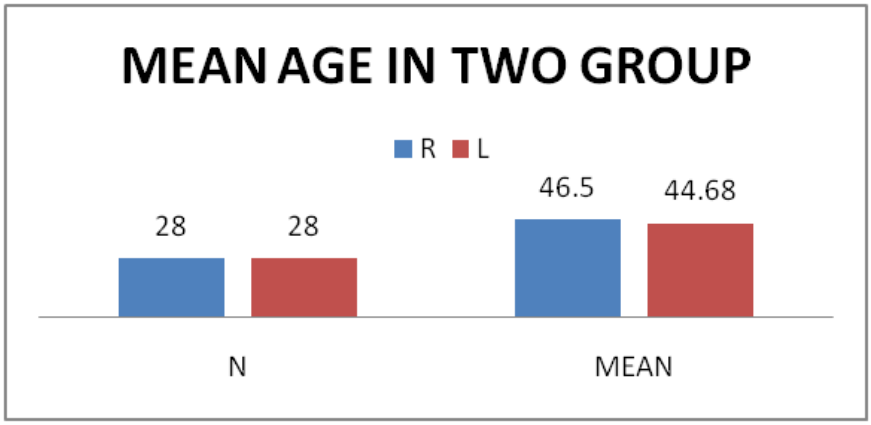
p>0.05 is not significant
p<0.05 is significant
p<0.01 is highly significant

RESULTS:

DEMOGRAPHIC PROFILES:
The age, sex, educational qualification and BMI of the patients included in both the groups were comparable with no statistically significant difference.(Table 1,2,3 ,4) and (Chart 1,2,3,4,5).

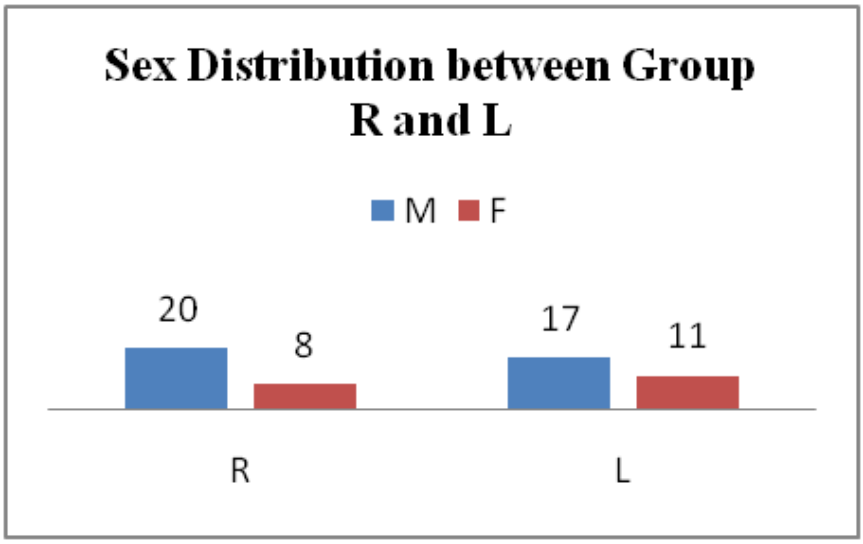
AGE				
GROUP	N	MEAN	SD	SE
R	28	46.5	16.68	3.15
L	28	44.68	11.31	2.13

Table 1: Age Distribution:



P value: 0.87 P value › 0.05 is not significant
CHART 1: AGE DISTRIBUTION
Table 1 and Chart 1 shows the mean age in Group R (Ropivacaine) and L (Levobupivacaine). P value › 0.05 is not significant TABLE 2: SEX AND ASA GRADE

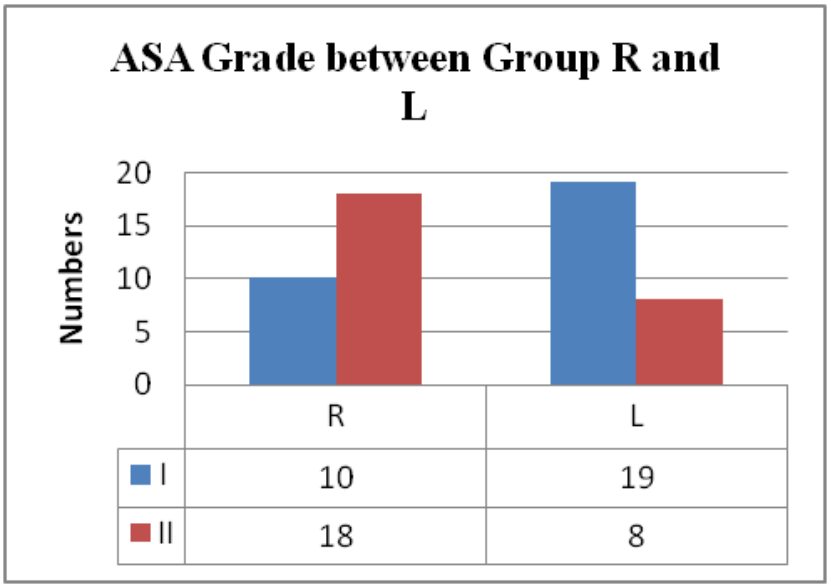
SEX	R	M	20
		F	8
	L	M	17
		F	11
ASA	R		
		I	10
		II	18
	L	I	19
		II	8



