Original Article

Quality of labor epidural analgesia and maternal outcome with levobupivacaine and ropivacaine: A double-blinded randomized trial

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Abstract

Background: Quality of labor analgesia plays a vital role in the maternal outcome. Very few literature are available analyzing the quality of epidural labor analgesia.

Aim: The aim of this study was to compare the effectiveness of 0.1% levobupivacaine and 0.1% ropivacaine with fentanyl as an adjuvant for epidural labor analgesia in terms of onset, duration, quality of analgesia, and degree of motor blockade.

Methodology: Sixty nulliparous parturients, with singleton uncomplicated pregnancy, were recruited by continuous sampling. Parturients were randomized to receive either levobupivacaine 0.1% or ropivacaine 0.1% with 2 µg/ml fentanyl as an intermittent epidural bolus. The epidural analgesia was initiated with 12 ml of study drug solution in the active stage of labor (cervix 3 cm dilated). Demand bolus was given whenever the visual analog scale (VAS) score >3. Onset, duration, and quality of analgesia and degree of motor blockade were analyzed. Maternal outcome was evaluated in terms of mode of delivery, duration of labor, and assisted vaginal delivery.

Statistical Analysis: All the data were recorded in Microsoft Office Excel. Statistical analysis was carried out using SPSS version 19.0 (IBM SPSS, USA) software with Regression Modules installed. Descriptive analyses were reported as mean and standard deviation of continuous variables.

Results: The mean onset of analgesia was shorter in ropivacaine (21.43 ± 2 min) than in levobupivacaine group (23.57 ± 1.71 min) (P = 0.000). Duration of analgesia was shorter in ropivacaine (60 ± 14 min) than levobupivacaine (68 ± 11 min) (P = 0.027). Levobupivacaine produced a better quality of analgesia in terms of not perceiving pain and uterine contraction during labor analgesia but was associated with 37% incidence of instrumental delivery. Duration of labor and rate of cesarean section were comparable between the groups.

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Conclusion: Quality of analgesia in labor epidural was superior to levobupivacaine but was associated with higher incidence of instrumental vaginal delivery.

Key words: Instrumental delivery, labor analgesia, levobupivacaine, quality of analgesia, ropivacaine

INTRODUCTION

Epidural labor analgesia is considered at present to be the most effective and innocuous technique for painless childbirth because of reasons such as, (1) allowing parturient to participate in birthing experience, (2) dramatically reducing the pain of labor, (3) ability to extend the duration of analgesia to match the duration of labor, (4) minimal motor block to allow ambulation, (5) minimal effects on fetus, (6) minimal effects on progress of labor, (7) reducing maternal catecholamine, (8) blunts hemodynamic effects of uterine contractions, and (9) less dystocia.[1] Comparative studies of ropivacaine and levobupivacaine as intermittent boluses in labor with or without the addition of opioids in analyzing quality of analgesia are not present. We hypothesize that intermittent bolus administration of levobupivacaine provides better analgesia than ropivacaine without affecting the maternal and fetal outcomes. Hence, we compared the effectiveness of 0.1% levobupivacaine and 0.1% ropivacaine with fentanyl as an adjuvant during epidural labor analgesia.

METHODOLOGY

Following approval from the Hospital Ethical Committee, this prospective, randomized, double-blinded study was conducted in our institute on all pregnant women requesting labor analgesia from December 2013 to May 2014. All parturients were educated on methodology and advantages of epidural labor analgesia. Sixty primigravidae of age between 18 and 32 years with a singleton pregnancy were enrolled in our study by continuous sampling. Parturients with high-risk complicated pregnancy, cephalo pelvic disproportion (CPD), fetal anomaly, and any contraindication for neuraxial block were excluded from the study. Written informed consent was obtained from all the parturients [Figure 1].

During the early stage of labor, parturient was shifted to the operating room, and epidural catheter was secured at L2–L3 space. Three milliliters of 1.5% lignocaine with 15 µg adrenaline was given as a test dose. Parturients were shifted to the labor ward after ruling out intravascular and intrathecal catheter placement. Parturients were randomly divided into two groups of thirty each, Group L and Group R by sealed envelope technique. The study solution was prepared aseptically by an anesthetist who was not directly involved in this study. Parturients in Group L received 12 ml of 0.1% levobupivacaine (Abbott Laboratories, Elverum, Norway) with 2 µg/ml fentanyl and Group R received 12 ml of 0.1% ropivacaine (Astra Zeneca, Zug, Switzerland) with 2 µg/ml fentanyl as an adjuvant. When the parturient had progressed to the active stage of labor (cervical dilatation >3 cm), the epidural analgesia was initiated after assessing the baseline pain score by VAS of 10 cm line from 0 to 10.[2]

The primary outcome measures were onset, duration, and quality of analgesia and degree of motor blockade. The secondary outcome measures were maternal outcome in terms of mode of delivery, percentage of instrumental delivery, maternal satisfaction score, and neonatal outcome (Apgar score at 1 and 5 min).

