Original article:

Prospective observational study of isobaric 0.5% levobupivacaine and isobaric 0.5% ropivacaine intrathecally in lower limb surgeries

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Abstract:

Introduction: Spinal or Intrathecalanaesthesia has recently become more popular due to an increasing number of ambulatory procedures and interventions, for which the ideal spinal anaesthetic would provide rapid and adequate surgical anaesthesia together with early ambulation to allow early discharge. Because of reports showing the potential neurotoxicity of intrathecallidocaine, the use of bupivacainefor outpatient spinal anaesthesia has increased.Butintrathecal bupivacaine has been shown to have selective cardiac effects more pronounced with R-isomer than S-isomer.

- Primary objectives: To assess onset, duration and effectiveness of sensory and motor blockade with two different local anaesthetics and total dose required.
- Secondary objectives: To study hemodynamic changes associated with two different local anaesthetics in same concentration 0.5%.

Methods: After institutional review ,board approval and written, informed consent, 100 patients with ASA physical status I–II aged 18–60 yr scheduled to undergo elective lower limb surgery with spinal anesthesia were enrolled in this prospective observational study. Patients with known hypersensitivity to amide local anesthetics or a history of severe renal, hepatic, respiratory,cardiac disease or neurological, neuromuscular or psychiatric condition were excluded.Patients were divided randomally in two groups with 50 patients in each group.Group L receiving isobaric levobupivacaine 0.5% and Group R receiving isobaric ropivacaine 0.5%.Adequate block to initiate surgery was defined as a sensory block bilaterally to dermatome T10.The onset,degreeand duration of motor block were measured in both legs by using a modified Bromage scale.

Observation and Results: The differences in paramteters were statistically significant.Onset was seen earlier in Group L than in Group R.sensory maximum Level T was seen at higher level in Group L than in Group R.Lesser time was required in Group R to achieve two segment regression than group L.Higher duration of sensory blockade was seen in Group L than in group R.Higher duration of Motor blockade was seen in Group L than in group R.There was no significant difference in basal and minimum pulse rate,basal systolic blood pressure and diastolic blood pressure,minimum systolic blood pressure and diastolic blood pressure ,mean basal SPO2 between two groups. In the study there was no complications noted among all the subjects in both the groups

Conclusion: This study concludes that both study drugs,pure enantiomers, Isobaric 0.5% Levobupivacaine and Isobaric 0.5% Ropivacaine when used intrathecally provides adequate level of analgesia and excellent hemodynamic stability,no incidence of any cardiac or CNS toxicity with 0.5% levobupivacaineproviding longer duration of sensory and motor blockade compared to 0.5% ropivacaine

Introduction

The spinal anaesthesia has the potential for being uniquely safe anaesthetic technique due to the combination of profound analgesia, muscle relaxation, less systemic and metabolic disturbances, Preservation of airway, Decrease in blood loss and Ability to provide residual post operative analgesia[4].Spinalanaesthesia has recently become more popular, due to an increasing number of ambulatory procedures and interventions, for which the ideal spinal anaesthetic would provide rapid and adequate surgical anaesthesia together with early ambulation to allow early discharge.

Because of reports showing the potential neurotoxicity of spinal lidocaine, over the past few years, the use of hyperbaric racemic mixture **BUPIVACAINE** for outpatient spinal anaesthesia has increased.ButIntrathecalBupivacaine has been shown to have selective cardiac effects more pronounced with R-isomer than S-isomer. Levobupivacaine and Ropivacaine are two relatively new long-acting local anesthetics,have been developed after reports of simultaneous seizure and cardiac arrest with prolonged resuscitation after accidental intravascular injection of bupivacaine.

Levobupivacaine is pure s(-) enantiomer of bupivacaine.It has demonstrated less affinity and strength of depressant effects onto myocardial and central nervous vital centers in pharmacodynamic studies and a superior pharmacokinetic profile.It is well tolerated in variety of regional anaesthesia.Reports of toxicity with levobupivacaine are scarce.Ropivacaine is enantiomerically pure (S-enantiomer) amide local anaesthetic,with a low lipid solubility which blocks nerve fibers involved in pain transmission (Aδ and C fibers) to a greater degree than those controlling motor functions(Aβfibers).It has been shown to provide effective ,well tolerated surgical anaesthesia via epidural route, for major and minor nerve blocks and field blocks with a reduction in CNS and cardiotoxic potential[7].