P value:068 P value › 0.05 is not significant

CHART 2: SEX DISTRIBUTION

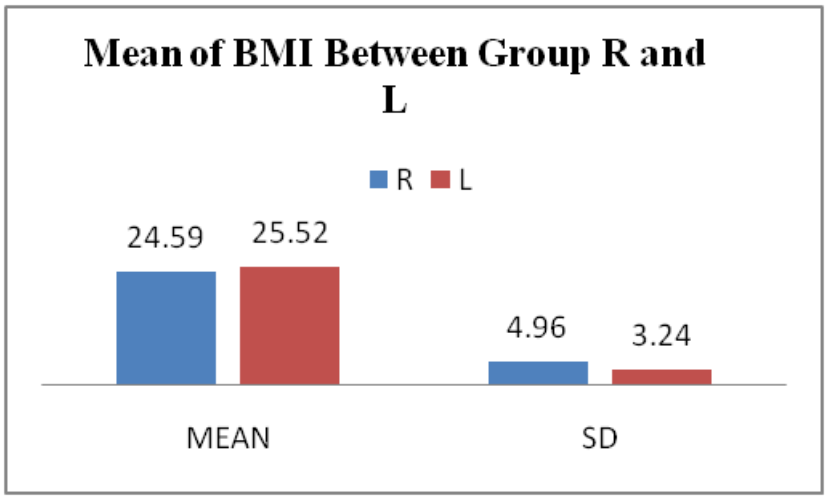
CHART 3: ASA GRADE I AND II DISTRIBUTION



2 and Chart 2 and 3 shows the distribution of Sex and ASA grade between Group R and L. P value › 0.05 is not significant. Both group patients were in ASA I and ASAII grades only.

TABLE 3: BMI

BMI	MEAN	SD
R	24.59	4.96
L	25.52	3.24



P value: 0.63 P value › 0.05 is not significant

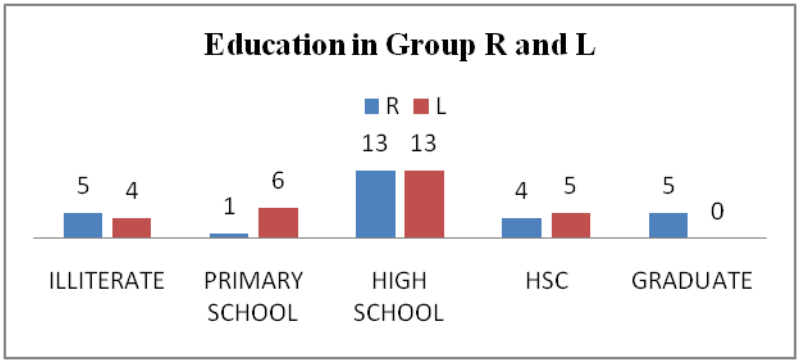
CHART 4: BMI DISTRIBUTION

Table 3 and Chart 4 displays the mean and standard deviation of BMI among Group R and L. P value › 0.05 is not significant

TABLE 4: EDUCATION

	EDUCATION	
	R	L
ILLITERATE	5	4
PRIMARY SCHOOL	1	6
HIGH SCHOOL	13	13
HSC	4	5
GRADUATE	5	0

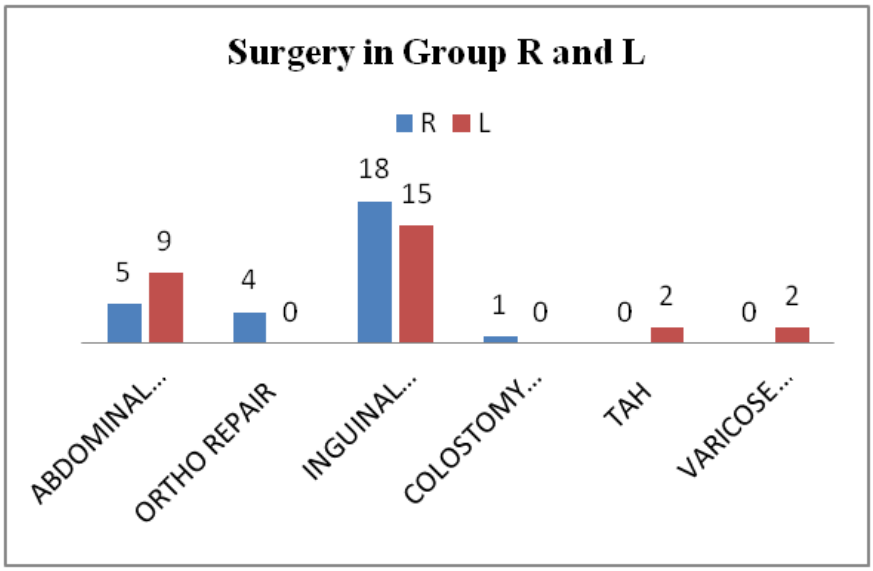
CHART 5: EDUCATION



P value › 0.05 is not significant

The Education qualification of patients in both group were similar (Table 4 and Chart 5). P value › 0.05 is not significant

CHART 6: TYPE OF SURGERIES



P value › 0.05 is not significant

SURGERY	R	L
ABDOMINAL HERNIA REPAIR	5	9
ORTHO REPAIR	4	0
INGUINAL HERNAI	18	15
COLOSTOMY CLOSURE	1	0
TAH	0	2
VARICOSE VEIN REPAIR	0	2

TABLE 5: TYPE OF SURGERIES

The type of surgeries in both group were similar (Table 5 and Chart 6). P value › 0.05 is not significant

SENSORY PROFILE:

TABLE 6: SENSORY BLOCK AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

SENSORY BLOCK			
TIME	R	L	p VALUE
5	7.07±2.58	11.07±1.01	0
10	5.71±1.78	9.64±1.09	0.04
15	5.21±1.57	8.29±1.69	0.78
20	4.86±1.38	7.29±1.74	0.09
25	4.79±1.37	6.57±1.31	0.98
30	4.79±1.37	6.07±1.01	0.02
60	4.79±0.99	6.21±1.13	0.09
90	4.86±1.00	7.07±1.58	0.01
120	5.57±1.47	8.00±1.96	0.32
150	6.79±2.13	9.07±1.67	0.98
180	7.71±2.91	10.14±1.53	0

