Comparative Study of Racemic Mixture of 0.5% Bupivacaine , 0.5 % Levo Bupivacaine And 0.75% Ropivacaine In Lumbar Epidural Anaesthesia In Patients Undergoing Lower Abdominal Surgeries

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Abstract: Background and aims: Epidural blockade is one of the most useful and versatile procedures in modern anaesthesiology. Bupivacaine a long acting amide local anaesthetic though widely used but associated with side effects like neuro and cardio toxicity. Study was done to compare the haemodynamic variations , onset time and duration of sensory and motor block and complications if any of epidural anaesthesia produced by 0.5% bupivacaine, 0.5% levobupivacaine and 0.75% r opivacaine which are possible alternatives to bupivacaine for lower abdominal surgeries. Methodology: 90 patients were randomly allocated into 3 groups of 30 each. The time for loss of pinprick at T_{10} and T_6, intensity of motor block, duration of sensory and motor block and variations in haemodynamic parameters, respiratory rate and SpO_2 changes were assessed. Results: The onset of sensory blockade at T_{10} level was 6.56 ± 1.69> 6.27±1.55 >6.13 **±** 1.81 minutes which was comparable ,but onset of motor blockade was 18.9±2.41 >15.5+1.98 > 14±2.03 minutes in levobupivacaine, ropivacaine and bupivacaine groups respectively which was highly significant. While the duration of sensory block was 340.5±28.6 < 355.83±34.98 < 371.5 ± 9.60 minutes (P < 0.001), duration of motor block was 202.6 ±9.35 **<** 265.17±29.29 **<** 304.9 ± 28.89 minutes in bupivacaine , ropivacaine and levobupivacaine groups respectively(p < 0.001). Conclusions: Epidural levobupivacaine and ropivacaine are excellent alternatives to bupivacaine for lower abdominal surgeries with little compromise on the onset of sensory and motor block with an added advantage of longer duration as well as decreased incidence of cardiotoxicity. [Deshpande S NJIRM 2017; 8(5):22-26]

Key Words: Epidural Anaesthesia; bupivacaine; levobupivacaine; Ropivacaine

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Introduction: Epidural anaesthesia is more versatile than the spinal anaesthesia giving an excellent option for lower abdominal surgeries. It decreases intraoperative blood loss, perioperative ischaemic events, postoperative hypoxic episodes & venous thrombosis offering an excellent sensory block The commonly used agents are lignocaine, bupivacaine, levobupivacaine and ropivacaine.[1]

Bupivacaine is commercially available as a racemic mixture containing equal proportion of the S (-) and R(+) isomers. Despite its popularity, it is associated with side effects like unwanted longer duration of motor blockade, central nervous system(CNS) and cardiotoxicity. There have been many reports of death attributable to bupivacaine induced cardiotoxicity after accidental intravenous injection resulting in continued search for new and safer local anesthetic agents.[2]

Levobupivacaine is local anesthetic drug belonging to the amide group, the S-enantiomer of bupivacaine which was developed as an alternative to bupivacaine, to achieve lower risk of cardiotoxicity[3]. It's longer lipid solubility makes it more potent than lower lipid soluble agent and results in longer duration of action. Another answer to bupivacaine induced cardiotoxicity is ropivacaine, a newer long acting amide local anesthetic which is stereo isomer of bupivacaine and has been shown to have less CNS and cardio toxicity than bupivacaine. It is pure S(-) enantiomer of ropivacaine, less lipophilic than bupivacaine and less likely to penetrate large myelinated motor fibers resulting in relatively reduced motor blockade. Its reduced lipophilicity is associated with decreased CNS and cardiotoxicity.[1]

Methodology: After approval from ethics committee, 90 patients between the age group 18-65 years of ASA I and II physical status, scheduled to undergo various lower abdominal surgical procedures under epidural anaesthesia with anticipated duration of surgery more than 1hr were included and randomly allocated into three groups of 30 patients each. A prospective double blind study was conducted after taking an informed consent from the patients. Patients with a history of hypertension, diabetes, and liver disease, acute or chronic renal disease, known case of neurological disease, psychiatric disorders with anticipated difficult airway, neurosurgical and

cardiovascular surgical cases and patients posted for emergency surgeries ,patients with BMI >28 kg/m^2 , patients shorter than 150 cm , infection at the site of injection , with congenital anomalies of spine and patients with coagulation abnormalities , history of seizures and patients in shock were all excluded from the study. Group bupivacaine received 15 ml of 0.5% bupivacaine, group levobupivacaine received 15 ml of 0.5% levobupivacaine and group ropivacaine received 15 ml of 0.75%ropivacaine, epidurally.