Thus, the objective of study is to establish the reliability and efficacy of plain isobaric 0.5% LEVOBUPIVACAINE and plain isobaric 0.5% ROPIVACAINE intrathecally in patients undergoing lower limb surgeries.

Aim: Prospective observational study of quality of spinal anaesthesia with two different Isobaric local anaesthetics,Levobupivacaine and Ropivacaine in 0.5% concentration.

Objectives:

- To determine effectiveness of sensory and motor blockade with two different local anaesthetics
- To study onset of sensory and motor blockade.
- To study total duration motor and sensory blockade with two different local anaesthetics in same concentration.
- To study duration required for two segment regression
- To study hemodynamic changes associated with two different local anaesthetics in same concentration 0.5%.
- To study intraoperative complications like hypotension,bradycardia, nausea,vomitingetc if any associated with two local anaesthetics under study.

Material and Methods

After institutional review board approval and written, informed consent, 100 patients with ASA physical status I–II aged 18–60 yr scheduled to

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undergo elective lower limb surgery with spinal anesthesia were enrolled in this prospective observational study. Patients with known hypersensitivity to amide local anesthetics or a history of severe renal, hepatic, respiratory, or cardiac disease or a neurological, neuromuscular, or psychiatric condition were excluded.Patients were divided randomally in two groups with 50 patients in each group.Group L receiving Isobaric 0.5% Levobupivacaine and Group R receiving Isobaric 0.5% Ropivacaine.

A pre-anesthetic checkup was done for all patients which included a detailed history, general physical and systemic examination. Basic investigations were done. Patients were kept nil per oral overnight. Baseline heart rate, blood pressure and oxygen saturation will be recorded. An intravenous line was secured and ringer lactate was started.

Spinal anaesthesia was given under all aseptic precaution,with patients in sitting position in L3-4 interspace with Quincke's needle 25 gauge with midline approach with 3ml of study drug. The end of injection of study drug was termed "time 0" for the purposes of subsequent patient assessment.Intraoperative monitoring was done using multiparameter monitor.

following parameters were studied.

1. Onset of sensory and motor blockade.
2. Maximum dermatomal level of sensory blockade attained and the time taken for the same.
3. Maximum level of motor blockade attained and the time taken for the same.
4. Hemodynamic changes and side effects if any.
5. Time for two segment sensory regression.
6. Total duration of sensory and motor blockade.
7. Total duration of surgeries.

Sensory block was measured by using the blunt end of a 27-gauge dental needle at 0, 2, 5, 10, 15, 20, 25, 30, and 60 min postinjection and every 30 min thereafter until complete regression of sensory block was observed.The onset, degree and duration of motor block were measured in both legs by using a modified Bromagescale.Motor block was measured at 0, 10, 20, and 30 min postdose (presurgery) and every 30 min postsurgery until the patient returned to a score of zero in both legs.Hemodynamic variables were recorded at baseline, at the end of injection, and at 30-min intervals until complete resolution of the sensory block.The onset, degree, and duration of motor block were measured in both legs by using a modified Bromage scale and scored as:

Grade 0:no paralysis full flexion of hips, knees, and ankles

Grade 1: inability to raise extended leg, able to move knees

Grade 2:inability to flex knees, able to flex ankles

Grade 3: inability to move any portion of the lower limb.

All other adverse events were recorded throughout the study.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data.Continuous data was represented as mean and SD. Independent t test was used as test of

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significance to identify the mean difference between two quantitative variables. Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram and Pie diagram.p value(Probability that the result is true) of <0.05 was considered asstatistically significant after assuming all the rules of statistical tests.

