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Chirality in Local Anaesthetics: "Comparison of Efficacy and Tolerability of Epidural 0.5% Levobupivacaine, Ropivacaine 0.75% and 0.5% Racemic Mixture Bupivacaine in Patients coming for Elecive Lower Abdominal and Lower Limb Surgeries

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ABSTRACT:

Aim:

The aim of the study is to compare the efficacy and tolerability of 0.5% Levobupivacaine, 0.75% Ropivacaine and 0,5% Racemic Mixture Bupivacaine, in patients undergoing lower abdominal and lower limb surgery.84 patients, ASA grade 1 and 2, were randomised to receive an epidural injection of study drug (17 ml 0.5% Levobpivacaine in Group L,17 ml of 0.75% Ropivacaine in group R and 17 ml 0.5% Racemic Mixture Bupivacaine in group B).

Objective:

The objective of the study was to compare sensory, motor, haemodynamic and side effect profile of the 3 drugs.

Result:

In our study comparing the efficacy and tolerability of epidural 0.5% Levobupivacaine,0.75% Ropivacine and 0.5% % Racemic mixture Bupivacaine**(Group L vs Group R vs Group B)** the mean time for onset of sensory block is faster in R group when compared to group L and B (p Value <0.05). The maximum dermatome reached (higher), the time taken to attain maximum sensory level, the two segment regression and the duration for regression of sensory block to T_{10} were faster in group R. Total duration of analgesia in R group was 301.96 versus 222.86 in B group versus 319.29 min in group L (p value <0.05).The time for complete reversal of sensory block was 345.54 in R group versus 400.71 in B group versus 418.95 min in group L (p value <0.05). 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 0.53, 0.06 and 0.11 respectively).The grade of motor block as per MBS score was significantly different in three groups.(Mean 2.86±0.35in R vs2.21±0.87 in L vs 2.65±0.66)(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, 17.86 min in group L and 23.57 min in group B. (p value of 0.04).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.

Conclusion:

All three groups-0.5% levobupivacaine, 0.75% Ropivacaine and 0.5% Racemic mixture Bupivacaine produced effective epidural anaesthesia. Ropivacaine produces lesser duration of

motor block hence they can be used for laboranalagesia. 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.

KEY WORDS:

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

INTRODUCTION:

Neuraxial anaesthesia is a technique in which the spinal nerves are temporarily blocked leading to sensory and motor paralysis. After a specific time, depending on the drug and its concentration, the patient develops complete sensory and motor recovery. Majority of central neuraxial blocks are performed by two techniques - Subarachanoid block and Epidural block. Theuseofregionalanaesthesiaand quest for new and safer local anaesthetics hasincreasedinrecentyear**s.**Althoughgreatimprovements havebeenmade, the toxicity issuescontinuetobeanimportantconsideration.[1]Bupivacaine, the widely used local anaesthetic in regional anaesthesia is available in a commercial preparation as a racemic mixture (50:50) of its two enantiomers, levobupivacaine, S (−) isomer and dextrobupivacaine, R (+) isomer. The fatal central nervous system (CNS) and cardiovascular adverse reactions reported in the literature after inadvertent intravascular injection or intravenous regional anaesthesia have been linked to the dextro form of Bupivacaine. [1, 2]

Most organic molecules are chiral ones, and this is usually determined by the presence of a carbon atom bonded to four different molecules. When a molecule has a chiral centre it is possible to obtain two different three-dimensional structures (stereoisomers) that remain different with respect to each other in the way that a right hand will not fit properly into a left-handed glove. A solution of bupivacaine contains equal amounts of the two enantiomers and is called racemic solution.The technological advancements allowed the production of solutions containing only one enantiomer of a chiral molecule, which is optically pure. As most of the amide local anaesthetics are chiral molecules, the pure S (−) enantiomers of bupivacaine like ropivacaine and levobupivacaine were thus introduced into the clinical anaesthesia practice. Although the physicochemical properties of such molecules are identical, significant differences exist in their interaction with biological receptors, the conformation of which favours interactions with one form over interactions with the other. This is important for amide local anaesthetics because it has been demonstrated that the levorotatory isomers were shown to have a safer pharmacological profile[1, 2] with less cardiac and neurotoxic adverse effects.[3, 4] The decreased toxicity of levobupivacaine is also attributed to its faster protein binding rate.[5] Animportantaspectof CNS and CVS toxicityisthat the receptor involvesstereo-specificity. R- and S- enantiomers of local anesthetics have been demonstrated to have a different affinity for the different ion channels of sodium, potassium, and calcium and this results in a significant reduction of central nervous system and cardiac toxicity of the S-enantiomer as compared with the R-enantiomer [4].The reduced toxic potential of the two pure left-isomers is used in the clinical situations where the risk of systemic toxicity is high as in, either overdosing or unintended intravascular injection, such as during epidural or peripheral nerve blocks. The studies that have compared these three local agents supports the evidence that all three study drugs have a similar clinical profile.The differences seen between the three anesthetics are mainly related to the slight difference in their anesthetic potency (racemic bupivacaine > levobupivacaine > ropivacaine). Many animal and

human volunteer studies have investigated their toxicology and clinical profiles and observed some differences, but the effects of these properties on clinical practice have not been done extensively. Again, very few clinical studies comparing efficacy of epidural levobupivacaine, ropivacine and racemic bupivacaine are there in literature. In this study we have made an attempt to compare the efficacy of equipotent local analegesic dose of levobupivacaine 0.5%, 0.75% Ropivacaine and racemic mixture of bupivacaine 0.5% for epidural anaesthesia for lower abdominal and lower limb surgeries.It is important to go back to basic science-anatomy,physiology, pharmacology and molecular level concepts, as its believed going back to basic science is essential to come out with newer thoughts and ideas that would motivate the scientific world to bring newer techniques,equipment ,drugs,drug delivery method etc...

AIM AND OBJECTIVES

AIM

In this study we have compared the efficacy of levobupivacaine 0.5%, 0.75% Ropivacaine and racemic mixture of Bupivacaine 0.5% for epidural anaesthesia for lower abdominal and lower limb surgeries. The study objectives were:

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

This study was approved by the Scientific Review Board of Saveetha Medical College and Institutional Ethics committee of Saveetha Medical College(Number: 009/06/2023/IEC/SMCH). Appropriate permission was taken from the hospital authorities for data collection. Written informed consent from study participants, voluntariness and confidentiality of data was assured. The study was carried out at Saveetha medical college Hospital from 2016 to 2024. During covid pandemic no data was collected.

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

After obtaining institutional ethical committee's approval and written informed consent, 84 patients belonging to both sex, who were scheduled to undergo lower abdominal surgery with epidural anaesthesia were included.Patients were randomized into three groups group R, group L and group B, by computer generated random numbers. The study was blinded (Patient and the anaesthesia provider were blinded of the groups).

Patients were randomized into three groups group R, group L and group B, 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

Group B- Received 17 ml 0.5% Racemic Bupivacaine

All the patients were visited on the pre-operative day and informed consent was obtained.

The sequence of events in the theatre was explained.

Before induction of epidural anaesthesia and after confirming adequate starvation, patient was preloaded with 500 ml of Ringer Lactate solution. After getting the patient on table, NIBP was attached. Continuous monitoring of ECG,HR 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 0.75% Ropivacaine over a period of 5 minutes. (6ml 1 min wait, 6ml 1 min wait and 5ml)

Group L: received 17 ml 0.5% Levobupivacaine over a period of 5 minutes. (6ml 1 min wait, 6ml 1 min wait and 5ml)

Group B: received 17 ml 0.5% Bupivacaine over a period of 5 minutes. (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_2were 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% of baseline value 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. The time taken for two segment regression was also noted. 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 Bromagescale 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 simple to apply in a clinical setting and analyses movement in various muscle groups. It is a qualitative measure of spread and intensity of block. Mechanical measurement of the isometric muscle force (IMF) in a single muscle group is a

more valid measurement of intensity of motor block, although it is difficult to apply in the clinical situation.

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.

15.3 STATISTICAL METHOD APPLIED

Statisticalanalysiswasdoneusing latest SPSSversion 29.0.Descriptivestatisticswasdonebycalculatingmean,standarddeviation,rangeandproportionappropriately.The inferentialstatistics (testof significance)was doneusing unpairedt-test andchi-squaretest. The comparision between three groups were carried out by ANNOVA.

p- value:itistheprobabilityrateat0.05levelofsignificanceforcorrespondingdegreefreedom.

p>0.05isnotsignificant

p<0.05issignificant

p<0.01 is highlysignificant

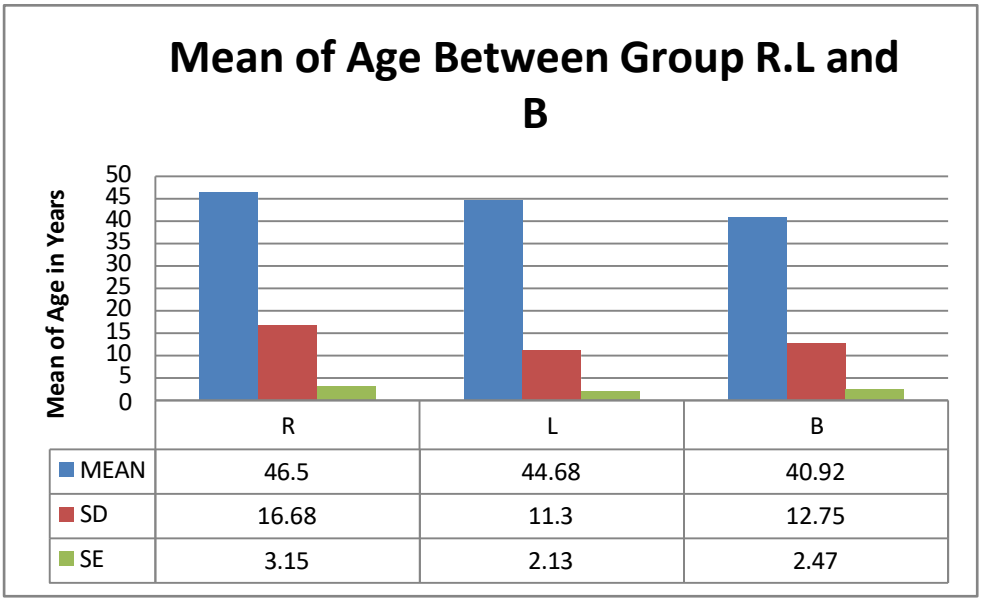
RESULTS:

DEMOGRAPHIC PROFILE:

The age, sex, ASA, educational qualification and BMI of the patients included in Ropivacaine(R), Levobupivacaine(L) and Racemic Mixture Bupivacaine(B) groups were comparable with no statistically significant difference.(Table 1,2,3 ,4) and (Chart 1,2,3,4,5).