The time of the initial dose was kept as time zero and assessments were scheduled accordingly. The adequacy of analgesia was assessed at 5 min interval. The onset of analgesia is defined as the time from the first dose to the time of achieving VAS <3. If analgesia was inadequate in 30 min, an additional 12 ml of the same drug solution was repeated, and VAS score was assessed at every 5-min interval. The parturient was excluded from the study if analgesia was still inadequate.

Quality of analgesia and extent of motor blockade were assessed 15 min after achieving adequate analgesia (VAS <3). Quality of analgesia was assessed by the verbal scoring system (score 0 - no pain and no awareness of uterine contractions, score 1 - aware of contractions but not painful, score 2 - aware of pressure but tolerable discomfort, score 3 - distressing pain or pressure).[3] The presence of any motor blockade was not directly involved in this study. Parturients in Group R received 12 ml of 0.1% ropivacaine (Astra Zeneca, Zug, Switzerland) with 2 µg/ml fentanyl and...
Side effects such as pruritus and nausea if reported were treated accordingly. Hypotension (defined as systolic blood pressure of <90 mmHg) was treated with a bolus of 6 mg intravenous mephentermine. Bradycardia (defined as heart rate <60 bpm) was treated with a bolus dose of 0.6 mg intravenous atropine sulfate. The study was terminated after baby delivery or when parturient required cesarean section.

Anesthesia for cesarean section was achieved by epidural injection with 12–15 ml of 2% lignocaine with adrenaline. Neonatal outcome was assessed with Apgar score at 1 and 5 min. Maternal satisfaction was graded as 3 - excellent pain relief, 2 - good pain relief, 1 - fair pain relief, and 0 - poor pain relief, and it was obtained during the 2nd postnatal day when the parturients were comfortable.

Sample size
From the previous study by Gautier et al., the mean onset time for ropivacaine was 14 min with standard deviation (SD) of 6 min. On hypothesizing that levobupivacaine has better potency than ropivacaine to find the difference of 4 min mean onset time with a power of 0.8 (α =0.05), the sample size required was 29 in each group. Considering the dropouts, we have included a sample size of thirty in each group.

Statistical analysis
All the data were recorded in Microsoft Office Excel. Statistical analysis was carried out using SPSS version 19.0 (IBM SPSS, Armonk, New York, USA) software with Regression Modules installed. Descriptive analyses were reported as mean and SD of continuous variables. Demographic data, onset of analgesia, duration of analgesia, and duration of labor were analyzed with unpaired Student’s t-test. Quality of analgesia, degree of motor blockade, and fetal Apgar score were assessed with Mann–Whitney U-test. Hemodynamic parameters were assessed with Student’s t-test. Mode of delivery, instrumentation among vaginal delivery, and maternal satisfaction were assessed by percentage.

**RESULTS**

The mean age (both Group L and Group R - 25 ± 3 years), weight (Group L - 70.3 ± 8.3 kg and Group R - 68 ± 8.4 kg), and height (Group L - 1.55 ± 0.05 m and Group R - 1.58 ± 0.04 m) of the parturients in both ropivacaine and levobupivacaine groups were comparable.

The mean onset time of analgesia in levobupivacaine group is 23.57 (22.93–24.21) min and for ropivacaine is 21.43 (20.59–21.90) min. Although the mean onset of analgesia with levobupivacaine and ropivacaine was statistically significant (P = 0.000), the difference of 120 s in the onset of analgesia between the two groups was not clinically relevant [Table 1].

The mean duration of analgesia with levobupivacaine and ropivacaine with fentanyl was 68.17 (64.04–72.29) min and 60.77 (54.92–65.56) min, respectively. The difference in mean duration of analgesia was found to be statistically significant (P = 0.027) [Table 1].