Results:

Mean sensory blockade onset in Group R was 3.68 ± 1.2 min and in Group L was 1.90 ± 0.99 min. This difference was statistically significant. i.e. Onset was seen earlier in Group L than in Group R. Table no.1 and figure no.1

Table 1: Sensory Parameters between two groups

	Group				P value
	Levobupivacaine		Ropivacaine		
	Mean	SD	Mean	SD	
Onset (min)	1.90	.99	3.68	1.20	<0.001*
Maximum Level T	8.80	1.21	10.24	1.38	<0.001*
Time for Max T (min)	16.04	3.32	16.90	3.09	0.183
Two Segment Regression (min)	128.08	25.22	92.20	5.51	<0.001*
Duration (min)	240.48	16.31	189.68	14.78	<0.001*

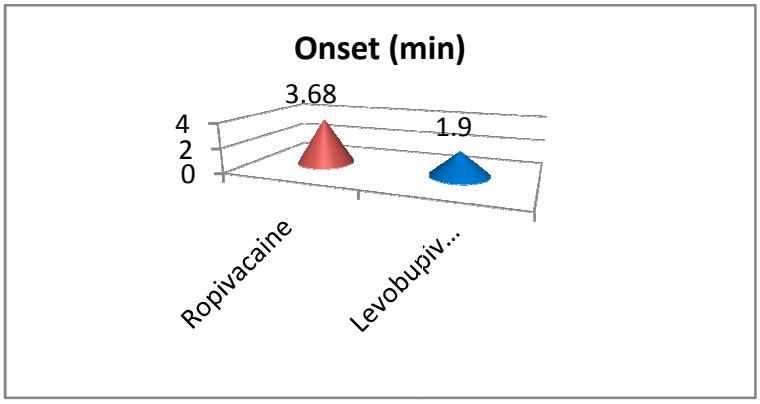

Figure 1: Bar diagram showing onset of sensory blockade between two groups

Mean sensory maximum Level T in Group L(Isobaric 0.5% levobupivacaine) was 8.8 ± 1.21 and in Group R(Isobaric 0.5% ropivacaine) was 10.24 ± 1.38 . This difference was statistically significant. i.e. sensory maximum Level T was seen at higher level in Group L than in Group R.

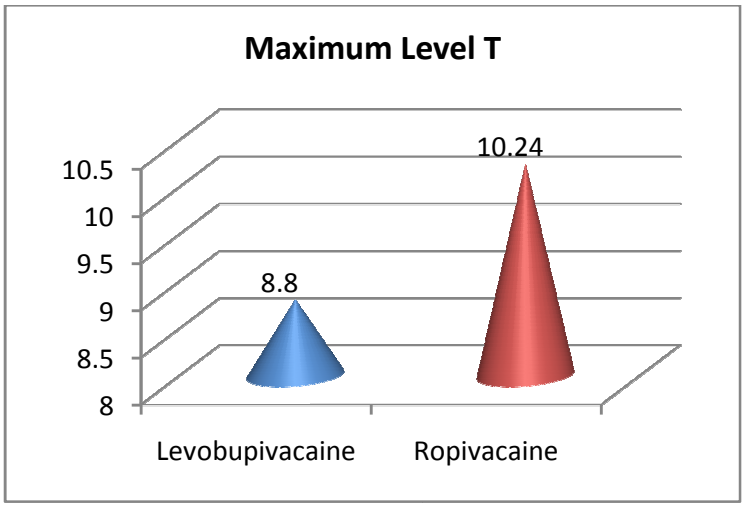

Figure 2: Bar diagram showing Maximum Level T between two groups

Mean sensory Time for Maximum T in Group L was 16.04 ± 3.32 min and in Group R was 16.9 ± 3.09 min. This difference was not statistical significant. Table no.1 figure no.3

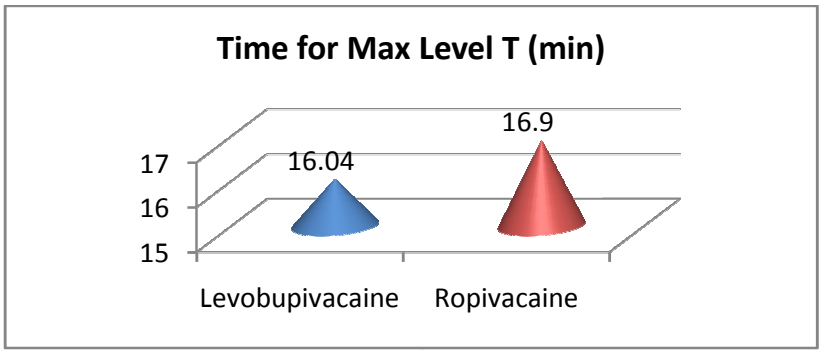

Figure 3: Bar diagram showing Time for Maximum Level T between two groups

Mean sensory two segment regression in Group L was 128.08 ± 25.22 min and in Group R was 92.2 ± 5.51 min. This difference was statistically significant i.e. Lesser time was required in Group R to achieve two segment regression than group L.