Table 1: Age Distribution:

GROUP	MEAN	SD	SE
R	46.5	16.68	3.15
L	44.68	11.3	2.13
B	40.92	12.75	2.47



P value: 0.30 P value › 0.05 is not significant

CHART 1: AGE DISTRIBUTION

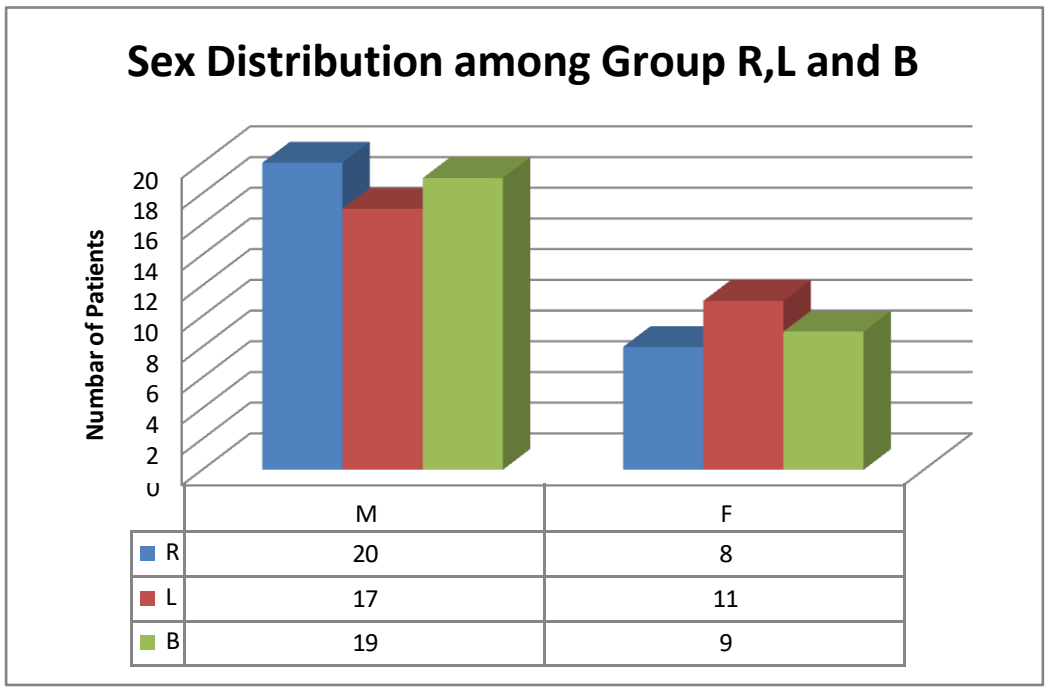
Table 1 and Chart 1 shows the mean age in Group R (Ropivacaine) ,L (Levobupivacaine) and Racemic Mixture Bupivacaine(B) . P value › 0.05 is not significant.

TABLE 2: SEX

SEX	R	L	B
M	20	17	19
F	8	11	9

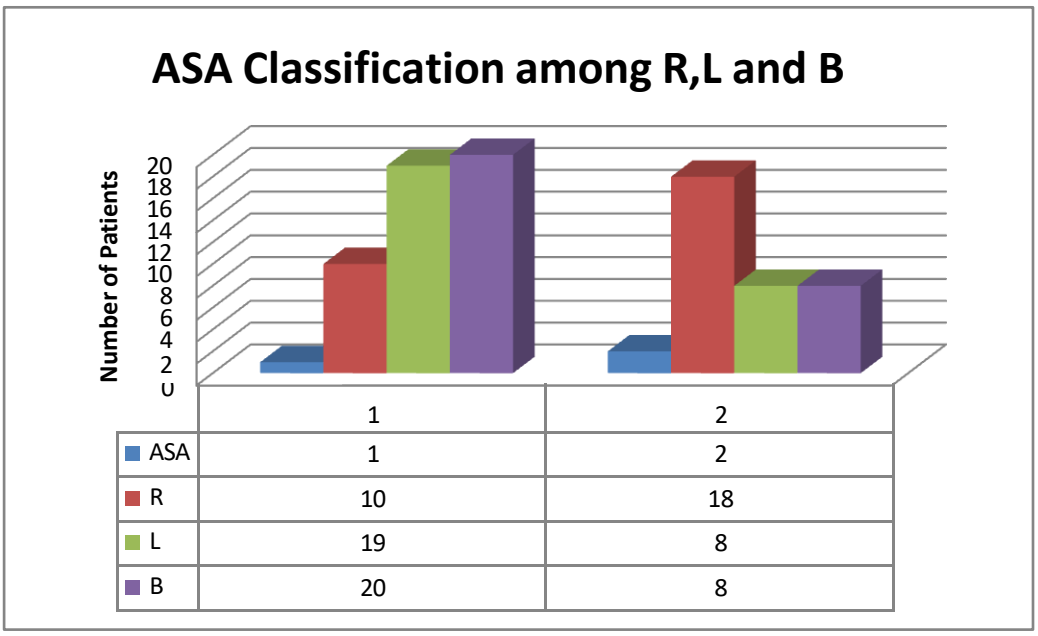
TABLE 3: ASA GRADE

ASA	R	L	B
1	10	19	20
2	18	8	8



P value: 068 P value › 0.05 is not significant

CHART 2: SEX DISTRIBUTION



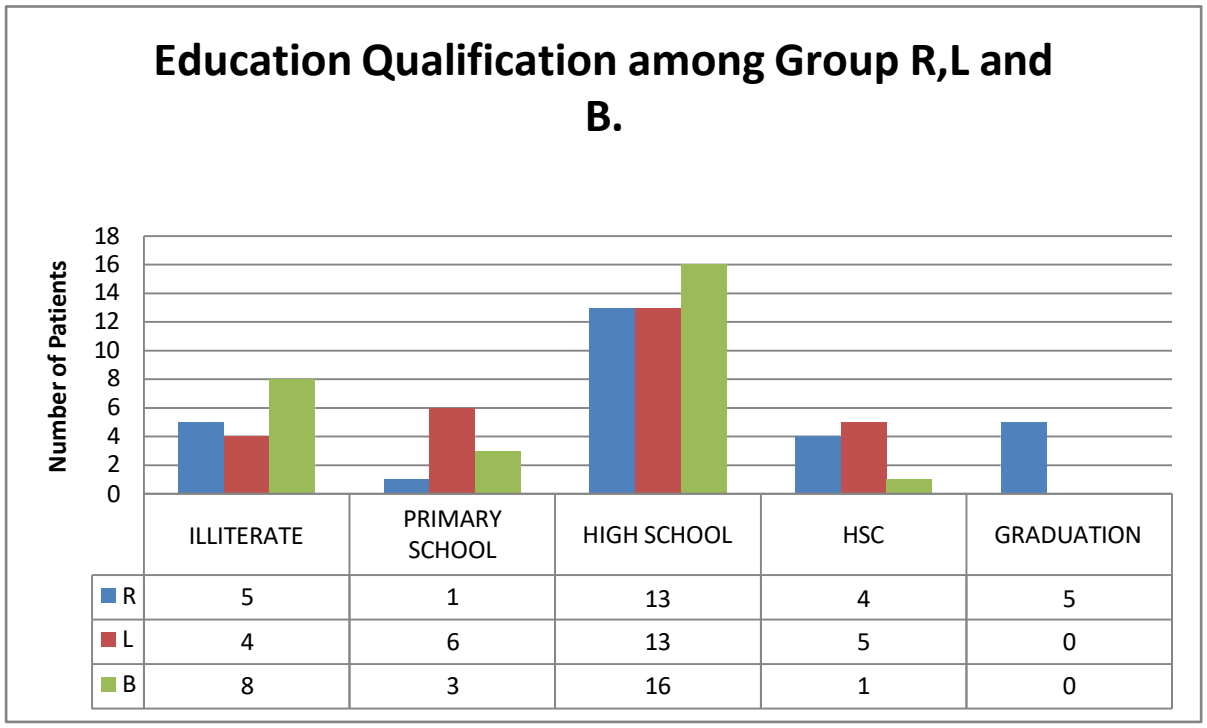
P value: 009 P value › 0.05 is not significant