On assessment of quality of analgesia, in levobupivacaine group (n = 30), 28% of parturients had no pain and awareness of uterine contraction, 69% of parturients were aware of uterine contractions but no pain and, in ropivacaine group (n = 30), 10% of parturients had no pain and awareness of uterine contractions and 83% of parturients were aware of uterine contractions but no pain. In either group, no parturient had distressing pressure or pain during uterine contractions [Figure 2]. In both groups, none of the parturients had any motor blockade. All parturients were ambulated to their preferences.

The maternal heart rate was stable in both groups throughout the study period. Only few had sinus tachycardia (rise of more than 20% from baseline). There was no significant (more than 20%) change in blood pressure (mean arterial pressure) in both groups.

The mean duration of labor in levobupivacaine and ropivacaine groups was 440.97 (331.23–550.70) min and 463.83 (364.63–563.03) min, respectively. The duration of labor between the groups was not statistically significant (P = 0.830) [Table 1].

<table>
<thead>
<tr>
<th>Parameters (min)</th>
<th>Group (n=30)</th>
<th>Mean (95%CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of analgesia</td>
<td>Group L</td>
<td>23.57 (22.93-24.21)</td>
<td>0*</td>
</tr>
<tr>
<td></td>
<td>Group R</td>
<td>21.43 (20.59-21.90)</td>
<td></td>
</tr>
<tr>
<td>Duration of analgesia</td>
<td>Group L</td>
<td>68.17 (64.04-72.29)</td>
<td>0.027*</td>
</tr>
<tr>
<td></td>
<td>Group R</td>
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<td>0.830</td>
</tr>
<tr>
<td></td>
<td>Group R</td>
<td>463.83 (364.63-563.03)</td>
<td></td>
</tr>
</tbody>
</table>

CI=Confidence interval, *Statistically significant

Figure 1: Consort diagram

Table 1: Outcome parameters
percent of parturients in both groups underwent cesarean section [Figure 3]. Instrumental vaginal delivery was found to be more in levobupivacaine group which was 32% and it was nil in ropivacaine group [Figure 4]. There was no significant drop in fetal Apgar score in any of the groups [Figure 5]. Maternal satisfaction was excellent in almost 90% of parturient in both groups. None in either group had complained poor pain relief [Figure 6].

**DISCUSSION**

Labor analgesia is still an unmet right for parturient in India because of lack of awareness and less availability of specialized centers to provide obstetric analgesia. With increasing awareness for labor analgesia and introduction of newer chiral alternative drugs, labor analgesia is becoming popular in recent times.

Studies looking at equipotent concentrations of ropivacaine and levobupivacaine in labor analgesia claimed that both are equipotent and safe at 0.1% concentration.[5,6] However, Benhamou et al. found levobupivacaine to be 19% more potent than ropivacaine in labor analgesia.[7] Robinson et al. proved that when fentanyl was added to local anesthetics in labor analgesia, it provided effective analgesia with minimum local anesthetic dose thus improving the local anesthetics safety margin.[8] Hence, we decided to use levobupivacaine and ropivacaine at 0.1% concentration with fentanyl as an adjuvant.

We looked at literature to decide on intermittent bolus or continuous infusion for epidural analgesia. Kaynar and Shankar et al.,[9] Wong et al.,[10] Fettes et al.,[11] Capogna et al.,[12] and Patkar et al.[13] found that parturient-controlled or programmed intermittent bolus method to be more efficacious in producing effective analgesia with low drug concentrations, because of the better spread of local anesthetics inside the epidural space than continuous infusion method and comparatively less dosage of drug is used. Hence, we preferred to provide analgesia by intermittent bolus technique.

In our study, the onset of analgesia was delayed in both levobupivacaine (23.57 ± 1.71 min) and (21.43 ± 2 min) ropivacaine groups when compared to studies by Gautier et al., Purdie and McGrady, and Sah et al.[4,5,14] This could be attributed to the lower concentration of local anesthetics (0.1%) and fentanyl (24 µg) used in our study. On comparing between these two drugs, the mean onset time of analgesia was higher for levobupivacaine than ropivacaine which we contribute to the pharmacokinetic property of ropivacaine which is less fat-soluble than levobupivacaine.
The mean duration of analgesia was 68 ± 11 min and 60 ± 14 min with levobupivacaine and ropivacaine, respectively, in our study. Our results were comparable to Supandji et al. and Purdie et al. who observed that 0.1% of levobupivacaine and ropivacaine with fentanyl 2 µg/ml did not have a significant difference in duration of analgesia during labor.[5,15] This minimal difference in duration of analgesia in our study may be attributed to more lipophilic nature of levobupivacaine than ropivacaine.

