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Original Research Article

Comparative Study of Efficacy of Racemic Bupivacaine 0.0625%-Fentanyl and Levobupivacaine 0.0625%-Fentanyl for Epidural Labour Analgesia

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Abstract:

Background and Aims: To provide good labour epidural analgesia, this study compares the analgesic efficacy of racemic bupivacaine (0.0625%) with 2 µg/ml fentanyl and levobupivacaine (0.0625%) with 2 µg/ml fentanyl in pregnant women at more than 37weeks of gestation in spontaneous labor and normal fetal heart rate monitoring.

Methodology: Sixty pregnant women who requested for labour analgesia were divided into two groups. Group B (n = 30) received racemic bupivacaine (0.0625%) and fentanyl 2 µg/ml and Group L (n = 30) received levobupivacaine 0.0625% and fentanyl 2 µg/ml. In both groups, 10-15ml of the study drug was given in 5 ml fractionated doses at 5 min interval. Parturients who did not experience analgesia within 15 min after the initial bolus were supplemented with an additional 5 ml of the same concentration of the solution. Epidural analgesia was maintained by timed doses at the end of 90 min with the dose equal to the initial dose of the drug. The Duration of labour analgesia, motor block, sensory block, visual analog scale, maternal hemodynamic parameters, mode of delivery, and maternal satisfaction was evaluated.

Results: In the present study, Maternal demographic characteristics were comparable. The Results indicate that both drugs were equally effective clinically in terms of pain scores, patient satisfaction, mode of delivery and total dose used. Statistically, bupivacaine (0.342±0.107) produced more motor blockade than levobupivacaine (0.229±0.025) while the highest level of sensory blockade achieved by bupivacaine was 20%-T10, 80%-T8,0%-T6 and with levobupivacaine was 3.33%-T10, 76.66%-T8, 20%-T6 which was statistically significant. Hemodynamic variations were found to be statistically significant between the groups but clinically they did not have any implications on maternal or foetal outcomes.

Conclusion: In this study, both drugs produced equivalent analgesia for labor at low concentration with fentanyl as an adjuvant providing good maternal satisfaction.

Keywords: Bupivacaine 0.0625%, epidural labor analgesia, fentanyl 2 µg/ml, low-dose epidural technique, levobupivacaine 0.0625%.

Introduction

The agonizing pain of labor is a significant trigger of stress and anxiety. Maternal and foetal hypoxemia is the outcome of painful uterine contractions leading to hyperventilation and increased catecholamine release. [1] Therefore, avoiding maternal and neonatal morbidity and decreasing the likelihood of a cesarean section due to maternal stress necessitates a good labour pain management. [2]

An optimal approach for labor analgesia should provide acceptable and sufficient pain relief without resulting in motor blockade or creating a detrimental effect on the expecting mother or fetus. The most widely used and successful way to treat pain during labor is the neuroaxial approach of epidural analgesia.[3] The key benefits of walking labor epidural analgesia are that the use of depressant general anesthetic drugs are minimized, and the mother can participate in the delivery while awake. The mother also claims a better satisfaction, lower pain scores and demonstrates stable hemodynamic parameters. [2] Low-dose epidurals (0.0625%–0.125%) aim to prevent motor blockage and lower the overall dose of LA administered.

The local anaesthetic drugs commonly used to effectively deliver epidural analgesia during labor is bupivacaine. Newer agents such as ropivacaine and

levobupivacaine have been designed to minimize cardiac and neurotoxicity, despite the widespread usage and relative safety of bupivacaine. [4] Reduced motor block is an additional advantage of these newer drugs in diluted concentrations for labor analgesia.

If highly lipid-soluble opioids (fentanyl) are introduced, the quality analgesia is excellent. Due to the synergistic action of opioid receptors in the spinal cord, the addition of opioids to LA decreases the dose of local anesthetics. This mitigates the likelihood of hemodynamic instability, motor blockade and undesirable impacts associated with anesthetic agents. [5,6]

The purpose of this study was to evaluate and contrast the effectiveness of levobupivacaine and bupivacaine in conjugation with fentanyl in the management of labor pain, as well as their effects on the fetus, maternal hemodynamics and possible negative effects.