CHART 3: ASA DISTRIBUTION

TABLE 4: EDUCATION

EDUCATION	R	L	B
ILLITERATE	5	4	8
PRIMARY SCHOOL	1	6	3
HIGH SCHOOL	13	13	16
HSC	4	5	1
GRADUATION	5	0	0

CHART 4: EDUCATION

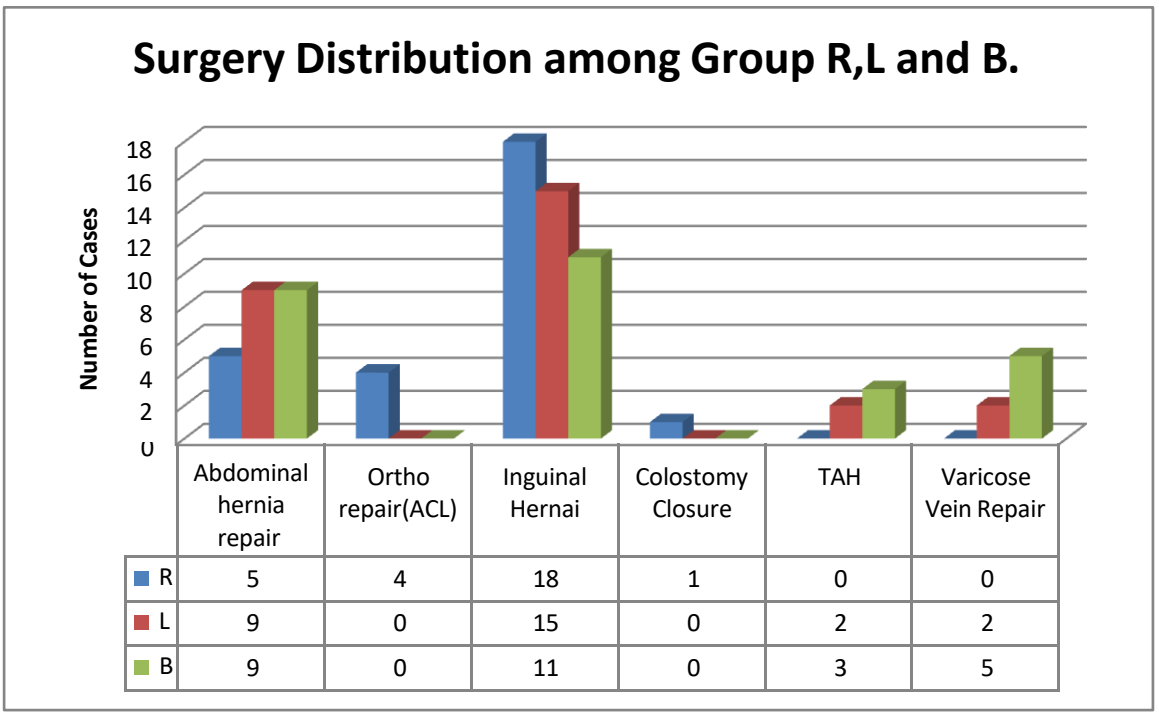


P value 0.019 P value › 0.05 is not significant

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

TABLE 5: TYPE OF SURGERIES

SURGERY	R	L	B
Abdominal hernia repair	5	9	9
Ortho repair(ACL)	4	0	0
Inguinal Hernai	18	15	11
Colostomy Closure	1	0	0
TAH	0	2	3
Varicose Vein Repair	0	2	5



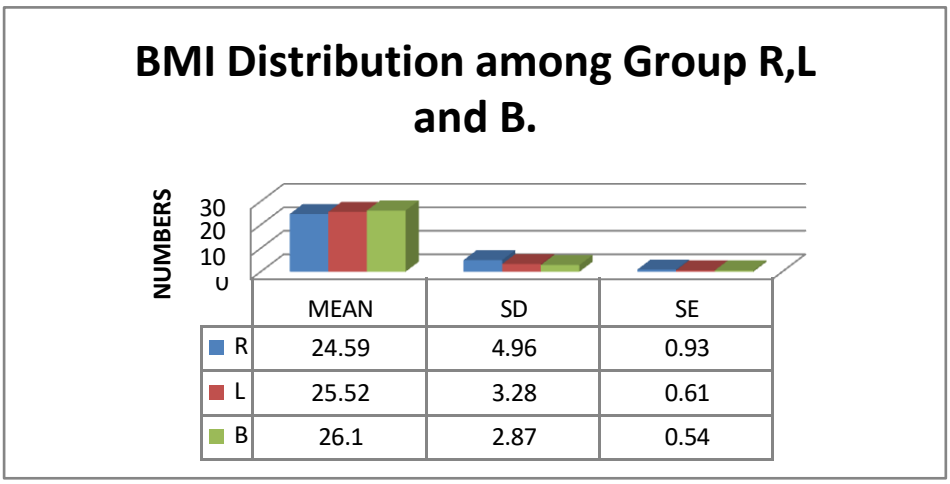
P value › 0.05 is not significant

CHART 5: TYPE OF SURGERIES

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

TABLE 6: BMI

BMI	R	L	B
MEAN	24.59	25.52	26.1
SD	4.96	3.28	2.87
SE	0.93	0.61	0.54



P value: 0.33 P value › 0.05 is not significant

CHART 6: BMI DISTRIBUTION

Table 6 and Chart 6 display the mean and standard deviation of BMI among Group R ,Land B.

SENSORY PROFILE:

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

SENSORY	R	L	B	pValue
5	7.07±2.58	11.07±1.06	11.07±1.15	0
10	5.71±1.78	9.64±1.09	10.14±1.53	0
15	5.21±1.57	8.29±1.69	8.64±1.81	0
20	4.86±1.38	7.29±1.74	7.29±1.74	0
25	4.79±1.37	6.57±1.31	6.14±1.32	0
30	4.79±1.37	6.07±1.01	5.64±1.22	0.01
60	4.79±0.99	6.21±1.13	5.57±1.26	0
90	4.86±1.00	7.07±1.58	6.07±1.58	0
120	5.57±1.47	8±1.96	7.07±1.84	0
150	6.79±2.13	9.07±1.67	8±1.88	0
180	7.71±2.91	10.14±1.53	8.86±1.75	0

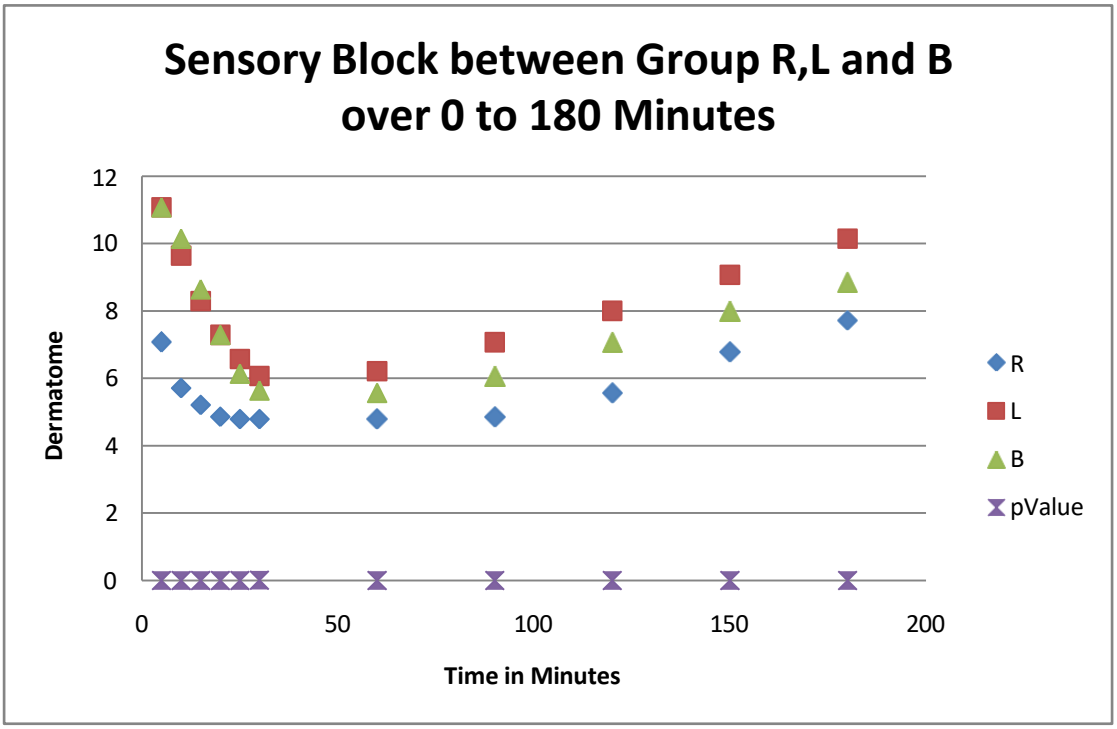
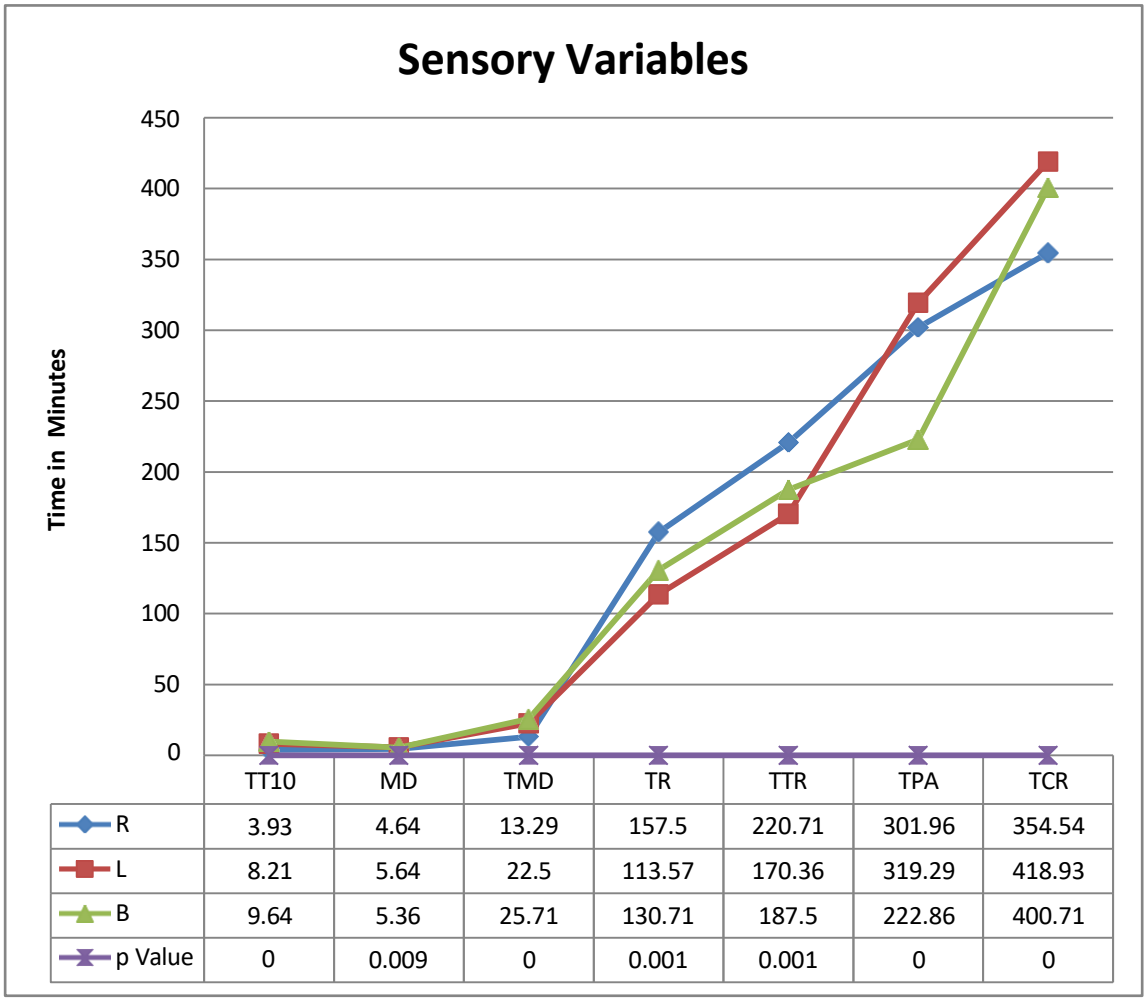