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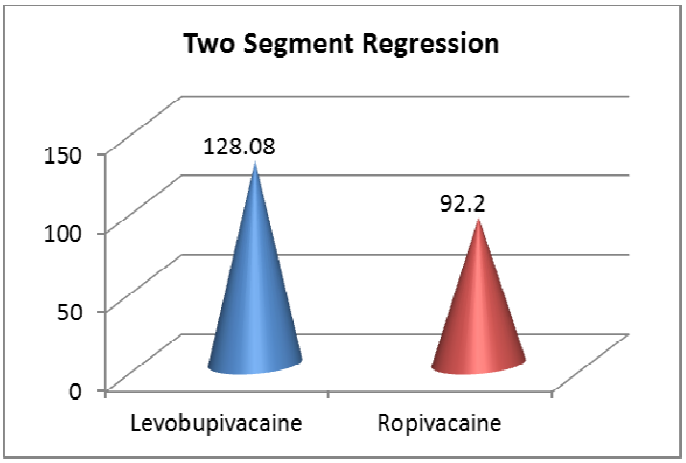

Figure 4: Bar diagram showing Time taken for Two Segment Regression between two groups

Mean duration of sensory blockade in Group L was 240.48 ± 16.31 min and in Group R was 189.68 ± 14.78 min. This difference was statistically significant i.e. Higher duration of sensory blockade was seen in Group L than in group R.

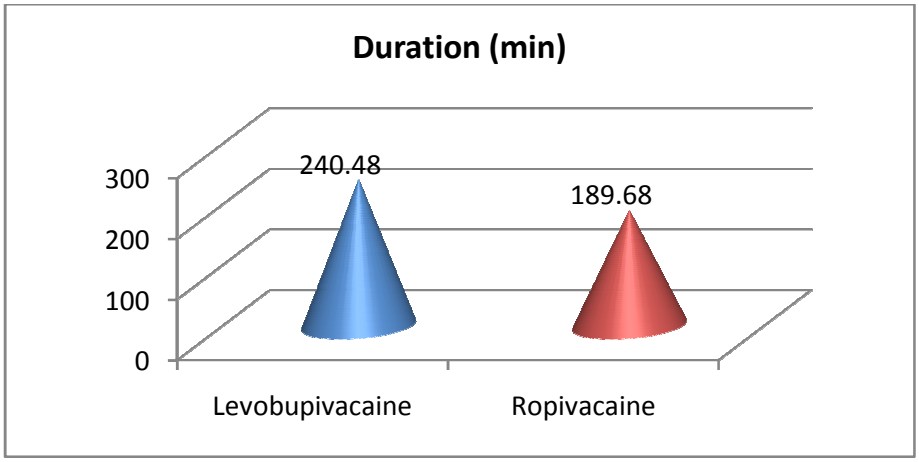

Figure 5: Bar diagram showing Duration of Sensory Block between two groups

Table 2: Motor Parameters comparison between two groups

	Group				P value
	Levobupivacaine		Ropivacaine		
	Mean	SD	Mean	SD	
Onset (min)	2.30	0.74	2.64	1.06	0.066
Time for max (min)	17.32	3.09	17.32	3.09	1.000
Duration (min)	221.44	15.81	149	15.41	<0.001*

Mean Motor blockade onset in Group L was 2.3 ± 0.74 min and in Group R was 2.64 ± 1.06 min. This difference in Mean onset of motor blockade was not statistically significant.