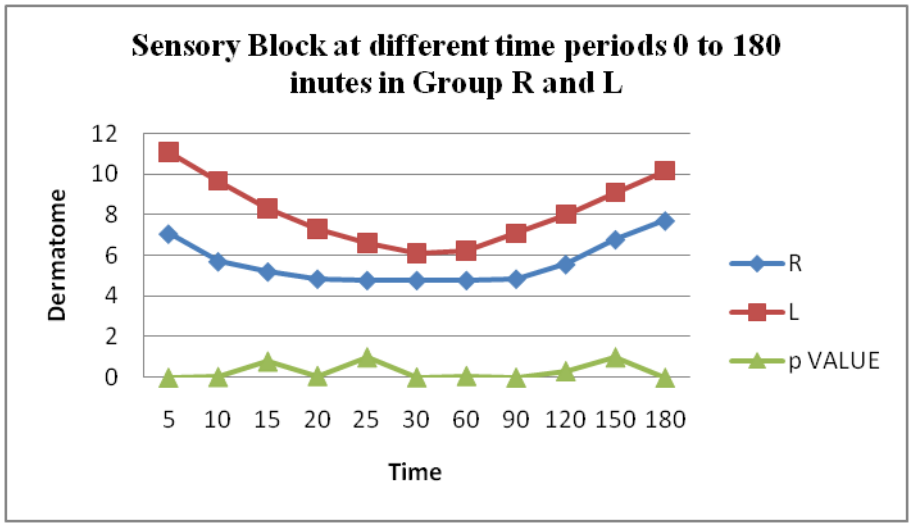


CHART 7: SENSORY BLOCK AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

The Sensory block (dermatome level) at different time period between 0 to 180 minutes among Group R and L are shown in the Table 6 and Chart 7.

TABLE 7: SENSORY VARIABLES/OBJECTIVES

SENSORY BLOCK VARIABLES	R	L	P VALUE
TT10	3.93±2.90	8.21±3.65	0
MD	4.64±0.95	5.64±1.44	0.36
TMD	13.29±11.32	22.5±5.0	0.65
TR	157.50±50.08	113.57±31.99	0.01
TTR	220.71±50.47	170.36±49.70	0
TPA	301.96±60.11	319.29±60.11	0.57
TCR	345.54±77.35	418.978.523±	0

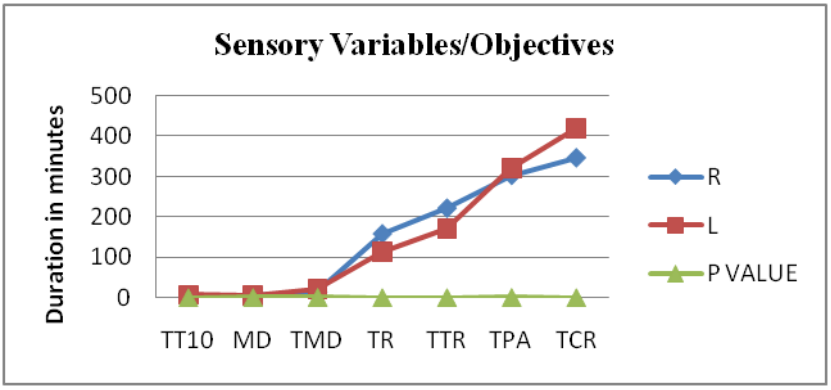


CHART 8 : SENSORY VARIABLES/OBJECTIVES

Table 7 and Chart 8 shows the mean time for onset of sensory block (TT10), mean values of maximum dermatome (MD) reached, time taken to attain maximum sensory level (TMD), time for 2 segment regression (TR), duration for regression of sensory block to dermatomal level T_{10} (TTR), total duration of analgesia (the time of request of analgesia by patient) (TPA) and time for complete reversal of sensory block (TCR) between Group R and L.

In our study the mean time for onset of sensory block (TT10) in ropivacaine (R) group was 3.93 min and 5.21 min in levobupivacaine (L) group ($P < 0.01$).

The mean values of maximum dermatome (MD) reached in R group and L group are 4.64 and 5.64 level respectively. (p value 0.008).In present study the time taken to attain maximum sensory level

(TMD) in two groups is similar, no statistically significant difference between the groups. (p value 0.652).The Time for 2 segment regression (TR) was found to be 157.50 min in R group and 113.57 min in L group, the p value being 0.001 with statistically significant difference. The duration for regression of sensory block to dermatomal level T_{10} (TTR) was 220.71 min in group R and 170.36 min in group L (p <0.05).Total duration of analgesia(the time of request of analgesia by patient) (TPA) in ropivacaine group was 301.96, whereas in levobupivine group it was 319.09.(p value 0.579). The time for complete reversal of sensory block (TCR) was 345.54 in ropivacaine group versus 418.93 in levobupivacaine group. The p value was statistically significant <0.05. (Table 7 and Chart 8)

MOTOR PROFILE:

TABLE 8: MOTOR BLOCK AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

MOTOR BLOCK			
TIME	R	L	P value
5	0.68±0.94	0.89±0.49	0
10	1.18±1.02	1.32±0.54	0.01
15	1.57±0.92	1.71±0.89	1
20	2.00±0.66	2.00±0.90	0.06
25	2.25±0.70	2.11±0.87	0.08
30	2.36±0.73	2.18±0.86	0.27
60	2.50±0.79	2.25±0.84	0.47
90	2.46±0.69	2.14±0.89	0.04
120	2.36±0.67	1.82±0.72	0.91
150	1.82±1.09	1.50±0.63	0.02
180	1.29±1.3	1.18±0.67	0

The table 8 shows the motor block as per MBS (Modified bromage score) at different time periods – from 0 to 180 minutes between Group R and L.