CHART 7: SENSORY BLOCK AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

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

TABLE 8: SENSORY VARIABLES/OBJECTIVES

SENSORY VARIABLES	R	L	B	p Value
TT10	3.93±2.90	8.21±3.65	9.64±4.89	0
MD	4.64±0.95	5.64±1.44	5.36±1.22	0.009
TMD	13.29±11.32	22.50±5	25.71±10.77	0
TR	157.50±50.08	113.57±31.99	130.71±45.61	0.001
TTR	220.71±50.47	170.36±49.70	187.5±39.68	0.001
TPA	301.96±86.59	319.29±60.11	222.86±38.66	0
TCR	354.54±77.35	418.93±78.52	400.71±36.71	0



	TT10	MD	TMD	TR	TTR	TPA	TCR
R	3.93	4.64	13.29	157.5	220.71	301.96	354.54
L	8.21	5.64	22.5	113.57	170.36	319.29	418.93
B	9.64	5.36	25.71	130.71	187.5	222.86	400.71
p Value	0	0.009	0	0.001	0.001	0	0

CHART 8: SENSORY VARIABLES/OBJECTIVES

Table 8 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 T10 (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 , L and B. In our study the mean time for onset of sensory block (TT10) in ropivacaine (R) group was 3.93 min ,5.21 min in levobupivacaine (L) group and min in racemic mxture Bupivacaine(B) group ($P < 0.01$). The mean values of maximum dermatome (MD) reached in R group, L group and B group are 4.64,5.64 and 5.36 level respectively. (p value 0.009).In present study the time taken to attain maximum sensory level (TMD) in three groups is 13.29(R),22.5(L) and 25.7(B) respectively ($P < 0.01$).The Time for 2 segment regression (TR) was found to be 157.50 min in R group ,113.57 min in L group and 130.7 min in B group, the p value being

0.001 with statistically significant difference. The duration for regression of sensory block to dermatomal level T10 (TTR) was 220.71 min in group R ,170.36 min in group L and 187.5 min in group B (p value < 0.05).Total duration of analgesia(the time of request of analgesia by patient) (TPA) in ropivacaine group was 301.96, whereas in levobupivine and Bupivacaine group was 319.09 and min respectively 222.86.(p value < 0.05). The time for complete reversal of sensory block (TCR) was 345.54 in ropivacaine group versus 418.93 in levobupivacaine group versus 440.71 min in bupivacaine group. The p value was statistically significant.

MOTOR PROFILE:

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

MOTOR	R	L	B	p Value
5	0.68±0.94	0.89±0.49	0.46±0.50	0.69
10	1.18±1.02	1.32±0.54	1.14±0.44	0.61
15	1.57±0.92	1.71±0.89	1.82±0.61	0.52
20	2±0.66	2±0.90	2.04±0.74	0.98
25	2.25±0.70	2.11±0.87	2.54±0.74	0.11
30	2.36±0.73	2.18±0.86	2.68±0.72	0.05
60	2.50±0.79	2.25±0.84	2.71±0.71	0.09
90	2.46±0.69	2.14±0.89	2.61±0,73	0.07
120	2.36±0.67	1.82±0.72	2.43±0.87	0
150	1.82±1.09	1.5±0.63	2.25±0.96	0.01
180	1.29±1.32	1.18±0.67	1.82±0.86	0.03

The table 9 shows the motor block as per MBS (Modified bromage score) at different time periods – from 0 to 180 minutes between Group R,Land B.

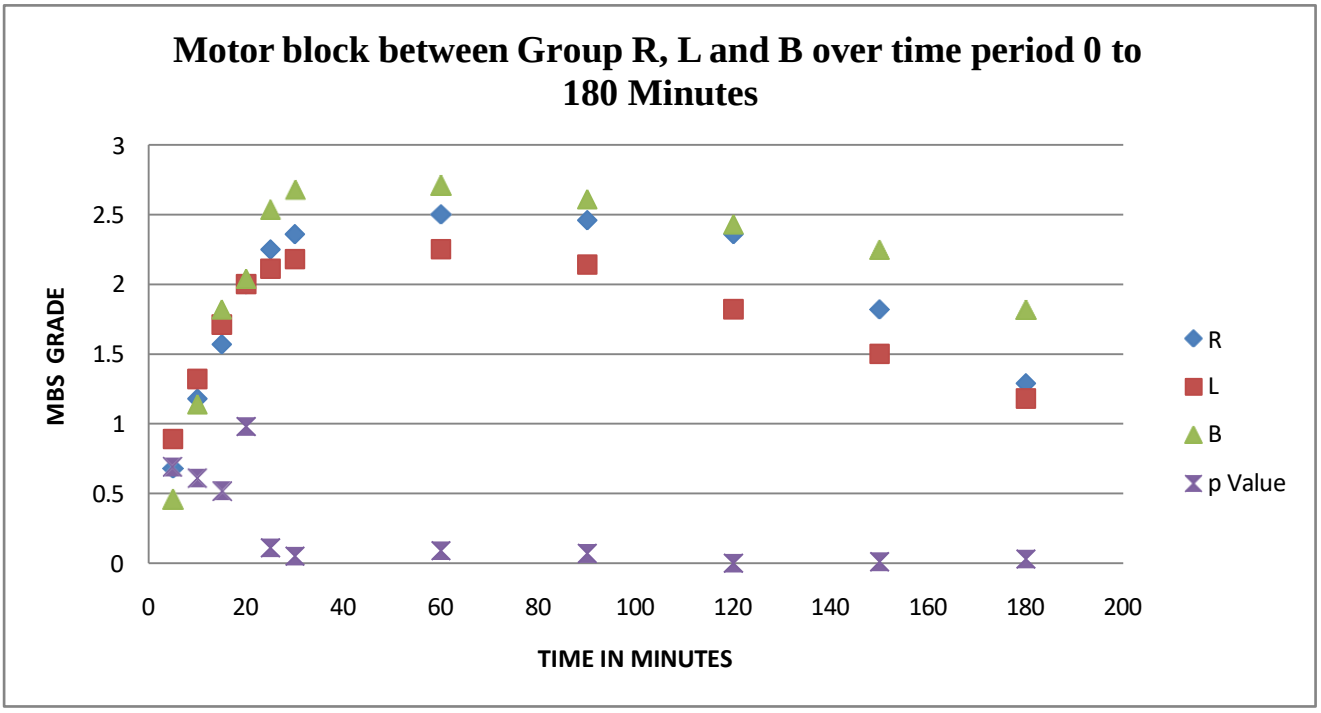


CHART 9: MOTOR BLOCK AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTE

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, L and B. 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 0.53, 0.06 and 0.11 respectively). The grade of motor block as per MBS score was significantly different in three groups.(Mean 2.86±0.35in R vs2.21±0.87 in L vs 2.65±0.66)(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, 17.86 min in group L and 23.57 min in group B.(p value of 0.04). The number of patients achieving MBS 3 in motor block is 71.4% versus 50% versus 85.71% in Group R, Group L and Group B respectively. The motor grade reached in Group B is denser than Group R and Group L. The number of patients achieving MBS 3 in motor block is more in Group B .The time taken to attain the maximum motor blockade is slower in Group R. The motor reversal is faster in group R. 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 was 146.25±48.58 min versus 160.71±46.64 in L group versus 172.78±44.9 min in Group B (p Value >0.05).(table 9 and Chart 10)

TABLE 10: MOTOR VARIABLES/OBJECTIVES

MOTOR VARIABLES	R	L	B	p Value
MO	24.64±31.11	16.43±11.74	20.56±26.11	0.53
MR	170.54±45.95	177.14±39	196±39.32	0.06
TTMBS2	146.25±48.58	160.71±46.64	172.78±44.9	0.11
MAX MBS	2.21±0.87	2.89±0.41	2.65±0.66	0
TTMMBS2	40.18±40.99	17.86±10.83	23.57±9.11	0.04

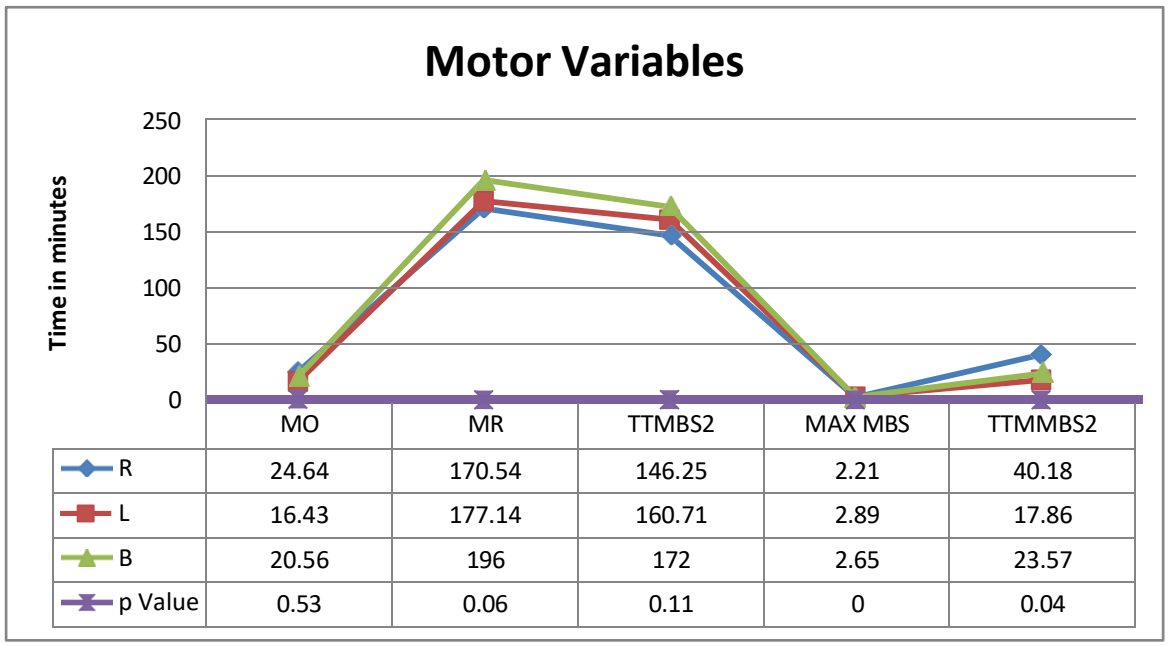


CHART 10: MOTOR VARIABLES/OBJECTIVES

Table 10 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,L and B.

