



## Comparative Evaluation of Bupivacaine Versus Ropivacaine Epidurally in Obstetrical Surgeries (LSCS): A Clinical Study

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### ABSTRACT

**Background:** A double blind prospective and randomized study was carried out in our institute to compare the anaesthetic effects of Ropivacaine and Bupivacaine epidurally in elective Lower Segment Caesarean Section (LSCS).

**Method:** A total of 50 patients aged 18-30 years of American Society of Anesthesiology (ASA) grade 1 and 2, scheduled for elective LSCS under epidural block, were enrolled for the study. Patients were divided into two groups of 25 each. Group 1 received 0.5% 15 ml Bupivacaine and group 2 received 0.5% 15 ml Ropivacaine. Heart Rate (HR), Mean Artery Pressure (MAP), SPO<sub>2</sub>, Respiratory Rate, Sensory Block, Motor Block, Maternal and Fetal outcomes and Blood loss were observed and recorded throughout the study period at regular intervals. At the end of research project data's were compiled systematically and were subjected to statistical analysis using student t-test. Value of  $p < 0.05$  is significant and  $p < 0.01$  as highly significant.

**Results:** No significant difference seen in both the groups for demographic characteristics, SPO<sub>2</sub>, RR, HR, MAP sensory and motor block and materno-fetal outcome. No significant difference seen for side effects and complications in both the groups.

**Conclusion:** Ropivacaine and bupivacaine given epidurally in the same concentration and volume provided similar and effective anaesthesia in patients undergoing elective LSCS.

**Key Words:** Ropivacaine, Bupivacaine, Epidural, Elective LSCS

## INTRODUCTION

Ropivacaine is a long acting amide local anaesthetic. All local anaesthetic drugs except Ropivacaine are racemic mixtures. Ropivacaine is unique in that it is produced in a pure chiral form, this results in a significant reduction in central nervous system (CNS) and cardiac toxicity of the S(-) enantiomer as compared with the R(+) enantiomer<sup>[1]</sup>. Ropivacaine has a lower CNS and cardiotoxic potential than bupivacaine in animals.<sup>[2]</sup> Ropivacaine has pharmacodynamic and pharmacokinetic properties in animals resembling those of Bupivacaine.<sup>[3],[4],[5]</sup> In human volunteers, ropivacaine has shown to be less prone than bupivacaine to produce mild CNS and cardiovascular changes after intra venous infusion.<sup>[6]</sup> Initial clinical studies in epidural anaesthesia have indicated that pharmacodynamic and pharmacokinetic properties of Ropivacaine are comparable to those seen with Bupivacaine.<sup>[7],[8],[9]</sup> During epidural analgesia for labour, ropivacaine has been found in metanalysis to be equivalent to bupivacaine in terms of quality of pain relief and side effects, mode of delivery and neonatal outcomes.<sup>[10]</sup> When comparing ropivacaine and levobupivacaine for epidural analgesia, there seems to be little difference in potency between the two local anaesthetics (LA). Similar doses and concentrations were administered for pain relief in abdominal surgery patients<sup>[11],[12]</sup> and parturients.<sup>[13]</sup> The results seem to suggest similar potency, either with or without opioids in the LA solutions. Both bupivacaine and ropivacaine cause reversible inhibition of sodium ion influx, and thereby block impulse conduction in nerve fibres.<sup>[14]</sup> This action is potentiated by dose dependent inhibition of potassium channels.<sup>[15]</sup> Ropivacaine is less lipophilic than bupivacaine and less likely to penetrate large myelinated fibres; therefore it has selective action on the pain transmitting AD and C fibres rather than A $\beta$  fibres, which are involved in motor function. Both bupivacaine and ropivacaine have been used in the practice of anaesthesia for over many years. They have been used for