Materials and Methods

A prospective randomized double-blinded study was conducted after the ethics committee approval at our institution Adichunchanagiri Institute of Medical Sciences, BG nagara, Mandya district, Karnataka India. 60 singleton term pregnant women in spontaneous labor with normal fetal heart rate monitoring who desired labor analgesia with the American Society of Anesthesiologists Classes I and II were recruited. The study excluded pregnant women with medical ailments obstetric complications, fetal malformations, and those who were not suitable candidates for regional analgesia. Written Informed consent was obtained, the participants were randomly allocated by a computer-generated table to two groups of 30 each such as the Group bupivacaine (B) (n = 30) and the Group levobupivacaine (L) (n = 30).

Anesthesiologist 1 performed the procedure, and anesthesiologist 2, who was not present for the procedure, made observations. An obstetrician, who was also blinded to group allocations evaluated the fetal heart rate (FHR), other obstetric information and the labor progress. Parturients were administered 500 ml of Ringer lactate solution intravenously, monitors (spO2, NIBP, ECG, and non-invasive blood pressure) were connected, and baseline parameters were documented prior to analgesia administration.

After positioning the parturients in the left lateral position and implementing all aseptic precautions, the epidural space was located using the loss of resistance to saline technique in a midline approach at the L3–L4 level with an 18-gauge Tuohy needle. The epidural catheter was inserted through the Tuohy needle after a negative blood and CSF aspiration. The catheter length was then meticulously adjusted to 3-4 cm inside the space, and the needle was pulled out. After confirming the placement of catheter in the epidural space, 10 ml of the study drug 0.0625% bupivacaine with fentanyl 2 µg/ml or 0.0625% levobupivacaine with fentanyl 2 µg/ml was administered in 5 ml fractionated doses in 5 min intervals. Parturients in the both the groups were familiarized with a visual analog scale (VAS) (0 = no pain, 10 = worst imagined pain). Parturients who did not experience analgesia (VAS >4) within 15min of the initial bolus were supplemented with an additional 5 ml of solution. If the parturient had no pain relief within 30 minutes, they were removed from the study.

The parameters like SpO2, heart rate, NIBP, FHR were monitored prior to catheter insertion, at intervals of 5, 10, 20, 30, 45, 60, min and every 30 min until delivery.

Analgesia was maintained by timed top ups at the end of 90 min whether the parturient had pain or not, without breakthrough pain experiences. The dose of additional doses was equal to the initial dose of the drug.

Detrimental reactions included pruritis, nausea, arterial desaturation, hypotension, and abnormal ECG readings were listed and dealt with appropriately. Hypotension was defined as fall in systolic blood pressure >20% from the baseline or <90 mmHg and was managed by left uterine displacement, accelerating IV fluid administration and intravenous bolus ephedrine 3-5 mg as needed.

After administration of the bolus dose and after giving timed top ups the following parameters were recorded: FHR, cervical dilatation, pain score (VAS), highest level of sensory block (assessed by loss of temperature discrimination to alcohol swab), motor block (intensity as per Bromage scale), total dose of LA consumed per hour and number of additional supplemental doses administered.

All parameters were assessed at 20 min after the initial bolus dose and every 30 min thereafter. The mode of delivery (spontaneous vaginal, instrumental vaginal, and cesarean section) was also noted. After the delivery, maternal satisfaction levels with epidural analgesia (on a numerical scale 0 = totally unsatisfied, 10 = totally satisfied) were noted.

Statistical Analysis

Software package SPSS 20 was employed to assess the dataset (IBM SPSS statistics for windows, version 20.0. Armonk, NY, USA). Odds variance was applied for the study of demographic data. Chi square and unpaired t tests were applied as needed. "P" values were determined using standard tests of significance; an outcome of $P < 0.05$ was deemed statistically significant. Bar graphs and trend graphs were generated appropriately.

Results

The 60 primigravida parturients who participated in the study had comparable demographic characters in both groups as depicted in Table 1. In addition, the time of establishment of labor epidural analgesia according to cervix dilation is also added in the Table.

