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Original Research Article

Comparison of effects of low dose ropivacaine with levobupivacaine on quality of analgesia, maternal satisfaction and neonatal outcome during labor through combined spinal epidural approach: A double blind randomized study

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ABSTRACT

Background: Regional techniques in labor analgesia have proven to be very effective, with bupivacaine being the most commonly used drug. This study compares the efficacy of local anaesthetics with lower cardiotoxicity and neurotoxicity such as levobupivacaine and ropivacaine in low doses, administered intrathecally followed by Patient Controlled Epidural Analgesia (PCEA). The primary outcome and secondary outcome of the study was to compare the quality of analgesia (verbal rating score) and maternal satisfaction respectively.

Materials and Methods: The Double blind prospective randomized study included 60 parturients of ASA I and II with 37-41 weeks of singleton pregnancy in active labor, cervical dilatation >4 cm, with no obstetrical or medical complication, requesting painless labor, randomized into two groups (30 each) by a computer generated randomized sequence:

Group R- received intrathecal 2.5 mg ropivacaine followed by epidural administration of 10 ml 0.125% ropivacaine Group L- received intrathecal 2.5 mg levobupivacaine followed by epidural administration of 10 ml 0.125% levobupivacaine. The primary and secondary outcome of the study was to compare the quality of analgesia and maternal satisfaction respectively. Statistical testing was conducted with the statistical package for social science system version (SPSS) 17.0.

Results: Group R had late onset and shorter duration of action with lesser motor blockade, however the results were statistically insignificant. Group L had slightly less total consumption of local anaesthetic and better maternal satisfaction, but was statistically insignificant. Patients in both groups had statistically similar pain scores at various intervals.

Conclusion: Both levobupivacaine and ropivacaine are highly effective for labor analgesia using the combined spinal epidural (CSE) technique.

1. Introduction

Labor is one of the most painful conditions that a woman can experience. The American College of Obstetricians and Gynecologists (ACOG) recognised maternal request as an indication which suffices for labor analgesia, in the absence of a medical contraindication.[1]

Among the current options for labor analgesia, neuraxial techniques such as epidural and combined spinal-epidural (CSE) are the most effective modalities for labor pain. These techniques provide complete analgesia for both stages of labor. Combined spinal- epidural has the advantage of achieving rapid onset profound analgesia through spinal injection along with the ability to prolong the duration of analgesia through epidural administration of local anaesthetics.[2]

Levobupivacaine, a new amide local anaesthetic seems to be nearly as potent as racemic bupivacaine, however, it demonstrated less cardio- depressant and neurotoxic effects. Ropivacaine, a amino amide local anaesthetic was

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developed later and has the desirable properties of racemic bupivacaine. Also due to its reduced toxic potential, it has a greater spectrum of safety as compared to bupivacaine.

This prospective randomized study compares the efficacy of these two drugs administered intrathecally (single dose) in terms of onset of block, duration of block and quality of analgesia during labor followed by their epidural administration via Patient Controlled Epidural Analgesia (PCEA).

2. Material and Methods

A double-blind randomized controlled trial was conducted in our institution from October 2014 to June 2016 on 60 parturients in active labor. We obtained the ethical clearance for conducting the randomized controlled study from the institutional ethical committee. A written, informed consent was obtained from all patients selected for the study. 60 parturients (nulliparous / multiparous) of ASA I and II with 37-41 weeks of singleton pregnancy in active labor, cervical dilatation >4 cm, with no obstetrical or medical complication requesting painless labor were included in the study. Women with a history of substance abuse, severe intrauterine growth retardation, presentation other than cephalic, bleeding disorder, morbidly obese, history of allergic reaction to local anaesthetic or having any fetal abnormality were excluded from the study. Patients with epidural wet tap, catheter dislodgement or blockade, positive test dose response and those converted to caesarean delivery were withdrawn from the study. The selected patients were randomized into two groups (30 each) by a computer generated randomized sequence:-

Group R- received initial intrathecal 2.5 mg ropivacaine followed by epidural administration of 10 ml 0.125% ropivacaine when the patient complained of first breakthrough pain.