subarachnoid block, epidural block, patient controlled epidural analgesia (PCEA) and peripheral nerve blocks. With the incidence of transient neurologic symptoms (TNS) being more with lidocaine, tetracaine, mepivacaine,<sup>[16],[17],[18]</sup> newer local anaesthetics have been developed which apart from their long duration of action also carried less incidence of TNS. However, Ropivacaine scores in terms of lesser incidence of transient neurologic symptoms (TNS) than Bupivacaine.<sup>[19],[20]</sup> Epidural techniques improve the post-operative outcome and attenuate the physiological response to surgery, significant reduction in pulmonary infections, pulmonary embolism, ileus, acute renal failure and blood loss.<sup>[21]</sup> The present study was designed to compare Ropivacaine and Bupivacaine in same concentration and volume given epidurally for elective LSCS.

## MATERIAL & METHODS

This is a double blind controlled clinical study. After taking permission from ethical committee, 50 primigravida patients with ASA 1/2 status, between 36-42 weeks of gestation, about 18-30 years of age weighing 50-80 kg. patients were randomly allocated to one of the following two groups in a randomized double blind fashion based on computer generated code.

Group 1- patients receiving bupivacaine 0.5% ,15 ml epidural

Group 2- patients receiving Ropivacaine 0.5%, 15 ml epidural

Informed and written consent was obtained after explaining the procedure to the patients. All patients were given tablet Ranitidine 150mg and tablet Metoclopramide 10 mg in the morning before surgery. In the OT good IV access was secured and monitoring devices were attached which included, ECG, SPO<sub>2</sub>, NIBP and baseline parameters were recorded. Drugs were in coded ampoules and the investigators were blinded to contents. patients were made to sit and part was painted and draped for epidural block. At L3-L4 level a skin wheal with 1 ml of 1% Lidocaine was

raised and then epidural block done with 18 G Tuohy needle and catheter was secured 3-4 cm. into epidural space and a test dose of 3 ml of 2% lignocaine hydrochloride solution containing adrenaline 1:200,000 was injected. After 2-3 minutes of administering test dose, 15 ml of study drug was given through epidural catheter at a rate of 5ml/min. After giving block parturients nursed in supine position with a wedge under right hip to avoid aorto-caval compression the effect of which may be aggravated by sympathetic blockade. Bilateral pin prick method was used to evaluate and check the sensory level while a Bromage scale (0= No paralysis, full flexion of hips, knees and ankles possible, 1= unable to move hip, 2=unable to move knee, 3=unable to move ankle) was used to measure motor blockade effect at 5,10,15,20,25 &30 minutes intervals after the epidural administration of the drugs. Surgical position was made approximately after 25-30 minutes of epidural administration of drugs in every patient after complete establishment of sensory and motor block. Monitoring of the maternal hemodynamic and cardio respiratory parameters was done continuously and recordings were made at every 5 minute until 30 min and at 10 minutes interval thereafter upto 60 minutes and then at 15 min interval for next hour. All the vitals and hemodynamic parameters were recorded in the recovery room also at every 10 minutes interval until return of sensation and return of normal motor function (Bromage scale 0). All women received oxygen (4L/min) via a Hudson mask until delivery of the baby. Injection Syntocinon (Oxytocin) 10 units were given intravenously in the infusion. Blood loss during surgery can be a confounding factor as it can mask hypotension caused by local anaesthetic drugs; hence the approximate amount of blood loss during surgery was also recorded. If the estimated blood loss was more than 1200 ml then, the patient was excluded from the study. Also no NSAIDs/opioids were given to the patients after the surgery as it would have masked the duration of the analgesia provided by the local anaesthetic

agent. Hypotension (defined as systemic arterial pressure falling >20% mmHg) was treated with injection mephentermine 3-6mg in bolus doses and bradycardia (HR<50 beats/min.) was treated 0.3-0.6 mg of atropine. APGAR score was recorded at 0 and 5 minute after the delivery of the new born. I.V. fluids were given as per body weight and operative loss requirement. Intraop and postop complications and adverse effects like bradycardia, hypotension, shivering, nausea, vomiting, pruritus etc were recorded. At the end of study, all the data was compiled systematically and analysed by student test. Value of  $p < 0.05$  was considered significant and  $p < 0.01$  as highly significant.