TABLE 11: USE OF IV FLUIDS, EPHEDRINE AND SUPPLEMENT

	R	L	B
IV	1.55±0.31	2.05±0.15	2.03±0.23
E	10.8±5.02	6.00±0	6.86±2.26
SUP	2±0	1.93±0.26	1.96±0.18

The table 11 depict use of Intravenous fluid (IV) ,Ephedrine and any supplementation in Epidural drug usage between Group R,L and B.

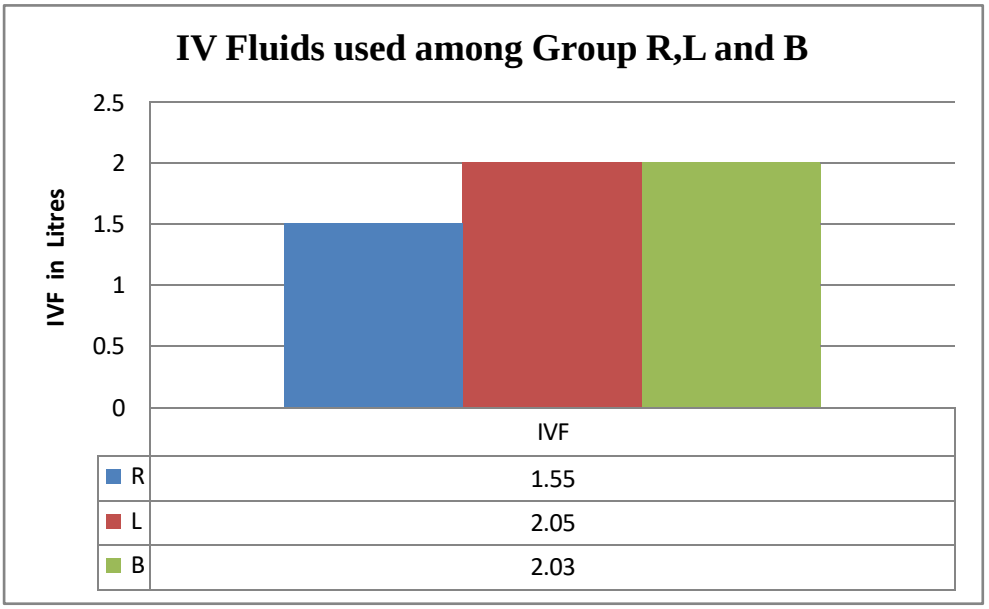


Chart: 11 Use of Intravenous (IV) fluids between Group R ,Land B.

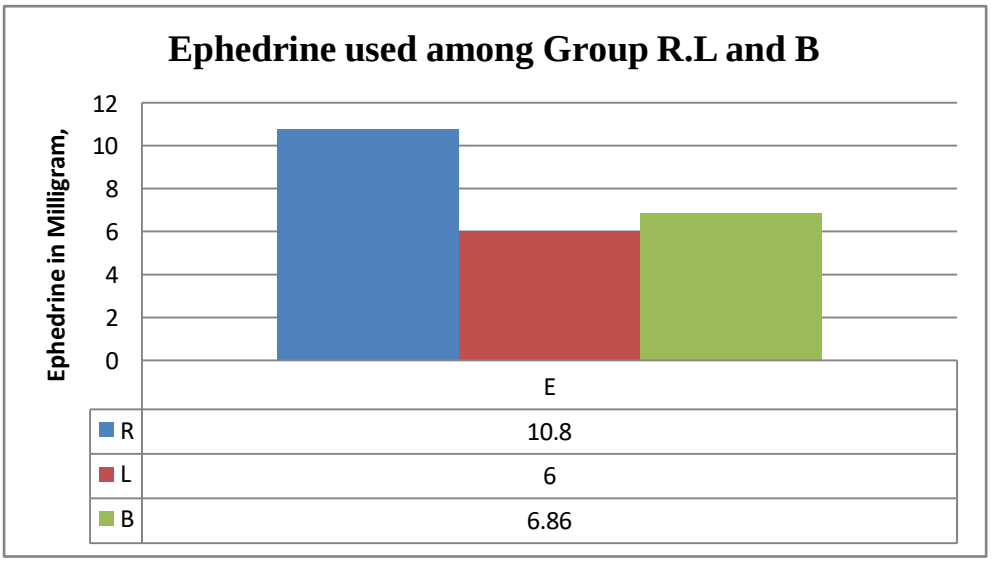


Chart 12: Ephedrine used between Group R, L and B

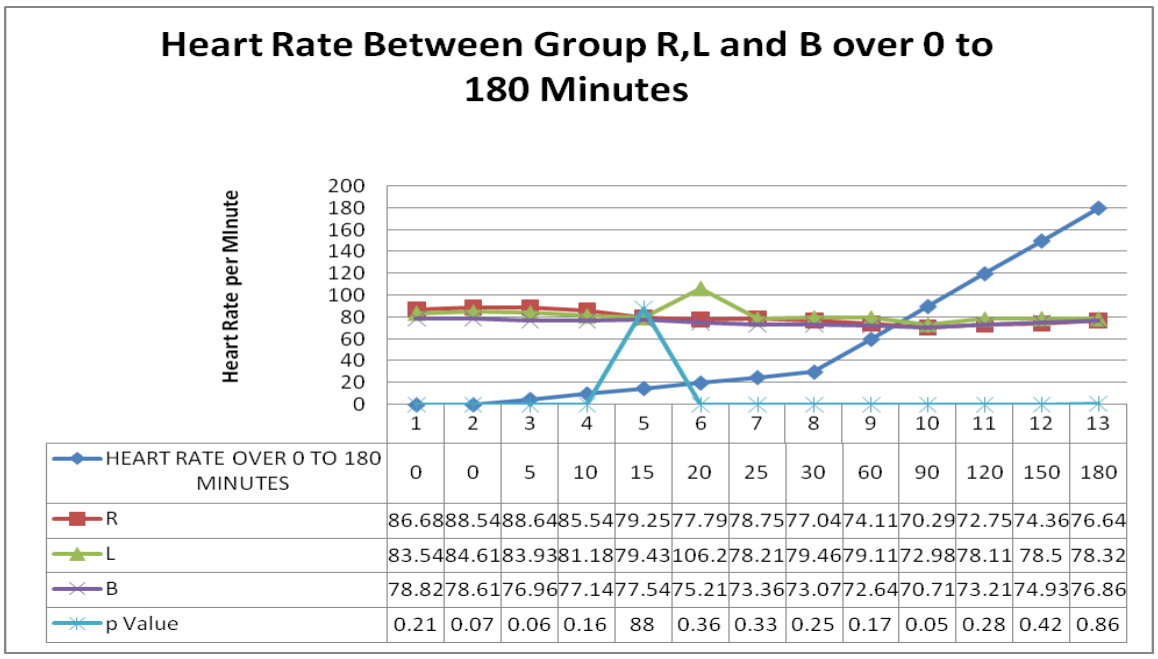
The Chart 12 display IV fluids used in Litre between Group R ,L and B.

The need for rescue analgesics, total IV fluid requirement and ephedrine usage was similar in all three groups. The haemodynamic profile MAP and HR were similar.(Table12,13,14and Chart 13,14 and 15). The time of request for postoperative analgesia was similar in all three groups

HAEMODYNAMIC PROFILE:

TABLE 12: HEART RATE AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTE

HEART RATE OVER 0 TO 180 MINUTES	R	L	B	p Value
PRE	86.68±19.22	83.54±17.31	78.82±12.59	0.21
0	88.54±19.11	84.61±17.05	78.61±10.80	0.07
5	88.64±24.43	83.93±17.68	76.96±10.33	0.06
10	85.54±16.69	81.18±19.39	77.14±12.06	0.16
15	79.25±16.73	79.43±18.77	77.54±9.53	0.88
20	77.79±14.04	106.21±154.71	75.21±9.95	0.36
25	78.75±15.63	78.21±16.66	73.36±11.93	0.33
30	77.04±14.77	79.46±16.54	73.07±11.4	0.25
60	74.11±14.05	79.11±15.28	72.64±10.11	0.17
90	70.29±13.47	72.98±13.37	70.71±9.59	0.05
120	72.75±14.06	78.11±16.25	73.21±11.02	0.28
150	74.36±14.02	78.5±14.18	74.93±9.21	0.42
180	76.64±15.37	78.32±13.19	76.86±9.28	0.86