Group L- received initial intrathecal 2.5 mg levobupivacaine followed by epidural administration of 10 ml 0.125% levobupivacaine when the patient complained of first breakthrough pain.

The anesthesiologist carrying out the study as well as the patients were blinded to the drug used. The study drugs were prepared in identical syringes by another anaesthesiologist who was not involved with the study. A total volume of 2ml isobaric drug solution (for intrathecal administration) was prepared by diluting either ropivacaine (group R) 2.5 mg (0.5 ml) or levobupivacaine (Group L) 2.5 mg (0.5 ml) with normal saline.

After pre anaesthetic workup and investigations, a 18-gauge cannula was used to secure an intravenous line after infiltrating the site with 1ml of 1% lignocaine and preloading with 500 ml Ringer lactate solution was done. Basal parameters such as pulse rate, systolic blood pressure and oxygen saturation were noted. Base line pain scores were assessed by Verbal Rating Score (VRS) (0- no pain; 1- aware of tightening or pressure; 2- tolerable pain, not distressing; 3-distressing pain or pressure). Fetal heart rate was monitored via external cardiotocogram throughout the study period. Occurrence of late or variable decelerations or fetal bradycardia (less than 110/min) was recorded as significant and obstetrician was notified immediately. The obstetrician was informed immediately in case of late or variable decelerations or fetal bradycardia (less than 110/min) and the event was recorded as significant. The patient was positioned in the left lateral position with the help of an assistant. Under strict aseptic conditions, the patient's back was prepared with 5% povidine iodine solution followed by 70% isopropyl alcohol and the area was draped. L2-L3 intervertebral space was identified and skin was infiltrated with 2 ml of 1% xylocaine. The loss of resistance to air technique was used to identify the epidural space using an 18 gauge tuohy needle through which 20 gauge epidural catheter was inserted into the epidural space in the cephalad direction. A test dose of 3ml of lignocaine 1.5% with 1:200000 adrenaline was administered through the catheter, after negative aspiration for blood and CSF. Five minutes after administering the test dose solution, L3-L4 intervertebral space was identified and dural puncture was performed by using a 26 gauge Quinke's needle. After ensuring free flow of CSF, the intrathecal solution was injected with the orifice of the spinal needle facing cephalic in direction. The patient was then made to lie down in the supine position immediately.

The onset of spinal analgesia time was taken to be the time for onset of tingling sensation in the legs after intrathecal injection. The duration of spinal analgesia was measured as the time from intrathecal injection to the point of first breakthrough pain. At first breakthrough pain, patients were administered 10 ml 0.125% solution of respective drugs via epidural catheter by anaesthesiologist and epidural catheter was connected to Patient Controlled Analgesia (PCA) pump with 0.125% solution of respective drugs in a 50 ml syringe for demand bolus with no background infusion. PCEA device was programmed to deliver a 5 ml dose of above solution with 10 minutes lockout interval and hourly limit of 15 ml. The patients were educated about using the PCEA pump while taking the informed consent. The maximum dose of both levobupivacaine and ropivacaine was taken as 2mg/kg and was not exceeded in any patient in order to prevent local anaesthetic toxicity.

Parameters like maternal non-invasive blood pressure and heart rate were measured at intervals of 2 minutes after spinal injection till haemodynamic stabilization. Thereafter the interval was set at 5 minutes for 30 minutes and then every 60 minutes throughout the study. Hypotension was defined as a systolic blood pressure of less than 90 mm Hg which was treated by increasing the intravenous fluid infusion rate or by giving bolus dose of Injection ephedrine

6 mg. A heart rate of less than 60 beats per minute was defined as bradycardia and was treated with Injection Atropine 0.6 mg.