### OBSERVATION & RESULTS

A total of 50 cases who underwent elective LSCS were enrolled for the study and were randomly divided into two groups of 25 each. (Table -1) shows the demographic distribution of cases among group 1 and group 2. All the patients in both the groups were of ASA 1 status. The difference in age, weight, height and ASA grade distribution between the two groups 1 and 2 are not significant,  $p$  value  $> 0.05$ . Table- 2, shows Onset and duration of analgesia. In maximum number of patients, time of onset of analgesia in group 1 and group 2 was between 11-15 min. The onset of analgesia and duration of analgesia in both the groups were not significantly different ( $P=0.8317$ ) and ( $P=0.3573$ ), respectively. Table-3, shows Mean  $\pm$  S.D. of mean blood pressure and heart rate, with time interval. The two samples (Group 1 & 2) are not significantly different ( $p > 0.05$ ) for mean blood pressure and HR. Table-4, shows Mean  $\pm$  S.D. of Respiratory rate and SpO<sub>2</sub>. Here also the two samples (Group 1 and 2) are not significantly different ( $P > 0.05$ ). Table-5, shows Maternal outcomes in relation to Pain relief (VAS SCALE), Degree of Motor blockade (BROMAGE SCORE) and Patient satisfaction. In our study, satisfactory analgesia (VAS  $\leq 4$ ) was observed in 22 patients in group 1 and all 25 patients in group 2. More than 4 VAS was observed only in 3 patients of group 1

The overall VAS scores were less in group 2 as compared to group 1. Degree of motor blockade was assessed by using Bromage scale. Maximum number of patients in both the groups had Bromage score of 3 (group 1=23 and group 2=20). P value for difference in Bromage score of both the groups was 0.2336 (Non significant=N.S.). maximum number of patients 64% in group 1 reported their analgesia as excellent while 12% reported their analgesia as good and rest 20% reported their analgesia was fair, as compared to group 2 in which 56% patients reported their analgesia as excellent, while 16% patients reported their analgesia was good and rest 28%

patients reported that their analgesia was fair. P value calculated for difference in maternal satisfaction between group 1 and group 2 was  $P=0.4127$  (NS). Table-6, shows Effect on foetus (Foetal outcomes). APGAR score at 0 minute showed 20 out of 25 neonates (80%) with score  $\geq 7$  in Bupivacaine group (group 1) while 22 out of 25 neonates (88%) showed with score  $\geq 7$  in Ropivacaine group (group 2). Calculated P value was 0.983 at 0 min (NS). While APGAR score at 5 min showed all 100% of the study neonates in both the groups having score  $\geq 7$ . Calculated P value was 0.987 at 5 min (NS). So effect on fetus in both the groups is also not significant  $P>0.05$ .

**TABLE 1:** Demographic Distribution of Cases Among Group 1 and Group 2

	Group 1 (Bupivacaine) (n=25)		Group 2 (Ropivacaine) (n=25)		P value
	Range	Mean $\pm$ SD	Range	Mean $\pm$ SD	
Age (yrs)	19-27	21.68 $\pm$ 1.99	19-25	21.80 $\pm$ 1.95	0.8308 (NS)
Height (cm)	150-168	157.12 $\pm$ 5.35	150-168	155.56 $\pm$ 4.84	0.286 (NS)
Weight (kg)	61-80	67.52 $\pm$ 4.90	54-80	66.68 $\pm$ 6.22	0.5556 (NS)
Gestational age (weeks)	36-42	38.28 $\pm$ 1.40	36-42	38.32 $\pm$ 1.31	0.9174 (NS)

No significant difference seen between the two groups regarding demographic distribution