All patients included in the study were visited on the previous day of surgery and a detailed pre-anaesthetic examination was carried out. An informed written consent was taken. Premedication with tablet lorezepam 2 mg and tablet ranitidine 150 mg was given orally the night before surgery. Patients were asked to maintain nil per oral status for at least 6 hours.

On the day of operation baseline blood pressure and pulse was recorded. An 18 G IV cannula was inserted and all patients were preloaded with received 20 ml/kg of ringer lactate solution.

A patient were given left lateral position and under aseptic conditions skin was infiltrated with lignocaine 2% and 2 ml was given. Epidural space was located with 18 G Tuohy needle in L_3-L_4 space using the midline approach with loss of resistance technique and after negative aspiration for blood epidural space was located, 3ml of lignocaine test dose was administered to exclude intrathecal and intravascular placement of the needle. After 5 min period, the study drug was injected incrementally over 2 min and later patients were made supine. All assessments were made by an anaesthetist who did not know the drug used. Measurement of blood pressure and pulse rate were recorded at 0,5,10,15,20 min and thereafter every 15min. Intraoperatively and postoperatively, complications like fall in blood pressure, variation in heart rate, respiratory rate and SpO_2 were noted. Sensory blockade using pinprick sensation was assessed until complete loss of sensation at T_{10} (taken as onset of sensory block) and then every 2 min to determine the time taken for maximum height of block and there after every 15 min to determine the time for two segment regression and regression of sensory block at T_{12} taken as duration of sensory block. When sensory block reached T_{10} motor block was assessed using a modified bromage score. (Table 1)

Table 1: Bromage Scale

Score	Description
1	Complete block (unable to move feet / knees)
2	Almost Complete block (able to move feet only)
3	Partial block (just able to move knees)
4	Detectable weakness of hip flexion while supine (full flexion of knees)
5	No detectable weakness of hip flexion while supine
6	Able to perform partial knee bend

Thirty was the number in each group, where any results could be statistically significant hence this number was selected. Student T-Test was used to find out significance between samples. Data was reported as mean value ±S.D. A *P*-value of < 0.05 was considered statistically significant, <0.001 as highly significant and > 0.05 as not significant.

Results: Demographic profile of three groups were similar regarding age , sex , height (Table2) type of surgery (Table 3) and duration (Table 4) of surgery and ASA status of the patients. Due to computerized generation of numbers to the patients, levobupivacaine group had more male: female ratio , leading to comparable weight and BMI datas. (Table 2) The onset of sensory blockade at T_{10} level as judged by loss of pinprick sensation, bilaterally at shin of tibia was 6.56 ±1.69 > 6.27± 1.55 > 6.1± 1.814 minutes and at T_6 level was 9.43±2.24 > 8.27±2.05> 8.17± 2.05 min in levobupivacaine, ropivacaine and bupivacaine groups respectively which was comparable. The onset of motor blockade ie. bromage score 1 or 2 was 18.9±2.41 >15.5+1.98 > 14±2.03 minutes in levobupivacaine, ropivacaine and bupivacaine groups respectively which was highly significant. While the time for regression of sensory block to T12 (duration of sensory block) 340.5±28.6 < 355.83±34.98 < 371.5 ± 9.60 minutes (P < 0.001) and the duration of motor block which was recorded from the time of injection to complete regression of motor block (bromage 5, 6 score) was 202.6 ±9.35 < 265.17±29.29 < 304.9 ± 28.89 minutes in bupivacaine, ropivacaine and