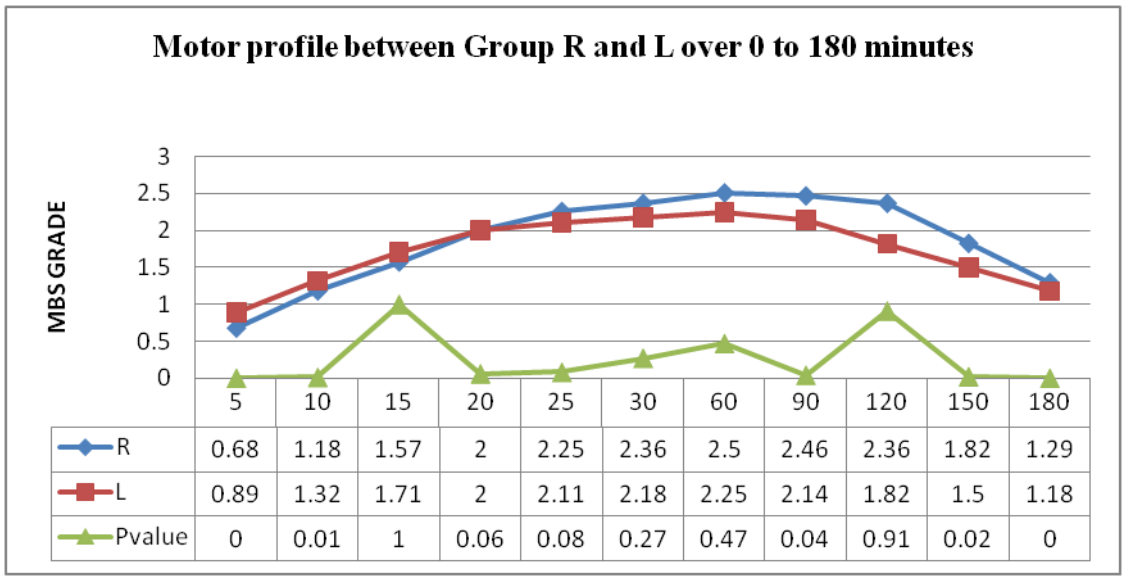


CHART 9: MOTOR BLOCK AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

The Chart: 9 displays the motor block as per MBS (Modified bromage score) at different time periods –from 0 to 180 minutes between Group R and L.

The onset of motor block (MO), regression of motor block (MR) and duration of motor block (TMD) was comparable in both the groups (P values 0.50, 0.84 and 0.53 respectively). The grade of motor

block as per MBS score was significantly different in both groups.(Mean 2.86±0.35in R vs2.21±0.87 in L)(p value:0.000) which is very highly significant.
The time taken to attain the maximum motor blockade (TTMBS2) was 40.18 min in group R and 17.86 min in group L.(p value of 0.043). The number of patients achieving MBS 3 in motor block is 71.4% vs 50 % in Group R and Group L respectively. The motor grade reached in group R is denser than in Group L.The number of patients achieving MBS 3 in motor block is more in group R. The time taken to attain the maximum motor blockade is slower in R group. Duration of motor blockade was assessed from the time of administration of drug to complete motor recovery. In our study, the mean duration of motor block in R group was146.25 ±48.58 min and in L group was 160.71 ±46.64 min (p value>0.05).(Table 9 and Chart 10)

TABLE 9: MOTOR VARIABLES/OBJECTIVES

MOTOR BLOCK VARIABLES	R	L	p VALUE
MO	24.64	16.43	0.5
MR	170.54	177.14	0.84
TTMBS≥2	146.25	160.71	0.53
MAXIMUM MBS	2.86	2.21	0
TIME TAKEN FOR MAX MBS	40.18	17.86	0.004