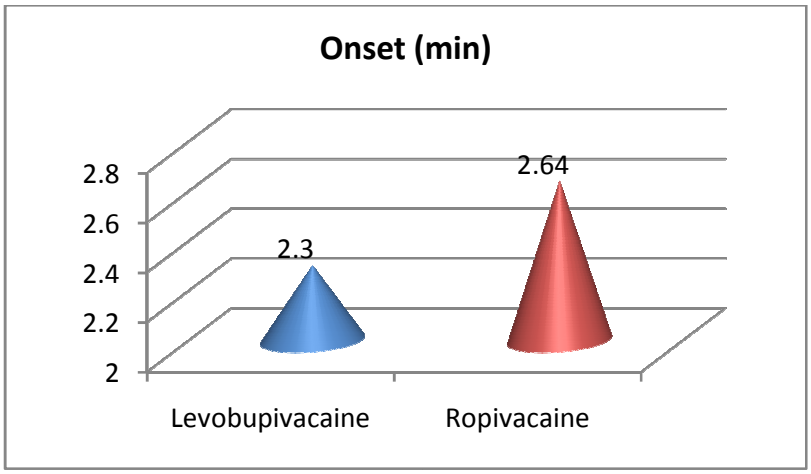

Figure 6: Bar diagram showing Onset of Motor Blockade between two groups

Mean Motor Time for Maximum in Group L was 17.32 ± 3.09 min and in Group R was 17.32 ± 3.09 min. There was no significant difference between two groups

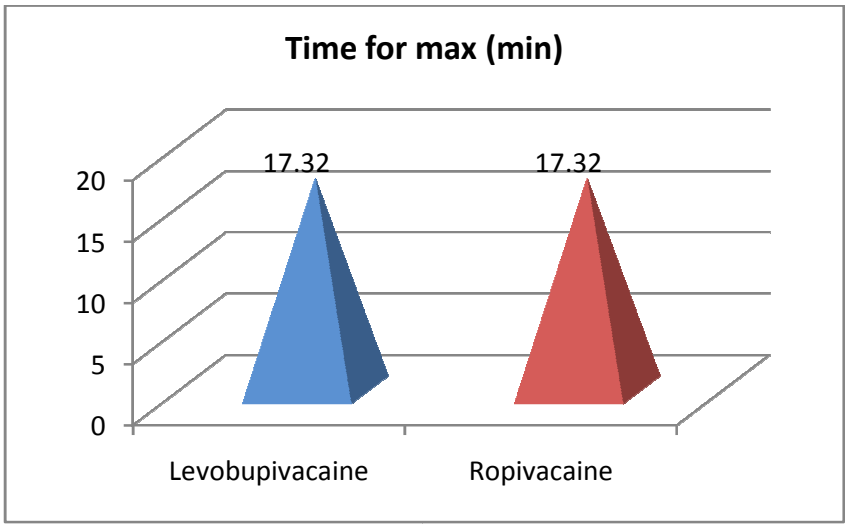

Figure 7: Bar diagram showing Time for Maximum between two groups

Mean duration of Motor blockade in Group L was 221.44 ± 15.81 min and in Group R was 149 ± 15.41 min. This difference was statistically significant. i.e. Higher duration of Motor blockade was seen in Group L than in group R.

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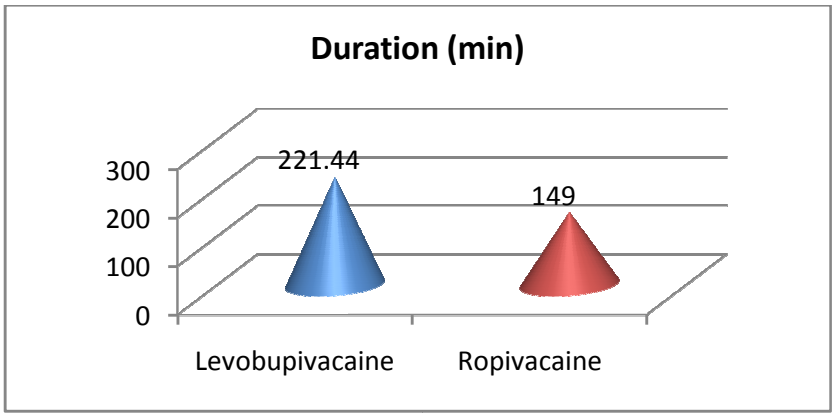

Figure 8: Bar diagram showing duration of motor blockade

Table 4: Bromage Score between two groups

		Group			
		Levobupivacaine		Ropivacaine	
		Count	%	Count	%
Bromage grade	2	1	2.0%	28	56.0%
	3	49	98.0%	22	44.0%

χ 2 = 35.41, df=1, p<0.001*

In Group L, 2% had Grade 2 and 98% had Grade 3 Bromage grade. In Group R, 56% had Grade 2 and 44% had Grade 3 Bromage score. This difference was statistically significant.