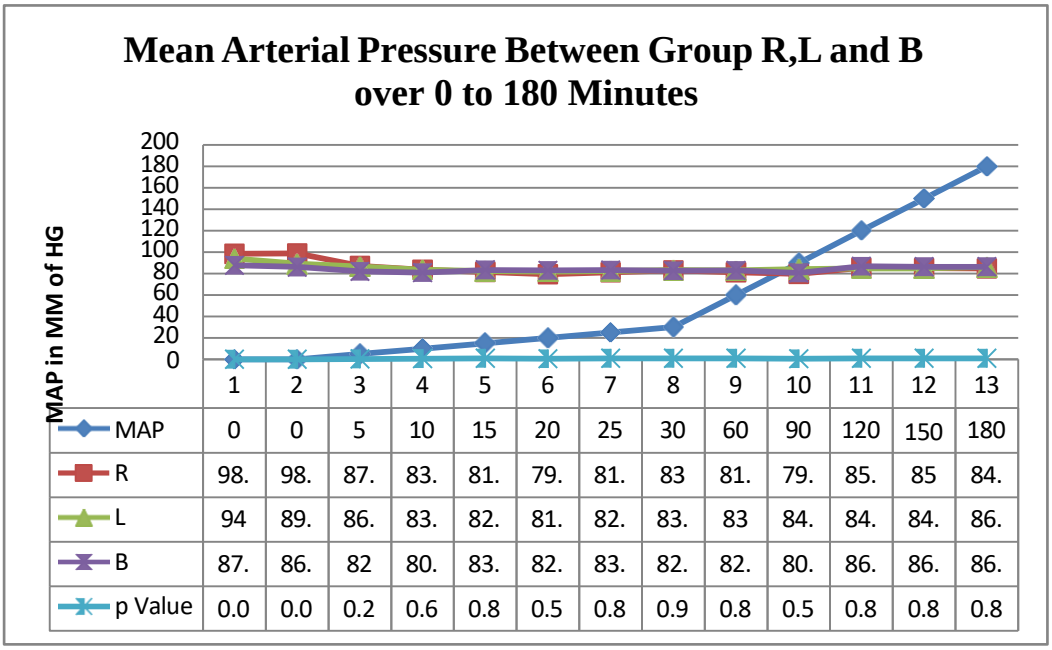
	1	2	3	4	5	6	7	8	9	10	11	12	13
HEART RATE OVER 0 TO 180 MINUTES	0	0	5	10	15	20	25	30	60	90	120	150	180
R	86.68	88.54	88.64	85.54	79.25	77.79	78.75	77.04	74.11	70.29	72.75	74.36	76.64
L	83.54	84.61	83.93	81.18	79.43	106.2	78.21	79.46	79.11	72.98	78.11	78.5	78.32
B	78.82	78.61	76.96	77.14	77.54	75.21	73.36	73.07	72.64	70.71	73.21	74.93	76.86
p Value	0.21	0.07	0.06	0.16	88	0.36	0.33	0.25	0.17	0.05	0.28	0.42	0.86

CHART 13: HEART RATE AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

Table 12 and Chart 13 display heart rate at different time period between 0 to 180 minutes between Group R,L and B.

TABLE 13: MEAN ARTERIAL PRESSURE (MAP) AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

MAP	R	L	B	p Value
PRE	98.4±15.71	93.97±10.62	87.62±9.63	0.06
0	98.8±15.65	89.16±10.28	86.05±11.82	0.01
5	87.09±14.70	86.68±10.62	82.04±14.26	0.29
10	83.68±15.68	83.64±10.83	80.90±14.15	0.68
15	81.47±17.18	82.52±12.56	83.33±11.94	0.88
20	79.40±10.71	81.81±12.76	82.84±11.70	0.53
25	81.27±15.46	82.48±12.82	83.24±14.85	0.87
30	83±17.75	83.37±12.51	82.64±11.47	0.98
60	81.29±20.84	82.98±9.51	82.86±10.26	0.88
90	79.66±15.74	84.05±8.97	80.56±18.06	0.5
120	85.34±20.8	84.85±10.98	86.70±7.43	0.88
150	85±14.71	84.65±11.42	86.29±7.41	0.85
180	84.71±13.29	85.79±11.74	86.29±8.54	0.86



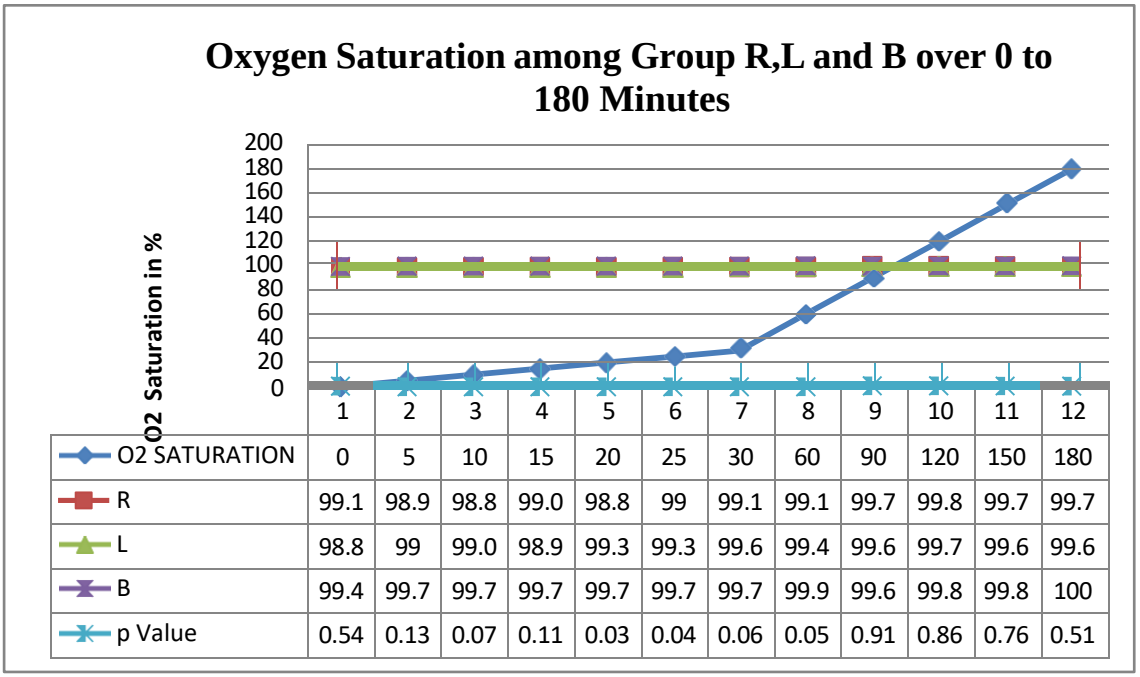
	1	2	3	4	5	6	7	8	9	10	11	12	13
MAP	0	0	5	10	15	20	25	30	60	90	120	150	180
R	98.	98.	87.	83.	81.	79.	81.	83	81.	79.	85.	85	84.
L	94	89.	86.	83.	82.	81.	82.	83.	83	84.	84.	84.	86.
B	87.	86.	82	80.	83.	82.	83.	82.	82.	80.	86.	86.	86.
p Value	0.0	0.0	0.2	0.6	0.8	0.5	0.8	0.9	0.8	0.5	0.8	0.8	0.8

CHART 14: MEAN ARTERIAL PRESSURE (MAP) AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

Table 13 and Chart 14 display Mean Arterial Pressure (MAP) at different time period between 0 to 180 minutes between Group R , L and B.

TABLE 14: ARTERIAL OXYGEN SATURATION AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

O2 SATURATION	R	L	B	p Value
PRE	99.14	98.86	99.46	0.54
5	98.93	99	99.71	0.13
10	98.83	99.07	99.75	0.07
15	99.07	98.93	99.75	0.11
20	98.82	99.39	99.79	0.03
25	99	99.39	99.79	0.04
30	99.14	99.61	99.79	0.06
60	99.18	99.46	99.93	0.05
90	99.75	99.64	99.64	0.91
120	99.86	99.75	99.86	0.86
150	99.71	99.68	99.86	0.76
180	99.79	99.64	100	0.51



	1	2	3	4	5	6	7	8	9	10	11	12
O2 SATURATION	0	5	10	15	20	25	30	60	90	120	150	180
R	99.1	98.9	98.8	99.0	98.8	99	99.1	99.1	99.7	99.8	99.7	99.7
L	98.8	99	99.0	98.9	99.3	99.3	99.6	99.4	99.6	99.7	99.6	99.6
B	99.4	99.7	99.7	99.7	99.7	99.7	99.7	99.9	99.6	99.8	99.8	100
p Value	0.54	0.13	0.07	0.11	0.03	0.04	0.06	0.05	0.91	0.86	0.76	0.51

CHART 15: ARTERIAL OXYGEN SATURATION AT DIFFERENT TIME PERIODS FROM 0 TO 180 MINUTES

Table 14 and Chart 15 show Oxygen saturation at different time period between 0 to 180 minutes between Group R,L and B.

DISCUSSION:

Bupivacaine is being regularly used for epidural anaesthesia for lower abdominal and lower limb surgeries in our hospital. Levobupivacaine and Ropivacaine with structural similarity to bupivacaine without its cardio toxic effects has been introduced for clinical use.. Few studies have compared racemic mixture Bupivacaine, Levobupivacaine and Ropivacaine for epidural anaesthesia. Hence Levobupivacaine and Ropivacaine were selected for our study to compare with routinely used racemic mixture bupivacaine. Equipotent doses of study drugs were chosen-0.5% of Racemic Mixture Bupivacaine and Levobupivacaine with 0.75% of Ropivacaine.The explanation for the differentl potency of Levobupivacaine,Racemic mixture Bupivacaine and Ropivacaine may be because of the different lipophilic property. The lipid solubility of Levobupivacaine and Racemic mixture Bupivacaine is is 30.The Lipophilicity of Ropivacaine is 25, lesser than the other two study group drugs.

CoxC R et al.,[6]in the year 1998, have mentioned that levobupivacaine iscurrentlybeingdevelopedforclinicaluseinanaesthesiaand postoperativepainmanagement.Thecomparableefficacyoflevobupivacaineandbupivacaineforsensoryblockforlowerabdominalsurgeryisinagreementwiththatfoundinpreviousclinicaltrialsofthese anaestheticsforextraduralanaesthesia inlowerlimbsurgery. The study done by **RobinsonA et al.,**[7]showednodifferencebetweentheMLACoflevobupivacaine(0083%)andbupivacaine(0081%). The rank order of the potency of inhibition of sodium channel conductance under voltage clamp is generally the same as the rank order of the drugs in producing clinical local anaesthesia, which is also the same order as the potency in producing cardiac toxicity.