CHART 10: MOTOR VARIABLES/OBJECTIVES

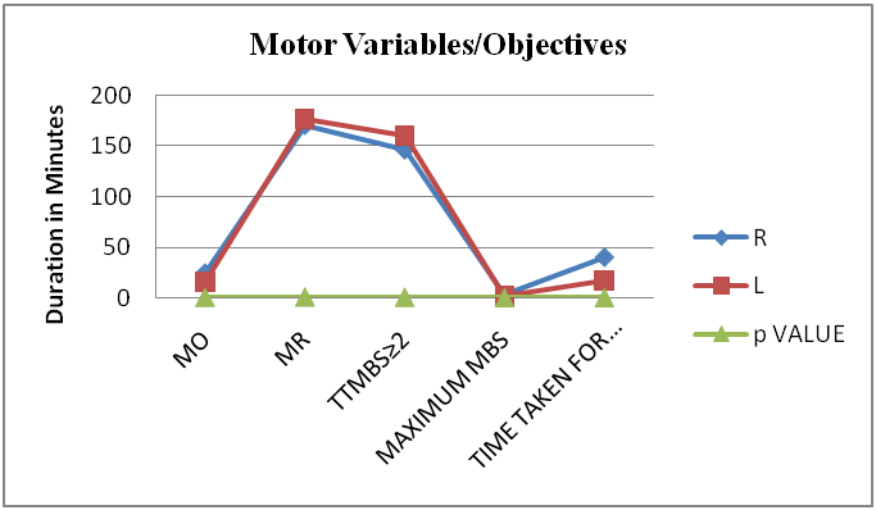


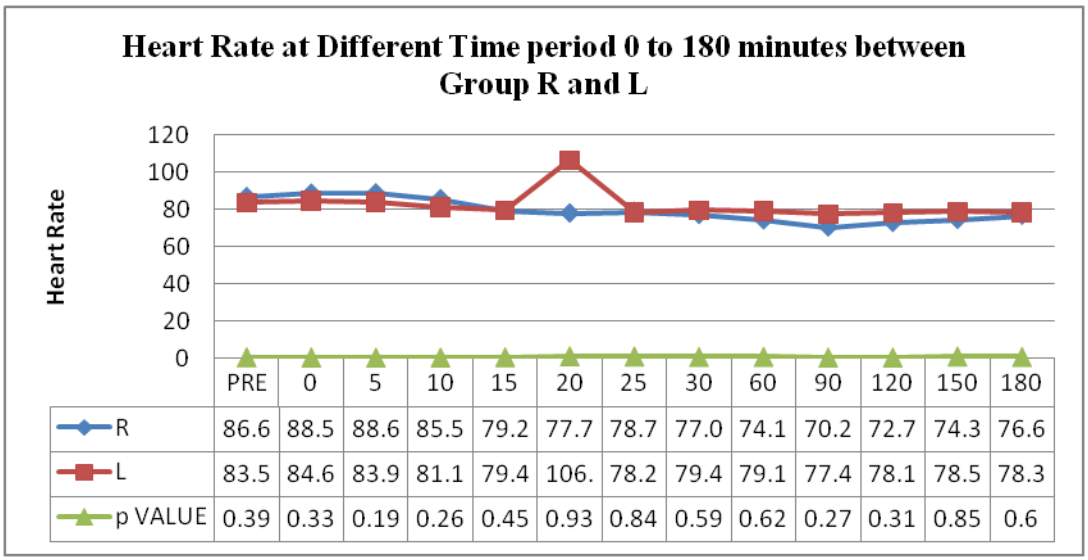
Table 9 and Chart 10 shows the time for motor onset(as defined by Modified Bromage Scale ≥2 (MO) ,time for motor reversal <2 (MR),Time to reach MBS ≥2 (TTMBS2), maximum MBS reached and time taken to reach maximum MBS between Group R and L**.**

HAEMODYNAMIC PROFILE:

TABLE 10: HEART RATE AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

HEART RATE			
TIME	R	L	p VALUE
PRE	86.68±19.22	83.54±17.31	0.39
0	88.54±19.11	84.61±17.05	0.33
5	88.64±24.43	83.93±17.68	0.19
10	85.54±16.69	81.18±19.39	0.26
15	79.25±16.73	79.43±18.77	0.45
20	77.79±14.04	106.21±154.71	0.93
25	78.75±15.63	78.21±16.66	0.84

30	77.04±14.77	79.46±16.34	0.59
60	74.11±14.05	79.11±15.28	0.62
90	70.29±13.47	77.43±15.43	0.27
120	72.75±14.06	78.11±16.25	0.31
150	74.36±14.02	78.50±14.18	0.85
180	76.64±15.37	78.32±13.19	0.6



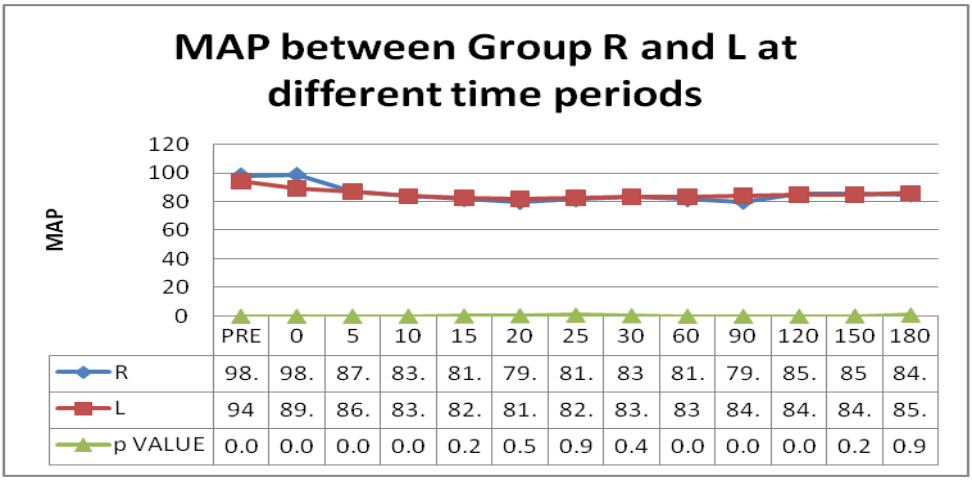
	PRE	0	5	10	15	20	25	30	60	90	120	150	180
R	86.6	88.5	88.6	85.5	79.2	77.7	78.7	77.0	74.1	70.2	72.7	74.3	76.6
L	83.5	84.6	83.9	81.1	79.4	106.	78.2	79.4	79.1	77.4	78.1	78.5	78.3
p VALUE	0.39	0.33	0.19	0.26	0.45	0.93	0.84	0.59	0.62	0.27	0.31	0.85	0.6

CHART 11: HEART RATE AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

Table 10 and Chart 11 display heart rate at different time period between 0 to 180 minutes between Group R and L.

TABLE 11: MEAN ARTERIAL PRESSURE (MAP) AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

MAP			
TIME	R	L	p VALUE
PRE	98.40±15.71	93.97±10.62	0.05
0	98.80±15.65	89.16±10.28	0.01
5	87.090±14.70	86.68±10.62	0.05
10	83.68±15.68	83.64±10.83	0.08
15	81.47±17.18	82.52±12.56	0.24
20	79.40±10.71	81.81±12.76	0.53
25	81.27±15.46	82.48±12.82	0.9
30	83.00±17.75	83.37±12.51	0.42
60	81.29±20.84	82.98±9.51	0.06
90	79.66±15.74	84.05±8.97	0.02
120	85.34±20.80	84.85±10.98	0.01
150	85.00±14.71	84.65±11.42	0.23
180	84.71±13.29	85.79±11.74	0.93