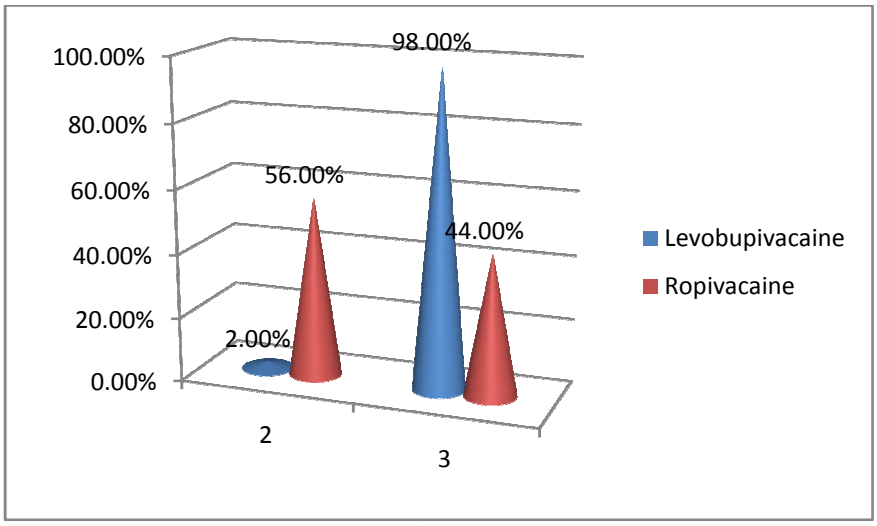

Figure 9: Bar diagram showing Bromage Score between two groups

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Table 4: Pulse Rate comparison between two groups

	Group				P value
	Levobupivacaine		Ropivacaine		
	Mean	SD	Mean	SD	
Basal PR	76.32	5.76	76.32	5.76	1.000
Minimum PR	68.04	3.74	67.72	4.02	0.681
Maximum PR	86.72	5.12	85.16	12.55	0.418

Mean basal pulse rate in Group L was 76.32 ± 5.76 per min and in Group R was 76.32 ± 5.76 per min. Mean minimal pulse rate in Group L was 68.04 ± 3.74 per min and in Group R was 67.72 ± 4.02 per min. Mean maximum pulse rate in Group L was 86.72 ± 5.12 per min and in Group R was 85.16± 12.55 per min. Thus mean Basal, Minimal and Maximum pulse rate werecomparable in both the groups. (P > 0.05).

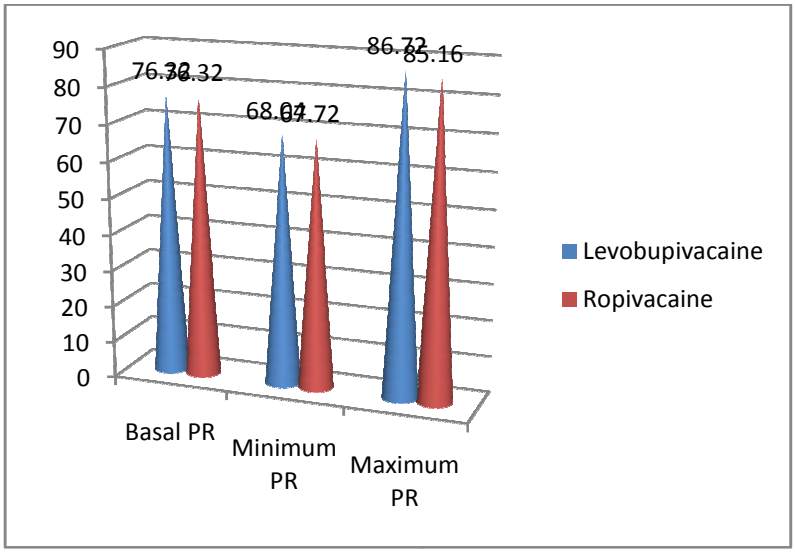

Figure 10: Bar diagram showing Pulse Rate comparison between two groups

Table 5: SBP comparison between two groups

	Group				P value
	Levobupivacaine		Ropivacaine		
	Mean	SD	Mean	SD	
Basal SBP	127.36	5.07	127.36	5.07	1.000
Minimum SBP	107.04	5.82	107.80	6.08	0.524

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There was no significant difference in Basal SBP and Minimum SBP between two groups.