**TABLE 2:** Onset and Duration of Analgesia

	Group 1 (Mean±SD)	Group 2 (Mean±SD)	P value
ONSET OF ANALGESIA (min)	13.88±1.42	13.80±1.22	0.8317(NS)
DURATION OF ANALGESIA (hrs)	5.90±0.48	5.76±0.58	0.3573(NS)

P value not significant in both the groups for onset and duration of analgesia

**TABLE 3 :** Mean±Sd Of Mean Blood Pressure And Heart Rate ,With Time Interval

HEART RATE				MEAN BLOOD PRESSURE		
TIME	GROUP 1 MEAN±SD	GROUP 2 MEAN±SD	P value	GROUP 1 MEAN±SD	GROUP 2 MEAN±SD	P value
0 min	84.08±6.74	82.56±8.26	0.4795	91.84±5.91	92.12±6.69	0.6886
5 min	84.24±7.01	82.56±7.56	0.4192	89.88±6.23	89.64±5.94	0.0659
10 min	85.04±8.62	85.84±11.37	0.7805	88.12±6.23	85.96±8.07	0.2951
15 min	89.52±13.43	88.24±13.67	0.7398	82.80±9.53	82.24±8.78	0.8298
20 min	94.16±12.33	90.24±13.59	0.2908	80.28±10.00	81.88±6.71	0.5097
30 min	93.60±11.27	91.92±8.05	0.547	82.40±7.27	81.72±5.51	0.711
40 min	91.68±6.99	90.32±5.88	0.4602	84.08±6.12	83.80±4.04	0.7449
After Surgery	90.64±5.53	89.52±5.24	0.4659	84.68±5.59	84.96±3.05	0.8269

No significant difference seen in both the groups regarding Heart rate and Mean Blood Pressure

**TABLE 4 :** Mean  $\pm$  SD Of Respiratory Rate And Spo2 With Time Interval

RESPIRATORY RATE				SpO <sub>2</sub>		
TIME	GROUP 1 MEAN $\pm$ SD	GROUP 2 MEAN $\pm$ SD	P value	GROUP 1 MEAN $\pm$ SD	GROUP 2 MEAN $\pm$ SD	P value
0 min	12.28 $\pm$ 0.54	12.36 $\pm$ 0.57	0.6128	99.24 $\pm$ 0.72	98.92 $\pm$ 0.76	99.32
5 min	12.44 $\pm$ 0.65	12.52 $\pm$ 0.71	0.6796	99.24 $\pm$ 0.78	99.04 $\pm$ 0.73	98-100
10 min	12.48 $\pm$ 0.71	12.64 $\pm$ 0.70	0.4263	99.12 $\pm$ 0.83	99.00 $\pm$ 0.71	0.5853
15 min	12.60 $\pm$ 0.76	12.60 $\pm$ 0.76	0.5431	98.92 $\pm$ 0.91	99.16 $\pm$ 0.80	99.40
20 min	12.44 $\pm$ 0.77	12.48 $\pm$ 0.65	0.8435	99.20 $\pm$ 0.76	99.28 $\pm$ 0.79	98-100
30 min	12.52 $\pm$ 0.77	12.36 $\pm$ 0.49	0.4469	99.20 $\pm$ 0.82	99.32 $\pm$ 0.75	0.65
40 min	12.48 $\pm$ 0.71	12.40 $\pm$ 0.50	0.6471	99.24 $\pm$ 0.78	99.40 $\pm$ 0.71	99.32
After surgery	12.44 $\pm$ 0.65	12.32 $\pm$ 0.48	0.4614	99.32 $\pm$ 0.69	99.40 $\pm$ 0.65	98-100

P value not significant in both the groups for Respiratory Rate and SpO<sub>2</sub>.