Verbal rating score was recorded before the block and then at intervals of 10 minutes up to 60 minutes and thereafter half hourly. Cumulative analgesia score (%) was calculated as a percentage of the total number of pain assessments for each study group. A loss of pin prick sensation in the mid- clavicular line after intrathecal injection of study drug was used to assess the highest dermatomal level of sensory block. After asking the patient to close their eyes, the patient's joint position sense of the metatarso-phalangeal joint of both big toes was tested in order to assess propioception. Motor block was assessed using the modified bromage scale (0-ability to lift leg against resistance, 1-ability to flex knees but unable to lift extended legs, 2-ability to move feet but unable to flex knees,3-no movement at all). Side effects such as nausea, vomiting, backache, shivering, urinary retention, systemic toxicity and neurological deficit were recorded. Duration of first and second stages of labor and the requirement for an instrumental or caesarean delivery were recorded. In case of caesarian delivery, the dose of local anaesthetic to be administered during the surgery was calculated considering the safe dose of local anaesthetic and the amount of local anaesthetic already given during the study in order to avoid local anaesthetic toxicity. APGAR score and birth weight were recorded and used as parameters for neonatal outcome. Patient satisfaction and obstetrician satisfaction were also noted. The primary and secondary outcome of the study was to compare the quality of analgesia and maternal satisfaction respectively.

The statistical package for social science system version (SPSS) 17.0 was used for statistical analysis. Data was expressed as mean and standard deviation. Mean values were compared using Students 't' test. Categorical data were expressed as number and percentages and difference between the groups was compared by fisher's exact test and chi square test. A p value of 0.05 or less was considered to be statistically significant. Power calculations suggested that a minimum of 20 subjects per group were required to detect 20 minutes difference in mean duration of sensory analgesia between groups, taking Type 1 error of 5%, Type 2 error of 20% and intergroup standard deviation of 20 minutes.

3. Results

There was no significant difference in the two groups regarding demographic and baseline parameters such as age, weight, height, gestational age, parity, cervical dilatation, verbal rating score and oxytocin use (Table 1). Group R had late onset and shorter duration of action with lesser motor blockade, however the results were statistically insignificant (Table 2). Group L had slightly less total consumption of local anaesthetic and better maternal satisfaction as compared to group R($p>0.05$; Table 2). Duration of labor was found to be comparable in both groups (Table 3). Patients in both groups had statistically similar pain scores at various intervals ($p > 0.05$) and similar hemodynamic profile. In group L, three patients experienced hypotension as compared to two in Group R. One patient had bradycardia in Group L. Six patients in Group L complained of nausea and vomiting as compared to five in Group R, however the differences were statistically insignificant.(Table 4)

4. Discussion

Bupivacaine has been the main stay of labor analgesia since a long period of time. Newer agents with lesser cardiotoxity and neurotoxity and higher differential sensory motor block ratio such as levobupivacaine and ropivacaine have been introduced but till date there are fewer studies comparing the potencies of the two agents. Also, use of these agents through the CSE technique has not been explored much. In a previous study conducted by K M Kuczkowski et al. in 2004, the CSEA technique for ambulatory analgesia in labor proved to have better efficacy and safety with minimal or no side effects.[3] Therefore through our study we planned to study levobupivacaine and ropivacaine in labor through the CSE technique, comparing the quality of analgesia, motor blockade, ambulation, adverse effects, maternal satisfaction and fetal outcome. In order to increase the accuracy of calculating the total amount of dose consumption, we chose to use the PCEA technique instead of manual top-ups on maternal requests which is often subject to error.