The potency of local anaesthetics is thus correlated to the lipid solubility of the drug, which is also correlated with its toxicity. **Brau et al**[8] reported that the ability to inhibit tetrodoxin-resistant sodium channels was nearly 50% less potent with ropivacaine than levobupivacaine or racemic bupivacaine; **Sinnott et al**[9] compared three concentrations of either ropivacaine or

levobupivacaine (0.0625, 0.125 and 0.25%) for sciatic nerve block in the rat.He demonstrated that, at lower concentrations, levobupivacaine produces a greater motor impairment and a longer duration of proprioceptive impairment relative to ropivacaine.At 0.125% concentration there were no differences between the two local anaesthetics. Another way of overcome the problem of potency comparison between these three long-acting local anaesthetic in a clinical setting is to determine the minimum effective local anaesthetic concentration (MLAC) required to produce adequate pain control in 50% of subjects using an up-and-down sequential allocation technique. This model has been applied for epidural analgesia during labour and initial reports demonstrated that, although no differences were observed between the MLAC of levobupivacaine (0.083%) and bupivacaine (0.081%), two different research groups estimated values nearly 40–50% higher for ropivacaine. [10,11]

In fact, based on the reported difference in the analgesic potency between ropivacaine and bupivacaine according to the MLAC studies during epidural analgesia for pain during labour.[10,11] Although the true equipotency ratio among these three long-acting local anaesthetics remains a subject of further investigation, results coming from different studies seem to suggest a rank order of potency of ropivacaine < levobupivacaine < bupivacaine.**Wang LZ, Chang XY et al.,[12]** in the year 2010, have stated that the analgesic efficacy mainly depends on the concentration of LA rather than the type of anaesthetics and at least 0.1% is needed for satisfactory analgesia. Hence, 0.5% concentration was chosen for both the drug R(Racmic mixture of Bupivaciane) and L(Levobupivacaine). The dosage of 0.5%bupivacaine and 0.5%levobupivacaine is 2 per kg body wt.(for a 50 kg patient the toxic dose is about 100 mg) The total volume used in our study in both the group is 17 ml(85 mg).The toxic dose of Ropivacaine is 3 mg per kg body weight.TheEuipotent dose of 0.5% racemic mixture Bupivacaine and Levobupivacaine is 0.75% Ropivcaine.(17 ml of 0.75% Ropivcaine gives 127.5mg)-In a50 kg person the toxic dose of Ropivcaine will be 50X 3=150

mg.(within toxic dose) Hence in the study group 17mlwasselectedasthevolumeofthedrugotherthanthetestdose.

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.[13] 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. Due to their reduced toxic potential, the two pure left isomers is been used increasingly in clinical situations where there is risk of systemic toxicity as a result of accidental overdosing or unintended IV injection as in epidural or peripheral nerve blocks.[14]

The age, sex, educational qualification and BMI of the patients included in three groups were comparable with no statistically significant difference.

19.1 SENSORY BLOCK:

Our study compare the efficacy and tolerability of 0.5% Levobupivacaine .0.75% Ropivacine and 0.5% % Racemic mixture Bupivacaine, **(Group L vs Group R vs Group B** respectively**).**The mean time for onset of sensory block is faster in R group when compared to group L and B (p Value <0.05). The maximum dermatome reached (higher), the time taken to attain maximum sensory level, the two segment regression and the duration for regression of sensory block to T_{10} were faster in group R. Total duration of analgesia in R group was 301.96 versus 222.86 in B group versus 319.29 min in group L (p value <0.05).The time for complete reversal of sensory block was 345.54 in R group versus 400.71 in B group versus 418.95 min in group L (p value <0.05).

Cok O Y et al.,[15]in the year 2011 compared the effects of epidural anaesthesia with Levobupivacaine**(L)** and racemic mixture of Bupivacaine**(B)** on block features and post-operative analgesia: Onset time of block (4.8±4.1 vs 4.8± 3.1 mins). **Kopacz D J et al**.,[16]in the year 2000, compared epidural Levobupivacaine 0.75% with racemic Bupivicaine 0.75% for lower abdominal surgery. The time to onset of adequate sensory block (T10 dermatome) was similar in both groups. **Cox et al**.,[6] in the year 1998 found that there was no difference in the onset time for sensory block which concurs with our study.

In a study done by **A Suri et al**[17] 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. **Maheshwari et al[18] (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.

The maximum dermatome(mean) reached in **L group** and **B group** are 5.73 and 5.21 level respectively. The p value is found to be 0.428 and hence there is no statistically significant difference. The mean values of maximum dermatome reached in the study done by **Kopacz D J et al.,** [16] in the year 2000, **Cox et al.,**[6]in the year1998, Murdoch et al., in the year2002 and Casati et al., in the year**.. Cok O Y et al**.[15],in the year 2011, observed that the number of blocked dermatomes was similar in both L and B groups (T8 vs T9).

Kopacz et al.,[16]in the year 2000 study found that the time taken to obtain the maximum dermatome level of sensory block was similar in both L and B groups (24.3± 9.4 and 26.5± 13.2 mins respectively).**Kountoudi et al[19]** compared epidural Levobupivacaine 0.5% with Ropivacaine 0.5% for inguinal hernia repair procedures in 30 patients and concluded that, there was no difference in the level of sensory block obtained. 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,[20]** 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. In a study conducted by **Finucane et al**,[21] 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. 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 to regression in L and B group was s similar in a study done by **Casati et al.,**[22]in the year 2003.**Concepcion et al**[23] found a mean time for two segment regressions as 164 ± 22 min for 0.75% ropivacaine, which was comparable to present study.

Duration of analgesia in our study was 170.36 mins in **group L** and 187.5 mins in **group B,** p value being 0.160, which shows there is no statistically significant difference. In contrast to our study**, Cox et al.,** [6] **in** the year 1998, showed significant difference in duration of sensory block caused by Levobupivacaine (longer), than racemic Bupivacaine. **Kopacz et al.,** [16]in the year 2000**,** obtained values of 505.9±71.1 mins for bupivacaine group and 550.6±87.6 mins for levobupivacaine group.(p value:0.016).Here the time for complete regression of sensory block in levobupivacaine group was found to be significantly longer.

Total duration of analgesia 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**[18] 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 ($p<0.05$).In a study conducted by **Concepcion et al**[23], 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. 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. The longer duration of analgesia here could be explained due to use of higher concentration of levobupivacaine. **Maheshwari et al**[18]**(2016)** conducted a similar study and found that time for first rescue analgesia was significantly longer ($p <0.001$) in group (L) II (6.43±2.12 hr) as compared to group(R) I (4.97± 0.89 hr) which is in accordance to our study. In a study by **Brockway et al**,[20] the duration of analgesia was increased by increasing the concentration of both drugs.This had minimal effect on onset time

or extent of block. The time for complete reversal of sensory block was 345.54 in ropivacaine group versus 418.93 in levobupivacaine group. (P value was <0.05- statistically significant).

The time of request for post-operative analgesia after the injection of study drug was found to be 319.28 min in group L and 222.85 min in group, B p value being 0.553 which shows there is no statistically significant difference

19.2 MOTOR BLOCK:

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 0.53, 0.06 and 0.11 respectively). The grade of motor block as per MBS score was significantly different in three groups.(Mean 2.86±0.35in R vs2.21±0.87 in L vs 2.65±0.66) (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, 17.86 min in group L and 23.57 min in group B. (p value of 0.04). 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 onset of motor block is defined as ≥ modified bromage grade 2.The motor block at the end of 5 min time interval (Bromage scale grade 1) after injection of study drug was noted in L group compared to B group with statistically significant difference (p value 0.002). The mean grade of motor block at 5 min time interval of study in group L was 2.5 ± 1.23 and in group B was 3.25 ± 0.79, the p value being 0.018, which shows there is statistically significant difference. Regression of Motor block to MBS grade 1 was found to be 177.14 mins in group L and 196.66 mins in group B, p value being 0.042 (statistically significant difference). Thus our study shows 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.

The time to reach MBS grade 2 was 16.42 mins in group L and 20.55 mins in group B, with p value being 0.160, which shows there is no statistically significant difference. This corresponds to the results of the study done by **Cox et al**.,[6] in the year 1998, and **Bergamaschi F et al.**,[24] A study by Casati **A et al**.[22], found that the onset of motor block was longer in Bupivacaine group which is contrary to our study.

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. 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[25](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(L) A and group(R) 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.

The grade of motor block as per MBS score was significantly different in L and R 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[26]** noted that Ropivacaine had slower onset and regression than Levobupivacaine, which could be due to its lower lipid solubility.

The grade of motor block as per MBS score was significantly different in L and B 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 B is denser than in Group L. Thetimetakentoattainthemaximummotorblockadewas 23.39±9.13 miningroup B and 17.85±10.8 min ingroup L.Thisisstatisticallyhighlysignificant. (p value:0.043).The number patient achieving MBS 3 in motor block is 62.5% vs 37.5% in Group B and Group L respectively.

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.[20]** showed thatonset of motor block produced by ropivacaine was slower. The mean duration of motor blockade of ropivacaine is lower than that of levobupivacaine.

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 **Kopacz et al.**,[16] in the year 2000, they observed that group L showed 355.4 mins vs Group B 375.7 mins, while analysing the total duration of motor block study. **Cox et al**.,[6] in the year 1998, found out that the duration of motor blockade in Group L was 185 mins vs Group B 192 mins.

In a study conducted by **Peduto et al**,[27] 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.It was observed by **Karz J A et al**[28] 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. 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.

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

19.3 Haemodynamic profile

The heart rate and MAP of the patients in L and B groups were comparable intra operatively with no clinical or statistically significant differences.

There is no statistically significant difference in heart rate between the R and L 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**,[29] 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.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.

19.4 Complications:

The incidence of hypotension was studied by **Bergamaschi et al.**,[24] in the year 2005 and was found to be similar (Group L 66.7% vs 43.5%in Group B) when either Levobupivacaine or Bupivacaine was used for epidural anaesthesia. **Kopacz et al.,** [16] in the year 2000, found out that the incidence of hypotension occurred in 82% of patients in Group L and 61% in Group B.

. In our study between group L and R 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. **Kumar GS et al[30]** says, 7% patients had hypotension, 3% had vomiting and 3% nausea in ropivacaine group. **Brockway et al**.[20] found similar side effect- the most common being backache (23%) followed by nausea (14%) and vomiting

(2%). **Finucane et al.**[21] reported nausea, vomiting, hypotension, headache, and backache as the most common adverse events in their study, which was similar to our study.

SUMMARY:

The summary of the study briefs about the comparision of efficacy and tolerability of 0.5% Racemic Mixture Bupivacaine,0.5% Levobupivacaine and 0.75% Ropivcine and among three groups.

A prospectiverandomizeddoubleblinded study was undertaken to evaluatethesensoryandmotorblockingpropertiesofepidurallyadministered 17 ml0.5% racemic mixture bupivacainecomparedwith 17mlof Levobupivacaine0.5% and 0.75% Ropivacaine inlower abdominal surgeries.

Eighty four patientsbetweentheagegroupof18-65yearsbelongingtoASAIandIIpostedforelectivelower abdominalsurgerieswererandomlydividedintotwogroups.Eachgroupconsistingof 28 patientstoreceiveepidurally17mlof Levobupivacaine0.5%(group L),17mlofbupivacaine0.5%(group B) and 0.75% of Ropivacaine(Group R).