**TABLE 5 :** Maternal Outcomes

	PAIN RELIEF VAS SCALE		DEGREE OF MOTOR BLOCK (BROMAGE)		PATIENT SATISFACTION	
	MEAN $\pm$ SD	RANGE	MEAN $\pm$ SD	RANGE	MEAN $\pm$ SD	RANGE
GROUP 1	2.96 $\pm$ 1.43	2-6	2.92 $\pm$ 0.28	2-3	3.48 $\pm$ 0.82	2-4
GROUP 2	2.56 $\pm$ 0.92	2-4	2.80 $\pm$ 0.41	2-3	3.28 $\pm$ 0.89	2-4
P value	0.183(NS)		0.2336(NS)		0.4127(NS)	

TABLE 6 : APGAR Score At 0 Minute and At 5 Minute

SCORE	APGAR SCORE AT 0 MIN.			APGAR SCORE AT 5 MIN.		
	GROUP 1	GROUP 2	P value	GROUP 1	GROUP 2	P value
1	0	0	0.983 (NS)	0	0	0.987 (NS)
2	0	0		0	0	
3	0	0		0	0	
4	0	0		0	0	
5	0	0		0	0	
6	5	3		0	0	
7	8	14		1	2	
8	12	8		13	9	
9	0	0		11	14	
10	0	0		0	0	

**DISCUSSION**

It shows that in equal doses and concentrations, ropivacaine and bupivacaine produce a comparable long acting sensory block . McClellan and KJ, Faulds D updated the use of

Ropivacaine in regional anaesthesia.<sup>[22]</sup> Ropivacaine is a long acting, enantiomerically pure (S- enantiomer) amide local anaesthetic with a high pKa and low lipid solubility which blocks nerve fibres involved in pain transmission (Delta

and c fibres) to a greater degree than those controlling motor function (A beta fibres). Drug was less cardiotoxic than equal concentration of racemic bupivacaine but more so than lidocaine (lignocaine) in vitro and had a significantly higher threshold for CNS toxicity than racemic bupivacaine in healthy volunteers. The drug had efficacy generally similar to that of the same dose of bupivacaine with regard to pain relief but caused less motor blockade at low concentration. They concluded that Ropivacaine is a well tolerated regional anaesthetic with an efficacy broadly similar to that of bupivacaine. However, it may be a preferred option because of its reduced CNS and cardiotoxic potential and its lower propensity for motor block. Brockway MS, Bannister J, et al compared extradural bupivacaine and ropivacaine.<sup>[23]</sup> Like very similar to our study, there was little difference between the groups with respect to speed of onset of sensory block. When the same concentration of each drug was administered, there were inconsistent differences in duration of sensory block, Ropivacaine produced a slower onset, shorter duration and less intense motor block than same concentration of bupivacaine. Griffin RP & Reynolds F compared 0.5% bupivacaine with 0.5% ropivacaine in extradural anaesthesia for caesarean section.<sup>[24]</sup> No significant difference in onset and intensity of motor block but duration of motor block was significantly shorter in ropivacaine group. There was no significant difference in neonatal outcome, as assessed by APGAR score. In our study, the time to achieve maximum height of block with level T6 (the onset of sensory block  $13.88 \pm 1.42$  min in group 1 (Bupivacaine group) compared to  $13.80 \pm 1.22$  in group 2 (Ropivacaine), (P value = 0.8317), which was not significant. The duration of block also has no significant difference between the two groups  $5.76 \pm 0.58$  hr in (group 1) Bupivacaine group as compared to  $5.90 \pm 0.48$  hr in (group 2) Ropivacaine group, (P value = 0.3573). In both the groups, the onset of analgesia in most of the patients was between 10-15 min. The results of