Table 2: Demographic Data

	Bupivacaine group	Levobupivacaine Group	Ropivacaine Group	P value
Mean age	42.63 ±8.58	50.73 ± 12.8	43 ± 0.45	>0.05
Mean wt (Kg)	57.06 ±8.14	67.00 ±8.1	55 ± 4.25	< 0.05
Mean Ht (mt)	1.56 ± 4.25	1.60 ± 5.19	1.55 ±6.28	>0.05
Male : female ratio	4: 26	12 :18	5 :25	
Mean BMI (kg/m2)	23.18 ±3.01	25.92 ±2.52	22.92 ±2.16	<0.05

Table 3: Type of surgery

	Bupivacaine group		levobupivacaine group		Ropivacaine Group	
	n = 30	%	n = 30	%	n = 30	%
Abdominal hysterectomy	13	43	15	50	10	33.33
Vaginal hysterectomy	6	20	1	3.33	6	20
P sling	1	3.33	-	-	1	3.33
Inguinal Hernioplasty	4	13.33	4	13.33	5	16.7
Appendicectomy	1	3.33	2	6.7	2	6.7
Tubal recanalization	1	3.33	1	3.33	1	3.33
Myomectomy	-	-	1	3.33	3	10
THR	4	13.33	6	20	2	6.7

Table 4: Characteristics of sensory and motor block

Mean		Bupivacaine group	Levobupivacaine group	Ropivacaine group	P value
Onset of Sensory Block (min)	T_{10} level	6.13 ±1.81	6.56 ±1.69	6.27 ±1,55	<0.05
	T_6 level	8.17 ±2.05	9.43±2.24	8.27 ±2.05	<0.05
Onset of Motor block (min)		14±2.03	18.9± 2.41	15.5±1.98	<0.001
Duration of surgery (min)		108.8 ±12.43	118.8 ±12.9	116.67± 29.25	>0.05
Duration of sensory block (min)		340.5±28.6	371.5 ± 9.60	355.83±34.98	<0.001
Duration of motor block (min)		202.6 ± 9.35	304.9 ± 28.89	265.17±29.29	<0.001

Table 5: Side effects

	Bupivacaine Group		Levobupivacaine Group		Ropivacaine Group	
	n=30	%	n=30	%	n=30	%
Headache	0	0	0	0	0	0
Nausea /Vomiting	1	3.33	0	0	1	3.33
Hypotension	0	0	1	3.33	0	0
Bradycardia	0	0	0	0	0	0
Urinary retention	0	0	0	0	0	0

levobupivacaine groups groups respectively as depicted in Table 4. Changes in heart rate, blood pressure and respiration were similar between the groups. We observed that there was a fall in the systolic and diastolic blood pressure below the baseline after epidural administration at various intervals in all the three groups. But this difference was not statistically significant (p>0.05). One patient in levobupivacaine group had clinically significant hypotension (SBP<30% baseline) which was corrected with Intravenous mephentermine 6mg bolus. Pulse rate was assessed at various intervals after the administration of epidural anaesthesia and the changes in mean pulse rate between the groups were not statistically significant (p>0.05). There was no difference in the respiratory rate between the groups when measured at various intervals after administration of epidural anaesthesia. One patient in bupivacaine and one patient in the ropivacaine group had vomiting episode intraoperatively which was treated with single intravenous ondansetron 8 mg.

We observed that there was a fall in the systolic and diastolic blood pressure below the baseline after epidural administration

Discussion: Epidural techniques are effective at providing dynamic analgesia allowing the patient to mobilize and resume normal activities unlimited by pain. It also improves the postoperative outcome and attenuates the physiologic response to surgery, with significant reduction in pulmonary infections, pulmonary embolism, ileus, acute renal failure and blood loss.[4]

Traditionally amide local anaesthetics have been used in regional anesthetic techniques and bupivacaine has emerged as the most commonly used drug for central neuraxial blockade. But it also carries undesirable effects like prolonged post-operative motor blockade and cardio toxicity.