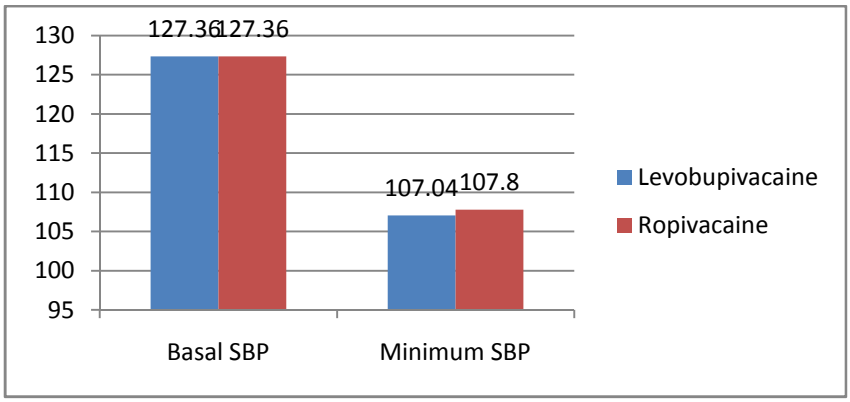

Figure 11: Bar diagram showing SBP comparison between two groups

Table 6: DBP comparison between two groups

	Group				P value
	Levobupivacaine		Ropivacaine		
	Mean	SD	Mean	SD	
Basal DBP	76.96	4.99	76.96	4.99	1.000
Minimum DBP	69.96	3.42	69.12	3.68	0.240

There was no significant difference in Basal DBP and Minimum DBP between two groups.

There was no significant difference in Basal SpO_2 and Minimum SpO_2, duration of surgery time between two groups. There was no complications noted among all the subjects in both the groups.

Discussion

With the introduction of the first long acting amino amide Bupivacaine into clinical practice in 1963, its use has been widespread for spinal anaesthesia. However, its cardio-toxic and central nervous system effects have made researchers to come up with newer drugs like Ropivacaine and Levobupivacaine whichare pure S-enantiomers with similarities in structure, pharmacokinetics, Pharmacodynamics and mechanism of action but with relatively less cardio-toxic and central nervous system effects.[7]

This study was a Prospective Observational Study conducted in 100 consenting patients of ASA grade I and II undergoing elective lower limb surgeries,divided in two groups. In our study both the groups were comparable with respect to the baseline demographic characteristics of Age, Weight, Height, Gender and ASA Grade. No significant difference was noticed in Mean Duration of surgery in both groups.

The mean time of onset of sensory blockade in Isobaric 0.5% Plain Levobupivacaine Group was 1.90 ± 0.99 mins and 3.68 ± 1.2 mins in Isobaric 0.5% Plain Ropivacaine Group.($P > 0.05$) (Table 1).The difference was statistically significant, the

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mean onset time of sensory block were significantly faster in Levobupivacaine compared to Ropivacain.

Maximum level spread of analgesia was variable in both the varying from as high as T_4 to sometimes as low as T12.Isobaric 0.5% levobupivacaine group median upper level of analgesia was found to be T8 (Range T6 – T12) and in Isobaric 0.5% ropivacaine group median upper level of analgesia was found to be T10 (Range T8-T12).This difference was found to be statistically significant *(P* <0.05) (Table No.1)

The difference between Mean time to achieve maximum level of sensory block was not statistically significant. (P > 0.05) (Table no.1).The difference between mean time to achieve two segment regression was statistically significant i.e.lesser time was required in ropivacaine group than in levobupivacainegroup.This difference in Mean duration of sensory blockade was statistically significant.i.e. Higher duration of sensory blockade was seen in Group L than in group R.