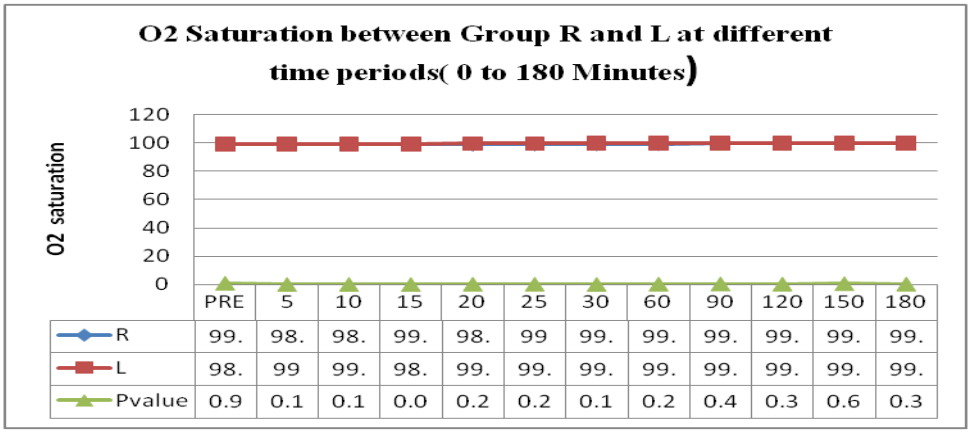
	PRE	0	5	10	15	20	25	30	60	90	120	150	180
R	98.	98.	87.	83.	81.	79.	81.	83	81.	79.	85.	85	84.
L	94	89.	86.	83.	82.	81.	82.	83.	83	84.	84.	84.	85.
p VALUE	0.0	0.0	0.0	0.0	0.2	0.5	0.9	0.4	0.0	0.0	0.0	0.2	0.9

CHART 12: MEAN ARTERIAL PRESSURE (MAP) AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

Table 11 and Chart 12 display Mean Arterial Pressure (MAP) at different time period between 0 to 180 minutes between Group R and L.

TABLE 12: ARTERIAL OXYGEN SATURATION AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

O2 SATURATION			
TIME	R	L	Pvalue
PRE PROCEDURE	99.14±2.52	98.86±2.17	0.91
5	98.93±1.08	99±2.43	0.1
10	98.93±1.18	99.07±1.94	0.17
15	99.07±1.05	98.93±2.38	0.03
20	98.82±1.61	99.39±1.54	0.26
25	99±1.36	99.36±1.22	0.25
30	99.14±1.22	99.61±1.13	0.1
60	99.18±1.56	99.46±1.20	0.29
90	99.75±0.79	99.64±1.54	0.42
120	99.86±0.44	99.75±1.32	0.35
150	99.71±0.85	99.68±1.36	0.68
180	99.79±0.56	99.64±1.89	0.35



	PRE	5	10	15	20	25	30	60	90	120	150	180
R	99.	98.	98.	99.	98.	99	99.	99.	99.	99.	99.	99.
L	98.	99	99.	98.	99.	99.	99.	99.	99.	99.	99.	99.
Pvalue	0.9	0.1	0.1	0.0	0.2	0.2	0.1	0.2	0.4	0.3	0.6	0.3

CHART 13: ARTERIAL OXYGEN SATURATION AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

Table 12 and Chart 13 show Oxygen saturation at different time period between 0 to 180 minutes between Group R and L.

TABLE 13: USE OF IV FLUIDS, EPHEDRINE AND SUPPLEMENT

	R	L
IV	1.55	2.05
E	10.8	60
SUP	2	1.93

The table 13 depict use of Intravenous fluid (IV) ,Ephedrine and any supplementation in Epidural drug usage between Group R and L.

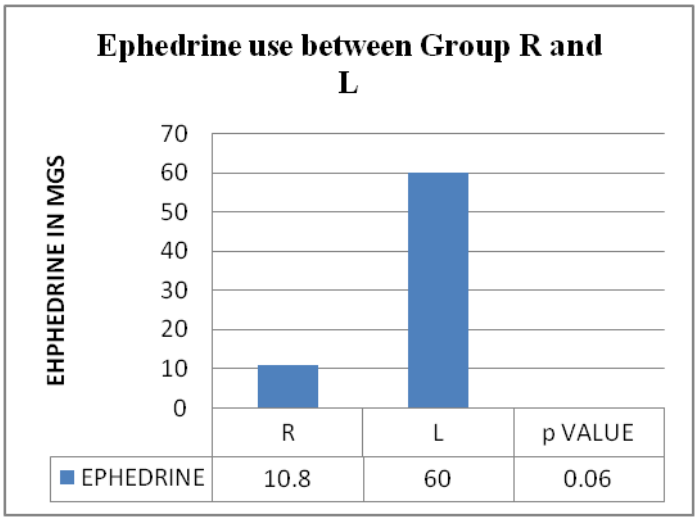


Chart 14: Ephedrine used between Group R and L

The charts 14 show Ephedrine usage between Group R and L.

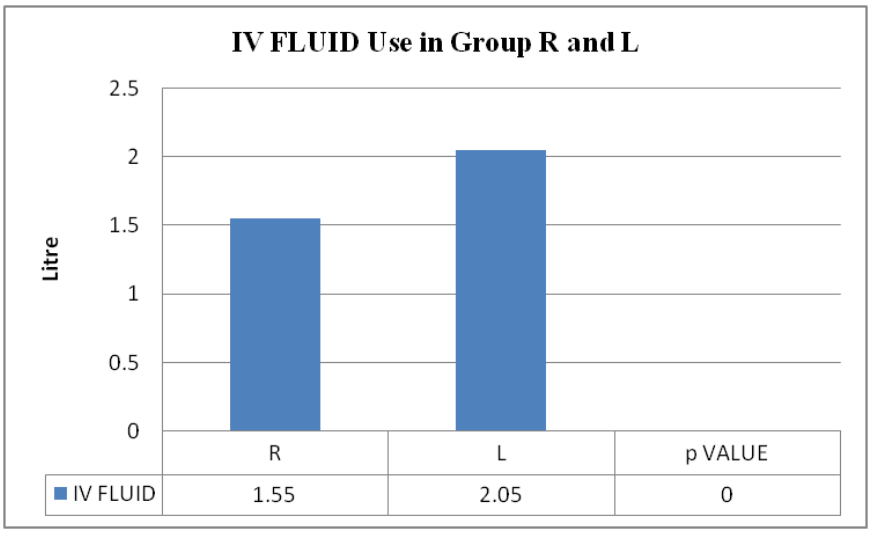


Chart: 15 Use of Intravenous (IV) fluids between Group R and L

The Chart 15 display IV fluids used in Litre between Group R and L.