Patientswhohadcontraindicationforepiduralanaesthesia,patientspostedforemergencysurgery,patients with BMI>30 andpregnantpatientswereexcludedfromthestudy.

In all three groupsepiduralspacewasidentifiedusinglossofresistance to air techniqueandepiduralcatheterwasintroducedfor 5 cmsinside.Afternegativetestdosewith3mloflignocaine2%with 1 in 2,00,000 adrenaline,17 ml of test drugwasgivenin left lateral decubitus position.

Theonset,maximumlevelandd urationofsensoryandmotorblockade,hemodynamicparameters and any side effects werestudied.

Therewas no statistically significant difference among the demographic profiles of the three groups.

Group	Sensory onset(mins)	Motor onset(mins)	Maximum sensory level	Time for maximum sensory level(mins)	Two segment regression (mins)	Duration of sensory block(mins)	Time for motor block to MBS 1(mins)	Duration of motor block(mins)
L	8.21 ± 3.65	16.42 ± 11.74	5.73 ± 1.37	22.50 ± 5.50	113.57 ±31.99	170.36 ± 49.70	177.14± 39.00	160±46.64
R	3.93±2.90	26.64 ± 31.11	4.64± 0.95	13.29±11.32	157.50±50.08	220.71±50.47	170.54± 45.95	146.25±48.58
B	9.64 ± 4.89	20.55 ± 26.17	5.36 ± 1.22	25.71 ± 10.77	130.71 ± 45.61	187.50 ± 39.68	196.66± 39.32	172.77±44.90

TABLE15:SUMMARY OF ANALYSIS OF STUDY

In our study the mean time for onset of sensory block (TT10) in ropivacaine (R) group was 3.93 min ,5.21 min in levobupivacaine (L) group and 9.64±4.89 min in racemic mxture Bupivacaine(B) group ($P < 0.01$).

The mean values of maximum dermatome (MD) reached in R group, L group and B group are 4.64, 5.64 and 5.36 level respectively. (p value 0.009).

In present study the time taken to attain maximum sensory level (TMD) in three groups is 13.29(R), 22.5(L) and 25.7(B) respectively ($P < 0.01$).

The Time for 2 segment regression (TR) was found to be 157.50 min in R group, 113.57 min in L group and 130.7 min in B group, the p value being 0.001 with statistically significant difference.

The duration for regression of sensory block to dermatomal level T10 (TTR) was 220.71 min in group R, 170.36 min in group L and 187.5 min in group B (p value < 0.05).

Total duration of analgesia (the time of request of analgesia by patient) (TPA) in ropivacaine group was 301.96, whereas in levobupivine and Bupivacaine group was 319.09 and min respectively 222.86. (p value < 0.05).

The time for complete reversal of sensory block (TCR) was 345.54 in ropivacaine group versus 418.93 in levobupivacaine group versus 440.71 min in bupivacaine group. (p value < 0.05).

The results of this study indicate that the sensory block produced by epidural 0.5% levobupivacaine and of 0.5% racemicbupivacaine .is equivalent to that produced by quipotent dose of 0.75% Ropivacaine

The onset of motor block (MO), regression of motor block (MR) and duration of motor block (TMD) was comparable in all three groups (P values 0.53, 0.06 and 0.11 respectively).

The grade of motor block as per MBS score was significantly different in three groups.(Mean 2.86±0.35 in R vs2.21±0.87 in L vs 2.65±0.66) (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, 17.86 min in group L and 23.57 min in group B.(p value of 0.04).

The number of patients achieving MBS 3 in motor block is 71.4% versus 50% versus 85.71% in Group R, Group L and Group B respectively. The motor grade reached in Group B is denser than Group R and Group L. The number of patients achieving MBS 3 in motor block

is more in Group B.The time taken to attain the maximum motor blockade is slower in Group R. The motor reversal is faster in group R.

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 was 146.25±48.58 min versus 160.71±46.64 in L group versus 172.78±44.9 min in Group B (p Value >0.05).

Thedurationofmotorblockadeand sensory blockadeingroup B was 172.77±44.90 minsand187.50 ± 39.68 mins respectively,whereasthedurationofmotorblockand sensory block,ingroup L was160±46.64 mins and170.36 ± 49.70 mins respectively and thedurationofmotorblockand sensory block,ingroupR was 146.25±48.58mins and 220.71±50.47 mins respectively.The duration of Motor Block in Group R was for shorter duration when compared to other two Groups.

The intraoperative hemodynamic profile (MAP and HR) of all three groups, showed no significant difference among them. The three local anaesthetics are well tolerated and effective in producing epidural anaesthesia for patients undergoing lowerabdominalsurgery.Sevenpatients ingroup B ,fivepatientsingroup L and five patients in Group R developedhypotensionofmorethan 20%fall from their baseline valuesin MAP which waseasilymanagedbyfluidsandvasopressors.Thisisstatisticallynotsignificant.Noneofthepatient sinboththegroupdevelopedbradycardia, bpm less than 50. Seven % of patientsingroup B and 4% ofpatientsingroup L requiredadditionalanalgesics. In our study none of the study patientshad complained of nauseaandvomiting.

CONCLUSION:

The study concludes that equipotent dose of 0.75% Ropivacaine, 0.5% levobupivacaine and 0.5% racemic mixture bupivacaine produces clinically indistinguishable, well tolerated and

effective epidural anaesthesia for patients undergoing lower abdominal and lower limb surgery.Severe central nervous system (CNS) and cardiovascular adverse reactions reported in the literature after inadvertent intravascular injection or intravenous regional anaesthesia have been attributed to the R (+) isomer of bupivacaine.The pure left-isomers have less toxic effects on the central nervous system and on the cardiovascular 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).

The present study's conclusion is:

1. The mean time for onset of sensory block is faster in R group when compared to group L and B (p Value <0.05). Therewasstatisticallysignificantdifferencein maximum dermatomal level of analgesia and time taken to reach maximum dermatomal blockbetween Levobupivacaine0.5%, Bupivacaine0.5% and Ropivacaine 0.75%. (p values being 0.009 and < 0.01 respectively).

2. The two segment regression (p value 0.001) and time taken to regress to T 10 level (p value < 0.05) is statistically significant among three groups..

3. The maximum dermatome reached (higher), the time taken to attain maximum sensory level, the two segment regression and the duration for regression of sensory block to $_{T10}$ were faster in group R.

4. Total duration of analgesia in R group was 301.96 versus 222.86 in B group versus 319.29 min in group L (p value <0.05).

5. The time for complete reversal of sensory block was 345.54 in R group versus 400.71 in B group versus 418.95 min in group L (p value <0.05).

6. But the demand for post-operative analgesia seems to be earlier in Group B (Bupivacaine) when we compare with Group L (Levobupivacaine) and Ropivacaine. p value is <0.05,statistically significant.

7. The onset of Motor block in the study groups was similar and their p value is 0.53, which is not significant.

8. The grade of motor block as per MBS score was significantly different in the study groups.The number of patients achieving MBS 3 in Motor block is 71.4% vs 50% versus 85.71% in Group R, L and B respectively. Implying the motor grade reached in group B is denser than in Group L.(GroupB>GroupL >group R).

9. The time taken to achieve the maximum MBS grade of motor block is slower in Group R.

10. The time for motor blockade regression to MBS 1 was earlier in Group R, (p value is 0.06, which is not significant.)

11. Durationofmotorblockadeis similar in the study groups. p value is 0.05.

12. The MAP, Heart Rate, oxygen saturation through pulsoximetry reading all showed no difference between the study groups from zero to three hours of the study.

13. The Intravenous fluid usage, requirement for rescue analgesia during surgery and need for ephedrine showed no difference between the two groups.

14. All three groups clinically, did not have significant adverse effects like nausea, vomiting and shivering.

From the above study, it is concluded that, 0.5% levobupivacaine,0.75% ropivacaine and 0.5% racemic mixture bupivacaine produces clinically indistinguishable, well tolerated and effective epidural anaesthesia for patients undergoing lower abdominal surgery.

FUTURE RESEARCH- A QUEST FOR CNS, CVS TOXICITY LESS LOCAL ANAESTHETICS –SELECTIVE BLOCK OF PERIPHERAL NERVOUS SYSTEM!

The chiral switch helped us to produce better Local Anaesthestic drugs for clinical use.The quest for safer drug should be produced to avoid LAST by virtue of developing Local Anaesthetics acting selectively on NA channels on PNS. The sodium channel is made of two types of subunit-alpha(one) and Beta(one or two).The alpha subunit has four domains,each having six helical membrane spanning segments.The alpha unit contains a volatagesensor,an ion selectivity filter,gating structures and P segment,which forms the pore.Nine different isoforms of sodium channels have been discovered,of which seven are in nerves;Na 1.4 is found in skeletal muscles and Na 1.5 is found in cardiac muscles.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, potassium and calcium ion,NA K ATPase Channel once gets attached to it (preventing dreaded, difficult to reverse/ resuscitate cardiac toxicity of Bupivacaine group of Local Anaesthesia drugs-substantiated by plasma levels of LA.Cardiac Toxicity-(Racemic mixture Bupivaciane>Levobupivcaine> Equipotent dose of Ropivcaine).However, despite electrophysiological evidence of stereoselective binding to sodium and potassium channels,

Groban et al[31]reported that the plasma concentrations resulting in a 35% reduction in dP/dtmax and ejection fraction were 4.0 and 3.0 mg/ml for ropivacaine, 2.4 and 1.3 mg/ml for levobupivacaine, and 2.3 and 2.1 mg/ml for racemic bupivacaine respectively. The safe plama level for racemic mixture Bupivacaine is about 1 microgram per ml,for Levobupivacaine it is 1.74±2.7 microgram per ml and for Ropivacaine it is 1.24±6.0 microgram per ml.Further PK and PD studies regarding safe dose for racemic mixture bupivacaine,levobupivacaine and ropivacaine by virtue of its plasma concentration-physiological model of PK of a drug when used in SAB,epidural and Peripheral nerve block should be carried out. The studies regarding cryo-EM structures of NaV channels can be used to understand their structure and, function which will help in designing selective drug delivery method using nanotechnology. The gene expert study for liver enzymes CYP 450 1A and 3A types can help in differentiating slow, intermediate, and fast metabolisers and hence can predict the increased side effects

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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.

Conflict of Interest:

None

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