In study conducted by Jigisha P Badheka*, Urmi Dave, Vasantha Kumar, Raghu S Parmeshwar, RakhiGoyal ,comparative study of 0.5% levobupivacaine and 0.5% ropivacaine in spinal anaesthesia for lower limb surgeries[11] ,the mean time of onset of sensory and motor block was faster in levobupivacaine group (9.09±1.63 minutes and 8.54±1.36 minutes respectively) than ropivacaine group (10.8±2.42 minutes and 10.7±1.5minutes respectively).The maximum sensory dermatome level attained in group levobupivacaine was T4 and in group Ropivacaine was T6, ranging from T4 -T12 and T6 –L1 respectively, with statistically significant difference. These results are also comparable with the certain studies conducted by Mantouvalou M. et al[38], Glaser C et al[76] and Orhan G et al[77].The mean duration of sensory blockade was comparable in group S (162.86±6.45 minutes) and in group R (161.29±5.05 minutes)

The mean time required for onset of motor block was 2.3 ± 0.74 mins in Isobaric 0.5% Levobupivacaine Group and 2.64± 1.06 mins in Isobaric 0.5% Ropivacaine. The difference was not statistically significant. (P >0.05) (Table no.2).complete motor block (Bromage Grade III) was obtained in 98% patients and Grade II motor blockade 2% of patients in Isobaric 0.5% levobupivacaineGroup.While in group 2 with Isobaric 0.5% Ropivacaine, Grade III motor blockade was seen in 44% of patients and in 56% of patients grade II motor blockade was seen.This difference between the two groups was statistically significant (P< 0.05) (Table 4).Our findings were consistent with the various studies[9,22,23,68,69] which state that ropivacaine has got less motor blockade due to its low lipid solubility resulting in less penetration of thick motor fibres Aα

III)Time for Maximum Motor Blockade was not statistically significant (P > 0.05) (Table 2)III)Time for Maximum Motor Blockade was not statistically significant (P > 0.05) (Table 2 In equal doses (15 mg) levobupivacaine has a faster onset (sensory and motor block) and longer duration (motor block and analgesia) as compared to ropivacaine. These studies suggest that ropivacaine may be suitable for short ambulatory surgical procedure. Levobupivacaine may be used as long acting local anaesthetic due to profound duration of motor block and analgesia.

Mean Basal, Minimal and Maximum pulse rate were comparable in both the groups(P > 0.05).There was no significant difference in Basal and Minimum SBP as well as Basal DBP and Minimum DBP between

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two groups.These findings were consistent with other studies mentioned above.Patients were hemodynamically stable in both groups. There was no significant difference in Basal SPO_2 and Minimum SpO_2 between two groups.Nopatient in our study had respiratory depression. No patient in our study required additional analgesia as sensory and motor blockade required for lower limb surgeries were adequate with both group of drugs.No procedure demanded conversion of regional anaesthesiainto generalAnaesthesia.

The incidence of complications apart from hypotension and bradycardia like nausea, vomiting and shivering was almost not seen in our study.

Conclusion

This study concludes that both study drugs,pure enantiomers, Isobaric 0.5% Levobupivacaine and Isobaric 0.5% Ropivacaine when used intrathecally provides adequate level of analgesia and excellent hemodynamic stability.There was no need of any supplemental analgesics in our study.No incidence of any cardiac or CNS toxicity.

w henIsobaric 0.5% Levobupivacaineused intrathecally,it was found that higher dermatome level with faster onset, adequate analegesia and great quality of motor blockade were achieved without any hemodynamic complications. So Levobupivacaine (isobaric 0.5%) can be used in surgeries where higher level of sensory blockade with good appreciation of muscle relaxation by surgeon is required such as in lower abdominal surgeries.Isobaric 0.5% Ropivacaine when used intrathecally gives good quality of subarachnoid block.WithRopivacaine level of analgesia and degree of motor blockade achieved is lower compared to Levobupivacaine.So it can be used in lower limb surgeries ,where muscle relaxation is less important.Time required for regression of effect of ropivacaine is less in comparison with long acting local anaesthetics, so we can provide early ambulation postoperatively.

Conflicts of interest –nil

Financial support and sponsorship- nil.

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