The need for rescue analgesics, total IV fluid requirement and ephedrine usage was similar in both the groups. The haemodynamic profile MAP and HR were similar. The time of request for post-operative analgesia was similar in both group.(Table 13 and Chart 14 and 15)

Discussion:

Ropivacaine and Levobupivacaine are pure S (-) isomers with similar physicochemical properties. Levobupivacaine is more lipophilic than ropivacaine hence it is theoretically more potent. But

Levobupivacaine has only a slightly greater protein binding than ropivacaine (95% vs 90%-92%). Therefore, clinical studies do not consistently show a longer duration of action with the S-isomer of bupivacaine. With the changes in molecular structure, it was hoped that ropivacaine and levobupivacaine would be less cardiotoxic. But (*S*)-enantiomers of mepivacaine and bupivacaine are metabolized by the liver more slowly than their (*R*)-enantiomers, which leads to greater systemic accumulation with prolonged infusions.[13] Ropivacaine and levobupivacaine were formulated to use stereo selectivity and limit CVS and CNS toxicity. Preclinical animal and volunteer studies showed Ropivacaine and levobupivacaine has a lower systemic toxicity than bupivacaine and has a shorter duration of action due to the lower affinity of the S (-) isomer to the cardiac sodium channels compared to the R(+) isomer.[14]
Theoretically and experimentally, some differences between ropivacaine and levobupivacaine have been observed, but the effects of these properties on clinical practice have not been shown..
The clinical trials that have compared racemic bupivacaine, ropivacaine and levobupivacaine gives the evidence that both levobupivacaine and ropivacaine have a clinical profile similar to that of racemic bupivacaine and that the differences reported between the three anesthetics are mainly due to the slightly different anesthetic potency, with racemic bupivacaine > levobupivacaine > ropivacaine. However, the reduced toxic potential of the two pure left isomers encourages their use in the clinical situations in which the risk of systemic toxicity related to either overdosing or unintended IV injection is high such as during epidural or peripheral nerve blocks.[1]
The age, sex, educational qualification and BMI of the patients included in both the groups were comparable with no statistically significant difference.

Sensory block
In our study the mean time for onset of sensory block in ropivacaine(R) group was 3.93 min and 5.21 min in levobupivacaine (L) group. The time to reach T10 dermatome in ropivacaine group was faster. There was very highly significant difference in the sensory block onset time between the groups ($P < 0.01$). In a study done by A Suri et al the onset time of analgesia was shorter in group R than group L(similar to our study), and the duration of sensory block was longer in group R than group L.[15] Maheshwari et al (2016) conducted a similar study to evaluate the efficacy of 15 mL of levobupivacaine 0.5% with that of 15 mL of ropivacaine 0.75% in patients undergoing lower limb orthopaedic surgeries under epidural anaesthesia. Time to achieve sensory onset was significantly lower in Ropivacaine Group (17.86 ± 2.51) as compared to Group Levobupivacaine (26.14 ± 2.45) with p value ($p<0.05$) which is in accordance to our present study.[16] Finucane *et al*. found that onset time for sensory block to T12 was shorter in 0.75% ropivacaine group[17]. Karki et al (2017), did a comparative study of epidural levobupivacaine 0.5% and ropivacaine 0.75%. There was no significant difference in the sensory onset time between group R and L ($p>0.05$) which is in contrary to our present study.[18]
The mean values of maximum dermatome reached in R group and L group are 4.64 and 5.64 level respectively. The p value was found to be 0.008 where there was statistically significant difference. In present study the time taken to attain maximum sensory level in two groups is similar, no statistically significant difference between the groups. In a study conducted by Kountoudi et al, where they compared epidural Levobupivacaine 0.5% with Ropivacaine 0.5% for inguinal hernia repair procedures in 30 patients, there was no difference as far as the level of sensory block is concerned.[19]
The time taken to reach maximum dermatome level was found to be 13.29 min in R group and 22.5 min in L group, the p value being 0.652, which shows there was no statistically significant difference. In a study by Brockway et al, where they compared different concentrations of Ropivacaine (0.5%, 0.75%, 1%) with Bupivacaine (0.5%, 0.75%),they stated that there is little difference between the groups with respect to speed of onset of sensory block.[20] In a study conducted by Finucane et al, where they compared different concentrations of Ropivacaine (0.5%, 0.75% and 1%) and Bupivacaine in concentration of 0.5% in 25 ml volume in patient undergoing lower abdominal surgeries with epidural anaesthesia, they observed no difference between the groups in terms of

maximum sensory block level.[17] However when duration of motor and sensory blocks were compared, as the ropivacaine dose was increased, they obtained a significant dose response effect.
The Time for 2 segment regression was found to be 157.50 min in R group and 113.57 min in L group, the p value being 0.001 with statistically significant difference. Concepcion *et al* found a mean time for two segment regression as 164 ± 22 min for 0.75% ropivacaine, which was comparable to present study[21]. The duration for regression of sensory block to dermatomal level T_{10} was 220.71 min in group R and 170.36 min in group L, p value being <0.05,which shows there was statistically significant difference.
Total duration of analgesia (the time of request of analgesia by patient) in ropivacaine group was 301.96, whereas in levobupivine group it was 319.09.The p value was 0.579, showing no significant statistical difference. Maheshwari et al conducted a similar study and found that the duration of sensory block was significantly higher in Group R(173.29 ± 6.29 min) as compared to Group L (156.71 ± 6.96 min) with p value (p<0.05).[15] In a study conducted by Concepcion et al, where they compared three different concentrations of Ropivacaine (0.5%, 0.75%, 1%),the duration of analgesia with 0.75% Ropivacaine is 255±73 minutes which is similar to our result.[21] In a study conducted by Simon et al, where they compared the clinical profile of levobupivacaine in epidural route in different age groups, the duration of analgesia with 0.75% levobupivacaine is 327±69 minutes.[22] The longer duration of analgesia here could be explained due to use of higher concentration of levobupivacaine. Maheshwari et al (2016) conducted a similar study and found that time for first rescue analgesia was significantly longer (p<0.001) in group II (6.43±2.12 hr) as compared to group I (4.97± 0.89 hr) which is in accordance to our study.[16]
In a study by Brockway et al, the duration of analgesia was increased by increasing the concentration of both drugs This had minimal effect on onset time or extent of block.[20] The time for complete reversal of sensory block was 345.54 in ropivacaine group versus 418.93 in levobupivacaine group. The p value was statistically significant <0.05.