In a previous study Sia et al. compared the effectiveness of 0.2% and 0.125% ropivacaine in PCEA and reported that sufficient analgesia had been obtained in both concentrations, but motor block had been less in low concentration of ropivacaine.[4] Thus, a lower concentration of 0.125% was selected as the epidural top up solution in order to minimize motor blockade. Intrathecally, 2.5 mg local anaesthetic was given which was like the drug regimen of Camborcia et al. who through their study determined the minimum analgesic dose as well as analgesic potency of local anaesthetics such as bupivacaine, levobupivacaine and ropivacaine.[5] Similar results were found by Lim et al. on comparing 2.5 mg intrathecal doses of bupivacaine, levobupivacaine and ropivacaine.[6] In studies done by Polley LS et al. and Lyons G et al., MLAC potency ratios for ropivacaine and levobupivacaine versus bupivacaine were determined to be 0.6:1.0 and 0.98:1.0 respectively.[7,8] Hence levobupivacaine was assumed to be 40% more potent than ropivacaine. Minimum local analgesic concentrations (MLAC) studies done for labor analgesia suggest that different relative analgesic potencies of local anaesthetics used in labor analgesia attributes to the favourable properties of ropivacaine such as reduced motor blockade and lesser cardiac toxicity.

Table 1: Demographic / Baselinedata of patients

	Levobupivacaine	Ropivacaine	P value
Age (years)	26.93 ± 1.87	26.4 ± 2.19	0.3853
Weight (cms)	59.33 ± 3.85	58.73 ± 2.77	0.4914
Height (cms)	159.95 ± 3.22	158.87 ± 2.7	0.1647
Gestational age (weeks)	273.20 ± 3.11	273.80 ± 3.41	0.4793
Parity (Primi/multi)	18/12	17/13	0.505
Cervical dilatation (Cm)	5.47 ± 0.73	5.33 ± 0.88	0.505
Oxytocin use (number of patients)	8	8	

Table 2: Comparison of various study parameters of patients

	Levobupivacaine	Ropivacaine	P value
Onset of spinal analgesia (seconds)	370.00 ± 33.37	383.12 ± 28.08	0.1048
Duration of spinal analgesia (minutes)	55.04 ± 11.67	50.87 ± 10.35	0.1485
Motor blockade (Modified bromage score ≥1)	4 (13%)	2 (6.6%)	0.732
Total Dose of local anaesthetic (mg)	30.83 ± 6.34	32.50 ± 6.23	0.3077
Instrumental delivery	2	1	0.641
Maternal Satisfaction (excellent/ good)	26/4	24/6	0.162
Verbal Rating Score	0.43 ± 0.35	0.6 ± 0.51	0.078

Table 3: Comparison of duration of labor (minutes) between the two groups

	Levobupivacaine	Ropivacaine	P value
1st stage of labor(minutes)	212.32±52.23	239.58±54.71	>0.05
2nd stage of labor (minutes)	43.18±19.56	39.67±18.66	>0.05

Table 4: Comparison of adverse outcomes between the two groups

Parameter	Levobupivacaine	Ropivacaine
Hypotension	3/30 (10%)	2/30 (6.67%)
Bradycardia	1/30 (3.3%)	0/30
Nausea	4/30 (13%)	3/30 (10%)
Vomiting	2/30(6.67%)	2/30 (6.67%)

No statistical difference was found between the groups with respect to age, weight, height, gestational age, parity, oxytocin use and cervical dilatation prior to the block. In our study the onset of analgesia was comparable in both the groups. The duration of sensory analgesia had a mean of 55.04±11.67 minutes in group L and 50.87±10.35 min in group R and a p value of 0.1485 showed the result to be statistically insignificant. There was no difference in the height of sensory blockade in two groups. 73% of patients in group L had sensory block up to T9 when compared to 66.67% in group R. Similar results were found in Purdie et al. and Ashok Das et al.[9,10]

The quality of analgesia in our study was assessed by Verbal Rating Scores (VRS). We used the cumulative analgesia score since it avoided bias related to duration of labor. This score also removed any discrepancy in the analgesia measurements related to the different stages and duration of labor. It was found that many assessments in group L were grade 0 (43%) while assessments in group R were grade 1 (67%) mostly. This was statistically significant (p value <0.05). This can be attributed to the difference in potency between the drugs.[7,8] However, when those experiencing effective analgesia (grade 0 or 1) were compared with those experiencing inadequate analgesia (grade 2 or 3), there was no significant difference between ropivacaine and levobupivacaine groups. The Verbal Analogue Pain scores in both groups were comparable signifying both the groups had effective equivalent analgesia. Though cumulative analgesia score was better in levobupivacaine group than ropivacaine group, being a subjective measurement, the extent to which it can be related to the potency of the study drugs is uncertain.