Table 1: Demographic data

Demography	Group B Bupivacaine (Mean±SD)	Group L Levobupivacaine (Mean±SD)	P-Value
Age (years)	22.633±3.09	22.867±2.97	0.766
Height (cm)	153.9±3.235	152.8±2.666	0.156
Weight (kg)	62.023±8.834	60.733±6.275	0.517
Gestational age (weeks)	39.18±0.88	38.78±1.024	0.11
Cervical dilatation (cms)	4±0.93	3.97±0.67	0.887

Table 2: Showing the distribution of highest sensory level in two groups and the P-value

Number of patients (%)	Highest sensory level	Group B Bupivacaine	Group L Levobupivacaine	Total	P value Chi=square
	T 10	6(20%)	1(3.33%)	7(11.66%)	0.00826[S]
	T 8	24(80%)	23(76.66%)	47(78.33%)	
	T 6	0(0%)	6(20%)	6(10%)	
	Total	30	30	60	

The chi-square statistics is 9.593. There P value is .00826. The result is significant at p<0. The sensory block achieved in each participant was vivid. The blockade level with respect to the dermatomal level was taken as a non-numerical variable and the mode from that data set in percentage was adopted in all the parturients and also separately in the two groups as depicted in Table 2.

Table 3: Showing the distribution of motor blockade grades in both groups

Highest sensory level	Group B Bupivacaine	Group L Levobupivacaine	Total
Grade 0	22 (73.33%)	27(90%)	49(81.67%)
Grade 1	8(26.67%)	3(10%)	11(18.33%)
Grade 2	0	0	0
Grade 3	0	0	0
N	30	30	60

Table 4: Mean motor blockade in both groups

	Group B Bupivacaine	Group L Levobupivacaine
N	30	30
Mean ±SD	0.342±0.107	0.229±0.025
P value	0.0001[s]	

Mean ±SD of the motor blockade and its p-value depicted a statistically significant difference as per table 4

Table 5: Showing the mean VAPS and SD in both groups and P-value

Group	Group B Bupivacaine	Group L Levobupivacaine
N	30	30
Mean ±SD	1.725±1.71	2.07±1.63
P Value	0.427[NS]	

The two tailed P value equals 0.427 by conventional criteria, the difference is not statistically significant.

Table 6: Showing the mean maternal satisfaction and SD in both groups and P value

Group	Group B Bupivacaine	Group L Levobupivacaine
N	30	30
Mean ±SD	6.566 ±1.924	6.10 ±2.383
P VALUE	0.408[NS]	

Mean maternal satisfaction were comparable and were statistically not significant.

Table 7: Showing the hemodynamic parameters in both groups and their p value

Parameter	Group B Bupivacaine (Mean±SD)	Group L Levobupivacaine (Mean±SD)	P-Value
N	30	30	
SPO2(%)	98.451± 0.22	99.1± 0.18	0.0001
Heart rate (bpm)	89.63±1.36	94.1±3.67	0.0001
Systolic blood pressure (mmhg)	117.44±7.76	122.48±2.58	0.0013
Diastolic blood pressure (mmhg)	76.4±1.693	78.26±2.184	0.0005
Mean arterial pressure	90.237±2.633	92.75±2.16	0.0002
Fetal heart rate(bpm)	141.049±1.52	140.324±1.612	0.078

Although we found statistically significant difference in hemodynamic parameters between two groups there were no clinically significant alterations in hemodynamic parameters.

Table8: Depicts the mode of delivery among the parturients of both groups and their p value

Mode of delivery	Group B Bupivacaine	Group L Levobupivacaine	Total	P value(chi square)
Spontaneous vaginal	19(63.33%)	21(70%)	40(66.66%)	0.852(0.318)
Instrumental	4(13.33%)	3(10%)	7(11.66%)	
c-section	7(23.33%)	6(20%)	13(21.66%)	
N	30	30	60	

There was no statistically significant difference between two groups with respect to the mode of delivery.