Motor block

The onset of motor block is defined as ≥ modified bromage grade 2.The time to reach MBS grade 2 was 24.64 min in group R and 16.43 min in group L, with p value 0.502 which shows there was no statistically significant difference. This finding was similar to finding by Yang et al Regression of Motor block to MBS grade <2 was found to be 170.54 min in group R and 177.14 min in group L p value being 0.84 (statistically not significant).[23] Thus our study finds that the regression of motor block was quick in R group and hence this drug can be used for surgeries which require early ambulation and obstetric analgesia.
Duration of motor block was similar in both the groups(p vale being 0.53 and mean values being 148.25 min in group R and 160.71 min in group L). Gandhi et al (2020) conducted a similar study on epidural levobupivacaine 0.5% (group A) and ropivacaine 0.75% (group B) with fentanyl 100 mcg (2ml) on patients undergoing elective lower limb orthopaedic surgeries. Motor blockade mean onset time was 20+3.35 minutes and 20.2+3.64 minutes in group A and group B respectively which is statistically not significant (p>0.05) and is similar to our study. The mean duration of motor block in group A was 248.4+13.60 minutes and 247.8+13.29 minutes in group B which also was not statistically significant (p>0.05) and is in accordance to our present study[24].
The grade of motor block as per MBS score was significantly different in both groups..(Mean 2.86±0.35in R vs2.21±0.87 in L)(p value:0.000) 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 40.18 min in group R and 17.86 min in group L. This is statistically highly significant. (p value:0.004). Olofsen, Erik et al noted that Ropivacaine had slower onset and regression than Levobupivacaine. This may be due to its lower lipid solubility.[22]
The number patient achieving MBS 3 in motor block is 71.4% vs 50 % in Group R and Group L respectively. This implies lesser grade motor block is observed in L group in this study.The motor grade reached in group R is denser than in Group L. The number of patients achieving MBS 3 in motor block is more in group R. The time taken to attain the maximum motor blockade is slower in R group. Duration of motor blockade was assessed from the time of administration of drug to complete

motor recovery. In our study, the mean duration of motor block in R group was146.25 ±48.58 min and in L group was 160.71 ±46.64 min. The variations in the time duration of motor block between ropivacaine and levobupivacaine group were not significant (*P* >0.05). Brockway *et al*. showed thatonset of motor block produced by ropivacaine was slower. The mean duration of motor blockade of ropivacaine is lower than that of levobupivacaine.[20]

In a study conducted by Peduto et al, where they compared epidural levobupivacaine 0.5% with ropivacaine 0.75% for lower limb procedures, it was concluded same clinical profile is seen in both drugs.[25] It was observed by Karz J A et al that, no significant difference was found in motor or sensory effects with 0.5% Bupivacaine with 0.75% Ropivacaine given epidurally which proves their equipotency at different concentration. [26]

In our study the motor onset was similar but the sensory onset was faster in ropivacaine group and it was statistically significant. Though clinically the time to reach maximum dermatomal sensory block was faster in ropivacaine group, there was no statistical significant difference between the groups (P> 0.05). Also, 0.75% ropivacaine produces a motor block deeper than that produced by levobupivacaine 0.5% but duration of motor block was longer in L group than R group clinically on observation but lacking statistical significance.

Haemodynamic profile

There is no statistically significant difference in heart rate between the two groups at various time intervals. No patient in either group develops significant bradycardia. There was no statistically significant differences in systolic blood pressure, diastolic blood pressure, mean arterial pressure monitored at various intervals between the two groups The heart rate and MAP of the patients in both the groups were comparable intra operatively at different periods with no clinical or statistically significant differences.

Senard et al, concluded that after equal doses of levobupivacaine and Ropivacaine administered via postoperative patient controlled epidural analgesia, the efficacy of both the drugs were similar except that the ropivacaine receiving patients could ambulate earlier.[27]

There were no clinically significant differences in the total amount of IV fluids infused, ephedrine used (4 in each group) and rescue analgesics given intraoperatively among both the groups.

Complications

Kumar GS et al says, 7% patients had hypotension, 3% had vomiting and 3% nausea in ropivacaine group.[28] Brockway *et al*. found similar side effect- the most common being backache (23%) followed by nausea (14%) and vomiting (2%).[20] Finucane *et al*. reported nausea, vomiting, hypotension, headache, and backache as the most common adverse events in their study, which was similar to our study. [17]Levobupivacaine toxicity is intermediary to ropivacaine and bupivacaine.[19, 29] It has CVS and CNS side effects as compared to Ropivacaine, when administered to volunteers.[30-34]

In our study there was no statistical difference in incidence of complications between the groups. The complication encountered in our study was hypotension. None of the cases encountered other expected side effects like- bradycardia, nausea, vomiting and shivering.

Conclusion:

Both 0.5% levobupivacaine and 0.75% Ropivacaine produced effective epidural anaesthesia. Ropivacaine produces lesser duration of motor block hence they can be used for labor analagesia. Both Levobupivacaine and ropivacaine causes less cardio and neurotoxicity when compared to racemic mixture buivacaine, hence both drugs can be widely used in epidural and regional block techniques where large volume of drug is used.

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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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Author Contribution Statement:
Dr. Ashok Kumar Balasubramanian conceptualized, designed, collected data and prepared the manuscript. He analysed the datas with the help of statistician Professor Dr. Ravanan, Joint director of Collegiate Education, Chennai Region.

Conflict of Interest:
None

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