In our study, none of the parturients had any degree of motor blockade. All parturients were allowed to mobilize (walk) under supervision at their preference. Our results were comparable to Purdie et al.[5] Capogna et al. observed that the incidence of motor blockade was 37% higher in continuous infusion group when compared to intermittent patient-controlled epidural bolus analgesia.[16] This effect could be due to cumulative accumulation of drugs in the setting of continuous infusion technique in epidural analgesia.

The quality of analgesia during peak uterine contractions was excellent in both levobupivacaine and ropivacaine groups. None of the parturients in either group complained pain during uterine contractions. Parturient who did not have any perception of uterine contractions was more in levobupivacaine group (23%) than in ropivacaine group (7%). Those who perceived uterine contractions with no pain were more in ropivacaine group (83%) than in levobupivacaine group (69%). Only 3% in levobupivacaine group and 7% in ropivacaine felt uterine contractions as tolerable discomfort (pressure/pain). There is no literature commenting on the quality of analgesia in terms of perceiving uterine contractions.

There were no significant hemodynamic changes noticed in both groups. More than 20% rise in heart rate was noticed in nine parturients, five in levobupivacaine and four in ropivacaine groups. Our results were comparable to the study of Purdie et al. and Patkar et al.[5,13] The rise in heart rate among parturients as observed in our study was attributed to administration of intravenous injection valethamate bromide for enhancing the dilatation of cervix.[17]

The mean duration of labor in levobupivacaine group was 7.3 ± 4.9 h and was 7.6 ± 4.3 h in ropivacaine group which was insignificant (P = 0.830) in the clinical settings. Our results were similar to the study by Lee et al.[18] Ohel et al. observed that the mean duration of labor with early initiation of epidural analgesia was 5.9 h which was shorter than late initiation of analgesia (cervical dilatation 4.6 cm) 6.6 h (P = 0.004).[19] In our study, the duration of labor was longer than the above study because we calculated the duration of labor from the time of initiation of analgesia (3 cm cervix dilatation) to the time of baby delivery.

The rate of cesarean section was 17% in both groups, which was comparable to the studies by Purdie et al.[5] Incidence of instrumental delivery was more in levobupivacaine (32%) group than in ropivacaine group (0%) in our study, whereas Purdie et al. showed that there was no difference in the incidence of instrumental delivery with 0.1% levobupivacaine and ropivacaine with fentanyl 2 µg/ml in setting of parturient-controlled intermittent boluses.[5] Agrawal et al., Patkar et al., and Chestnut et al., in their studies, observed that the incidence of instrumental delivery does not relate to epidural analgesia or its method of administration or its time of initiation, respectively, when low-dose local anesthetics with or without opioids were used.[13,20,21]

We looked at the relation between the motor blockade and vaginal delivery. In our study, both groups had no lower limb motor blockade. However, the incidence of operative vaginal delivery was high in levobupivacaine group due to laxity in pelvic floor muscle producing a delay in the internal rotation of the fetal head. In addition, the greater sensory deafferentation of the pelvis produced by levobupivacaine blunted Ferguson’s reflex, decreasing oxytocin secretions, causing ineffective uterine contractions, bringing down the urge to bear down in the second stage of labor.

Maximum Apgar score at 1 min and 5 min was 8 and 9, respectively. The good fetal outcome can be attributed to hemodynamic stability due to the usage of low local anesthetic concentration. Manaa et al. observed the fetal response to epidural analgesia by using ultrasound indices. After epidural bolus injection, transient drop in Doppler indices corresponded to fall in maternal blood pressure.[22]
Maternal satisfaction in our study was excellent in more than 90% of mothers in both groups, which was comparable to observations by Purdie et al. This was due to good preprocedural counseling, better pain relief, less anxiety due to no motor blockade, and good neonatal outcome.

CONCLUSION

We conclude that both the drugs are safe to both mother and neonate. Levobupivacaine provides a better quality of analgesia (parturient perceived neither uterine contraction nor pain) but associated with increased rate of instrumental vaginal delivery than ropivacaine. Both groups had a similar incidence of cesarean delivery.

Limitations of the study

We did not calculate the duration of each stage of labor; hence, we cannot conclude on the possible effect of these drugs on each stage of labor. We did not calculate the total local anesthetics consumption. The experience of obstetrician was not looked into while analyzing the mode of delivery. Studies also should be directed to assess the extent of motor paralysis of pelvic floor muscles with low-dose local anesthetics and its effect on labor outcome.

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Conflicts of interest

There are no conflicts of interest.

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