Discussion

The drawbacks of labor pain are eliminated with effective analgesia, which alleviates the major source of stress and anxiety of a laboring mother. The gold standard method for that moment is central neuraxial analgesia. [3] Many research on the use of PCEA as a continuous epidural analgesic during labor compare various LAs with or without opioids in which the subjects receive demand-only or demand-plus-infusion regimens.[7,8] It is hypothesized that difference in the success rate of analgesia with intermittent doses compared to continuous infusion may be related to differences in dispersion of solution in the epidural space. The solution injected into the epidural space spreads more evenly when injected as a bolus due to the large volume and high injectate pressure. [9] In order to achieve superior analgesia with less breakthrough pain and fewer LA needs than continuous infusions, regular intermittent dosages were used in the current study.

Levobupivacaine, the S (-) enantiomer of bupivacaine, has a wider therapeutic index than the racemic mixture. With less toxicity and motor blocking efficacy than bupivacaine. [10] Clinical efficacy is more significant in labor analgesia than potency. There is not much research to back up this claim as there was no access to the levobupivacaine for a long time. [10]

Benhamou D. et al. (2002) examined 0.125% bupivacaine without opioids and 0.0625% bupivacaine with opioids; they discovered that the addition of lipophilic opioids, such as fentanyl or sufentanyl, at a dose of 1 to 3 mcg/ml could lower the concentration of local anesthetics and less motor blockage with a comparable decrease in pain scores, minimizing additional top-ups. [11] However, anesthetic intervention did not significantly change the obstetric result.

The mean of the following numerical data was taken into account in our study: age, height, weight, gestational age, cervical dilatation, Bromage score, VAP score, maternal satisfaction, duration of labor, LA requirement, oxygen saturation, heart rate, NIBP (SBP, DBP, MAP), and fetal heart rate throughout the duration. The mode of delivery and the highest level of sensory block were taken into consideration for the non-numerical data.

In terms of demographic information, the two groups were similar in terms of age, height, weight, and gestational age.

In our study, cervical dilation was not considered as criterion for the initiation of labour epidural analgesia. The maximum maternal desire for analgesia average at a cervical dilation of 4 cm. This may be due to the parturient's ignorance about the available services and lack of trust in the method due to erroneous assumptions of interventions during delivery. Early epidural initiation in labor is associated with a higher incidence of cesarean sections, according to the majority of observational research. [12] However Wong et al [13] study shows no difference in operative delivery between neuraxial analgesia started at 2 cm and 4-5 cm.

Motor blockade varies significantly with labour epidural analgesic regimens. Motor blockade depends mainly on the potency, concentration and volume of LA solution used. In our study, timely mean bromage scores were recorded. The Mean±SD Bromage score in group B was 0.342 ±0.107 and in group L was 0.229 ±0.025 with a P value of 0.0001 which was statistically significant. But this statistical significance is of no clinical relevance because among 60 parturients 81.66% - Bromage 0, 18.33% - Bromage I and none of them had grade 2 or grade 3 motor blockades. Therefore, whatever blockade was achieved did not have an impact on obstetric outcome. Merson et al. [14] investigated the motor blocking potencies of ropivacaine and bupivacaine at concentrations of 0.125% and 0. 25%, respectively, and found that the motor blocking potency was higher with bupivacaine 0.25%. Therefore, it shows that lowering the LA concentration by adding opioids and low dose of local anaesthetics can significantly reduce the motor blocking potencies. [14] Medge D et al in 2002 found that between 0.075% bupivacaine and ropivacaine with fentanyl 2mcg/ml, the degree of sensory and motor block was similar. 48% of patients receiving bupivacaine developed grade 1 motor block on a 0-3 scale, compared to 32% of the ropivacaine group. Although motor blockade between the two groups is statistically significant, the clinical degree of block had no clinical importance. [15]

The highest level of sensory block achieved in each patient was variable and the dermatomal level achieved was a non-numerical variable. We considered the most frequent value (mode) achieved as a percentage in all 60 patients and also separately in group B and group L. Among the 60 parturients 47(78.33%) of them had the blockade level at T8 while the level T6 and T10 was achieved in 6(I0%) and 7(11.66%) respectively. Among the two groups the level of T6 was the highest level attained in group L while the level of T8 was the highest in group B, this produced a statistically significant difference in the highest level of sensory blockade obtained between levobupivacaine and bupivacaine in labor epidural analgesia. Purdie NL et al. compared ropivacaine 0.1% and Levobupivacaine 0.1%, the level of sensory blockade obtained by the two drugs did not differ statistically [16]. Atienzer MC et al. compared levobupivacaine 0.125%, bupivacaine 0.125% and ropivacaine 0.2% with the addition of fentanyl 1mcg/ml in all groups. The author observed that the highest sensory level was similar in all the three groups. Upper sensory level, median [IQR] found to be TIO [T8-Tl 1] in all the groups. [4]