There were no statistically significant differences in the incidence or severity of motor block between the groups. 13% in group L experienced grade 1 block when compared to 6.7% in group R. This was statistically insignificant (p value <0.05). Grade 2 or 3 block was not observed in both the groups. This was comparable to the studies by Purdie et al.[11] The patients could ambulate once their motor blockade score returned to 0. Thus, in this context both levobupivacaine and ropivacaine can be safely used for ambulatory labor analgesia. The degree of motor block

during epidural analgesia depends not only on the drug used, but also on the cumulative dose of local anaesthetic used and the duration of labor.

The total dose of local anaesthetic used was slightly less in group L when compared to group R with a mean value of 30.83±6.34 mg and 32.5±6.23 mg respectively. The p value of 0.3077 was statistically insignificant. Similar results were found by Purdie et al.[9] Considering our previous assumption of levobupivacaine being 40% more potent than ropivacaine, it was expected that a larger dose of ropivacainewould be required in maintaining labor analgesia, but the difference in the doses was not significant enough to prove this previous assumption.

The two groups (Group L vs Group R) had comparable and similar duration of first (212.32±52.23 versus 239±54.71 minutes) and second stages of labor(43.18±19.56 versuss 39.67±18.66), like the study conducted by Nageotte M.P et al.[11] Studies have shown CSE to be associated with shorter duration of first stage of labor among nulliparous women when compared to epidural analgesia alone.[12,13] More than 90% of parturients in both the groups had spontaneous normal vaginal delivery and no significant difference was observed in the two groups with respect to the mode of delivery. This was comparable with the study by Wong CA et al. in 2005 which revealed that the rate of caesarian delivery was not increased by neuraxial analgesia in early labor, infact it resulted in better analgesia and shorter duration of labor.[14] APGAR scores in all newborn were more than 8. The mean APGAR score at 1 and 5 min were >9 for both the groups and hence no significant difference was found between the groups (p value >0.05). The findings were comparable with the findings of Bolukbasi et al.[15]

There was no significant difference between the two groups regarding heart rate and mean arterial blood pressure (P value >0.05). This may be due to the use of low concentrations of the study solution. Adverse effects such as hypotension, bradycardia, nausea and vomiting in both the groups had similar incidence with hypotension observed in 3 patients in group L whereas in 2 patients in group R. The nausea and vomiting incidence was also low in our trial, the etiology of which is multifactorial (hypotension or side effects attributed to intravenous oxytocin and epidural opioids) as suggested by Purdie et al. who used epidural fentanyl in their study.[9]

All the parturients and obstetricians were asked about acceptance and opinions about the technique applied. The level of maternal satisfaction was found to be excellent in 87% of patients in group L and 80% in group R and was statistically insignificant. Also there was no significant difference between the two groups with respect to obstetrician satisfaction (87% of patients in group L and 80% in group R). The overall response of parturient and obstetrician was considered favorable to walking epidural analgesia for labor.

The limitations of this study could be a requirement of a larger sample size in order to have a better understanding of maternal and neonatal side-effects.