our study are supported by Griffin RP & Reynolds F<sup>[24]</sup> & Crosby E, Sandler A, et al.<sup>[25]</sup> Though Ropivacaine showed significantly slower onset and shorter duration of block in the study conducted by Brockway MS, Bannister J, et al.<sup>[23]</sup> No significant difference seen in maternal hemodynamic parameters which were similar to studies done by Brockway MS, Bannister J, et al.<sup>[23]</sup> But Kampe S, Tausch B, Paul M, et al.<sup>[26]</sup> reported significant decrease in heart rate with use of 0.75% Ropivacaine than the with 0.5% Bupivacaine. But the blood pressure did not show any difference between the two groups. We had also recorded approximate amount of blood loss in every surgery to remove the confounding bias of hypotension being a variable entity with excessive bleeding. None of the patients in our study found to have more than 1200 ml of blood loss during the surgery and hence, no rescue agent in the form of blood, colloid was used. There was no significant difference between the two groups regarding the amount of blood loss during surgery (P value = 0.4519). Similarly no significant difference seen between the two groups regarding Induction – delivery time (P value = 0.9253). The maternal outcome was assessed on three parameters that were recorded during surgery, they are pain relief on VAS scale, degree of motor block on Bromage scale, and patient satisfaction. Pain relief on VAS score in the study was as, 22 out of 25 patients (88%) in Bupivacaine group (group 1) experienced  $VAS \leq 4$  as compared to 25 out of 25 patients (100%) Ropivacaine group (group 2). VAS score recorded between two groups was 0.183 (not significant). This is similar to the comparable study done by Griffin RP and Reynolds F<sup>[24]</sup>, Crosby E, Sandler A<sup>[25]</sup>, and Kampe S, Tausch B, Paul M, et al.<sup>[26]</sup>. The degree of motor blockade showed no significant difference in both the groups (P value = 0.2336). In Bupivacaine group (group 1), 23 out of 25 patients (92%) experienced score 3 in motor block on Bromage scale as compared to 20 out of 25 patients (80%) in Ropivacaine group (group 2). Our study showed similar results with the study done by Griffin RP

and Renolds F, <sup>[24]</sup> and Kampe S, Tausch B, Paul M, et al <sup>[26]</sup> which reported no significant difference with the intensity of motor block, while Brockway MS, Bannister J, <sup>[23]</sup> and Crosby E, Sandler A, et al <sup>[25]</sup> reported less intense motor block with the use of similar concentration of Ropivacaine. No significant difference seen in the two groups regarding patient satisfaction (P value =0.4127). The most commonly reported adverse events in our study are nausea which was equally distributed between two groups. Three patients (12%) in Bupivacaine group (group 1) had vomiting which was treated with 4 mg Ondansetron intravenously and seven patients (28%) in Ropivacaine group (group 2) had vomiting and required the use of Ondansetron. Incidence of shivering (16% in Bupivacaine group as compared to 8% in Ropivacaine group) and backache (12% in Bupivacaine group as compared to 8% in Ropivacaine group). In our study hypotension, bradycardia and nausea was comparable in both the groups. Crosby E, Sandler A, <sup>[25]</sup> reported equal incidence of hypotension in both the groups while reported more incidence of nausea observed in the Bupivacaine group (group 1) as compared to the Ropivacaine group (group 2). The mean values of systolic and diastolic blood pressures were also similar and any hypotension was treated with Mephentermine boluses of 6mg, while bradycardia was treated with 0.3 mg of Atropine boluses. Regarding foetal outcome, no significant difference seen in APGAR Score at 0 min (P value=0.983) and at 5 min (P value=0.987), between the two groups in our study, that is similar to study conducted by Brockway MS, et al, <sup>[23]</sup> Griffin RP & Renolds F, <sup>[24]</sup> Crosby E, Sandler A, <sup>[25]</sup> and Kampe S, et al. <sup>[26]</sup>

## CONCLUSION

To conclude Ropivacaine 0.5% 15ml & Bupivacaine 0.5% 15 ml given epidurally were tolerated and provided similar and effective anaesthesia in patients undergoing elective LSCS. In equal doses and concentration Ropivacaine and Bupivacaine produced almost

similar sensory and motor block. Thus both 0.5% bupivacaine and 0.5% ropivacaine in epidural space are recommended for caesarean section.

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