Keeping such factors in mind, long acting amide local anaesthetic, S (-) enantiomers of bupivacaine, levobupivacaine and ropivacaine have been developed. The advantages of levobupivacaine over bupivacaine are decreased cardiovascular toxicity and motor nerve fiber penetration and block, thereby a decreased post-operative motor blockade and thus early ambulation of the patients. Ropivacaine a newer long acting regional anesthetic is also developed for similar purpose is pure S (-) enantiomer. R and s-enantiomers of local anesthetic have been demonstrated to have a different affinity for the different ion channel of sodium, potassium and calcium which results in significant reduction of CNS and cardiotoxicity of the s (-) compared to r (+) enantiomer.[5]

Casati et al.[6] compared the onset, time and duration of epidural anaesthesia produced by levobupivacaine, bupivacaine and ropivacaine they found the onset time of sensory block was 31±16minutes, 25±19 minutes and 30±24 minutes (p = 0.98), recovery of pinprick sensation ie duration of sensory block occurred after 214±61 minutes with levobupivacaine, 213±53 minutes, and 233±34 minutes with levobupivacaine bupivacaine and ropivacaine respectively (p = 0.26) , which was similar to the study of Peduto VA et al[7] where onset time with levobupivacaine was 29±24 min, with ropivacaine it was 25±22 min (P = 0.41). Complete resolution of motor block (duration of motor block) required 105±63 min and 95±48 min (P=0.86). The time for regression of sensory block to T12 was 185±77 min and 201±75 min with levobupivacaine and ropivacaine respectively (P=0.46). Shaikh, K Rohini, et al [8] did a clinical study for evaluation of epidural 15ml 0.5% bupivacaine with 15ml 0.75% ropivacaine for lower limb orthopaedic procedures was done where the mean time of ropivacaine for sensory block at T10 was similar to bupivacaine (16.06± 3.82/15.76±2.95 min). Time for two segment regression was almost similar in ropivacaine and bupivacaine (99.5±13.34/102±13.87 min).Total duration of motor block was slightly shorter in ropivacaine than bupivacaine (134±12.41/151±11.09 min).

Thus there was no statistically significant difference in the onset and duration of sensory blockade. The motor blockade was more intense and of longer duration in bupivacaine than ropivacaine. The results of onset time of sensory and motor block correlated with our study but the results of duration of sensory and motor block were in contrast where the duration of sensory block was 340.5±28.6 < 355.83±34.98 < 371.5 ± 9.60 minutes (P < 0.001) and the duration of motor block was 202.6 ±9.35 < 265.17±29.29 < 304.9 ± 28.89 minutes in bupivacaine, ropivacaine and levobupivacaine groups groups respectively.

Chandran S etal.[9] compared 20ml 0.75% ropivacaine and 20ml 0.5% bupivacaine given for epidural anaesthesia in lower extremity orthopaedic surgery . Time for onset of sensory block was 6.24 minutes and 6.92 minutes, time for onset of motor block was 10.32 minutes and 10.20 minutes , time for total duration of sensory block was 389.80 minutes and 370.60 min & for motor block it was 336.30 minutes and 338.10 min in group ropivacaine and bupivacaine group respectively and concluded that there were no significant differences in the block parameters but ropivacaine was associated with relatively longer duration of postoperative analgesia correlating with our study results. Koch T, Fichtner A et al.[10] studied efficacy of 0.5% levobupivacaine versus 0.5% bupivacaine and 0.75% ropivacaine administered as epidural anaesthesia. The efficacy of epidural levobupivacaine was equivalent and showed a comparable clinical profile to bupivacaine and 50 – 60% higher concentrated ropivacaine, involving 88 patients undergoing hip surgery.

Conclusion: To conclude ropivacaine a less lipophilic than bupivacaine and less likely to penetrate the large myelinated motor fibres results in a relatively reduced motor blockade. Thus it has a greater degree of motor

and sensory differentiation which is useful when motor blockade is undesirable. Levobupivacaine's longer lipid solubility makes it more potent than lower lipid soluble agent and results in longer duration of action but slower in onset but both study drugs produced adequate surgical anaesthesia for lower abdominal surgery when administered epidurally.

Both levobupivacaine and ropivacaine developed as an alternative to bupivacaine can be used for lower abdominal surgeries with an added advantage of lower risk of cardio and CNS toxicity.

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