5. Conclusion

Hence, through our prospective randomized study we conclude that both levobupivacaine and ropivacaine are equally effective for labor analgesia using the combined spinal epidural technique with desirable effects such as negligible motor block, high maternal satisfaction and minimal adverse maternal or neonatal outcomes. We suggest the use of these newer agents for use in labor analgesia as they provide effective analgesia with minimal side effects.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. American College of Obstetricians and Gynecologists Committee on Obstetric Practice. ACOG committee opinion. No. 339: Analgesia and cesarean delivery rates. *Obstet Gynecol*. 2006;107(6):1487–8.
2. Pandya ST. Labor Analgesia: Recent Advances. *Indian J Anaesth*. 2010;54(5):400–8.
3. Kuczkowski KM. Ambulation with combined spinal and epidural labor analgesia: the technique. *Acta Anaesthesiol Belg*. 2004;55(1):29–34.
4. Sia ATH, Ruban P, JLChong, Wong K. Motor blockade is reduced with ropivacaine 0.125% for parturient-controlled epidural analgesia during labour. *Can J Anesth*. 1999;46(11):1019–23. doi:10.1007/bf03013195.
5. Camorcia M, Capogna G, Columb MO. Minimum Local Analgesic Doses of Ropivacaine, Levobupivacaine, and Bupivacaine for Intrathecal Labor Analgesia. *Anesthesiology*. 2005;102(3):646–50. doi:10.1097/00000542-200503000-00025.
6. Lim Y, Ocampo CE, Sia AT. A Comparison of Duration of Analgesia of Intrathecal 2.5 mg of Bupivacaine, Ropivacaine, and Levobupivacaine in Combined Spinal Epidural Analgesia for Patients in Labor. *Anesth Analg*. 2004;98(1):235–9. doi:10.1213/01.ane.0000094338.80430.c5.
7. Polley LS, Columb MO, Naughton NN, Wagner DS, Ven CJM. Relative Analgesic Potencies of Ropivacaine and Bupivacaine for Epidural Analgesia in Labor. *Anesthesiology*. 1999;90(4):944–50. doi:10.1097/00000542-199904000-00003.
8. Lyons G, Columb M, Wilson RC, Johnson RV. Epidural pain relief in labour: potencies of levobupivacaine and racemic bupivacaine. *Br J Anaesth*. 1998;81(6):899–901. doi:10.1093/bja/81.6.899.
9. Purdie NL, McGrady EM. Comparison of patient-controlled epidural bolus administration of 0.1% ropivacaine and 0.1% levobupivacaine, both with 0.0002% fentanyl, for analgesia during labour. *Anaesthesia*. 2004;59(2):133–7. doi:10.1111/j.1365-2044.2004.03582.x.
10. Das A. Comparison of the effects of intrathecal bupivacaine, levobupivacaine and ropivacaine for lower abdominal surgeries: A double blind randomized controlled study using isobaric preparations. *Int J Inf Res Rev*. 2015;2(4):636–41.
11. Nageotte MP, Larson D, Rumney PJ, Sidhu M, Hollenbach K. Epidural Analgesia Compared with Combined Spinal–Epidural Analgesia during Labor in Nulliparous Women. *N Engl J Med*. 1997;337(24):1715–9. doi:10.1056/nejm199712113372402.

12. Tsen LC, Thue B, Datta S, Segal S. Is Combined Spinal–Epidural Analgesia Associated with More Rapid Cervical Dilation in Nulliparous Patients When Compared with Conventional Epidural Analgesia? *Anesthesiology*. 1999;91(4):920–5. doi:10.1097/00000542-199910000-00010.
13. Bhagwat AG, Dua CK, Saxena KN, Srinivasan S, Dua K. Comparison of combined spinal epidural technique and low dose epidural technique in progress of labor. *Ind J Anaesth*. 2008;52:282–7.
14. Wong CA, Scavone BM, Peaceman AM. The risk of cesarean delivery with neuraxial analgesia given early versus late in labor. *N Engl J Med*. 2005;352(7):655–65.
15. Bolukbasi D, Sener EB, Sarihasan B, Kocamanoglu S, Tur A. Comparison of maternal and neonatal outcomes with epidural bupivacaine plus fentanyl and ropivacaine plus fentanyl for labor analgesia. *Int J Obstet Anesth*. 2005;14(4):288–93. doi:10.1016/j.ijoa.2005.04.007.

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