Pain scores were evaluated using the 0-I0cm scale, where 0 is no pain and 10 is the worst possible pain that the parturient can imagine. The Mean±SD VAP score in group B was 1.725±1.71 and in group L was 2.07±1.63 with a P-value of 0.427 that was not statistically significant. The VAP score distribution of the 2 groups was comparable with a P value of 0.427. In our study, Onset of analgesia was highest at 20 min and was similar between the groups. However, the levobupivacaine group showed higher VAP score compared to bupivacaine. Analgesia remained excellent during the initial period of labor. There were few episodes of break-through pain at I80min, 270min and 300 min but VAP scores were <4. The use of ultralow concentration of LA solution at regular intermittent interval and not as continuous infusion and a few patient factors like increased intensity of pain towards the second stage of labor, misinterpretation of discomfort due to head-on-perineum as pain could be attributed to this. However, this finding was not clinically significant because the VAP scores were within 4 cm and maternal satisfaction remained good. In similar studies conducted by Benhamou D et al. and Purdie NL et al. using low dose local anesthetic solutions with opioids, the reduced need for additional top-ups and comparable VAP scores among both analgesic regimens. [11,16] Augmentation of labour using IV oxytocine infusion prior to epidural catheterization was not standardized between the groups. This had an influence on the VAP scores.

Although we found statistically significant differences in maternal hemodynamic parameters between the two groups there was no significant clinical alterations in hemodynamic parameters and no significant detrimental events were recorded requiring further treatment. However, the fetal heart rate trend in both groups was comparable with no statistically significant differences.

The duration of labor is highly variable. In our study using ultra-low dose regimens of bupivacaine and levobupivacaine with opioids, the duration of labour was comparable. The mean duration of labor was 214 ± 69.906 min in group B and 213 ± 69.29 min in group L. Additionally, the total consumption of the volume of drug used in either group was comparable.

After delivery, the parturients were asked to rate their satisfaction with epidural analgesia on a numerical scale 0=totally unsatisfied, 10= totally satisfied. The mean maternal satisfaction in group B was 6.566 ±1.924 and in group L it was 6.16 mg ±2.383 with a P value of 0.408 that was not statistically significant. Atienzar MC et al. in 2008 found the mean maternal satisfaction on the 0 - 10 numerical scale to be 9.1 ± 0.8, 9.1 ± 0.6 using 0.125% bupivacaine and levobupivacaine with fentanyl 1mcg/ml respectively.[4]

The mode of delivery achieved in each patient is variable, and the result achieved is a non-numerical

variable. Therefore, we considered the most frequent value (mode) achieved in percentage in all 60 parturients and also separately in group B and group L. In group B, 19 parturients (63.33%) underwent spontaneous vaginal delivery, 4 parturients (13.33%) instrumental delivery and 7 parturients (23.33%) cesarean delivery. In group L, 21 parturients (70%) spontaneous vaginal delivery, 3 parturients (10%) instrumental delivery and 6 parturients (20%) cesarean delivery. Compared to the studies done by Atienzar MC et al. and Purdie NL et al. Our study results showed reduction in instrumental delivery with the use of very low concentration of LA's with opioids [4,16]

In our study there were no clinically significant adverse effects such as, bradycardia, hypotension and desaturation which required active intervention.

Conclusion

From our study we conclude that racemic bupivacaine 0.0625% and levobupivacaine 0.0625% both mixed with 2 µg/ml of fentanyl, were comparable for delivering a potent and an efficient labour epidural analgesia with a good level of maternal satisfaction. Considering the safety profile and characteristic differential blockade, levobupivacaine can also be considered as a better alternative over bupivacaine for labour epidural analgesia.

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