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A Comparitive Study Between Bupivacaine with Fentanyl And Levobupivacaine with Fentanyl for Combined Spinal Epidural Labor Analgesia in Multiparous Parturients

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Abstract

Background and Aim: *Epidural analgesia with local anesthetics and adjuvants, though proved to be a versatile technique in providing labor analgesia, it is associated with delayed onset of analgesia when administered in advanced stages of labor.Combined spinal-epidural analgesia (CSEA) is gaining popularity as a better neuraxiallabor analgesic technique compared to sole epidural analgesia in multiparous women as the second stage of labor rapidly progresses in this population demanding rapid analgesic onset. This combined method with low dose local anesthetic supplemented with adjuvants increases the duration of sensory blockade, augments maternal satisfaction, and minimizes side effects of local anesthetics. Although bupivacaine has been extensively used for labor analgesia, the newer enantiomer local anesthetics like levobupivacaine have become popular for intrathecallabor analgesia owing to its less cardiovascular and neurological side effects and less propensity for a motor blockade.*
Therefore this study was aimed at comparing the efficacy and fetomaternal outcome profiles between bupivacaine with fentanyl and levobupivacaine with fentanyl in multiparous women.

Material and Methods: *Sixty multiparous parturients in active labor, were randomly allocated into two equal groups. Group B:Received Intrathecal 1.25 mg of 0.5% Hyperbaric Bupivacaine + 25mcg Fentanyl followed by epidural top-ups on demand using 10mlsolution containing 0.125% Bupivacaine + 2 ug/ml of Fentanyl. Group LB:receivedintrathecal 2.5mg (1ml of 0.25% isobaric levobupivacaine + 25mg fentanyl followed by epidural top-ups on demand using 10mlsolution containing 0.125% levobupivacaine + 2mg/ml fentanyl. Onset, duration of spinal analgesia, Mode of delivery, fetomaternal outcomes, and maternal satisfaction were assessed.*

Results: *Demographic and baseline variables were comparable in both the groups.Both groups had a rapid analgesic onset. Onsetin group B (n=30) was 2.96 mins(S.D=0.47) and that group LB (n=30) was 3.01 mins(S.D=0.40). This difference is not statistically significant.The mean duration of spinal analgesia in the levobupivacaine group (80.16±10.54) minutes when compared to that in the bupivacaine group (77±8.05) minutes. This difference is not statistically significant.Twenty-eightparturients in the bupivacaine group and 27 parturients in the levobupivacaine group delivered vaginally. All the neonates in both the groups had an APGAR > 7 at the end of the 5th minute of delivery.*
Two parturients in the bupivacaine group have experienced a mild motor blockade of Bromage 4, while none of the women in the levobupivacaine group had a motor block. Maternal satisfaction was excellent in both groups. Four out of thirty parturients in the bupivacaine group had transient hypotension.Two parturients in the bupivacaine group and one of the parturients in the levobupivacaine group had episodes of vomitings. Fifteenparturients in the bupivacaine group and 12 parturients in the levobupivacaine group have complained of self-limiting pruritis.

Conclusion: *The newer S- enantiomer of bupivacaine is levobupivacaine which, when administered intrathecally, exhibited similar analgesic properties compared to bupivacaine with no adverse fetomaternal outcomes. Owing to its less cardiovascular and neurological side effects and better sensory block propensity at low concentrations, it can be a safe alternative to bupivacaine in the CSE technique of labor analgesia.*

Introduction

Labor pain is an emotional experience involving complex psychological and physiological mechanisms such as an increase in catecholamine surge, which in turn compromises uteroplacental blood flow, thus affecting the fetomaternal outcomes[1]. These concerns lead to the emergence of more and more analgesic techniques to relieve maternal pain, and among these neuraxial analgesic techniques have proved to be most effective in terms of fetomaternal safety and maternal satisfaction[2,3].The active phase of labor rapidly progresses in multiparous women demanding a rapid onset of analgesia for proper maternal satisfaction. Several authors like Karadjova D et al.[4], Heesen et al[5], and Simmons et al. .[6] have stated that in specific population like multipara and parturients in advanced stages of labor, combined spinal-epidural (CSE)labor analgesia supplemented with intrathecal local anesthetic and adjuvants provides superior labor analgesia with a more rapid onset, less motor block, and excellent maternal satisfaction. Levobupivacaine is a relatively newer S enantiomer of traditional bupivacaine which has a significantly lesser cardiovascular and neurological toxicity. The differential affinity for sodium, potassium and calcium channels explains this desirable property of levobupivacaine[7,8].When administered at low doses, intrathecallya pure sensory block could be achieved which is desirable for ambulatory labor analgesia and effective maternal contractions[9].

Hence, the present study is conducted to compare the efficacy and safety profile of levobupivacaine intrathecally supplemented with fentanyl in CSEA in multiparous women in terms of fetomaternal outcomes, analgesia, and maternal satisfaction.

Aim

To compare the efficacy of levobupivacaine with fentanyl and bupivacaine with fentanyl in combined spinal epidural technique of labor analgesia in multiparous parturients.

Objectives

To assess the following parameters between the two groups:

- Onset of spinal analgesia
- Duration of spinal analgesia
- Mode of delivery
- Neonatal outcome
- Maternal satisfaction
- Feto-maternal complications.

Material and Methods

The present study was conducted at KING GEORGE HOSPITAL, Visakhapatnam after the approval from the Institutional Scientific and Ethics committee (ANDHRA MEDICAL COLLEGE) and written informed consent from all the parturients who participated in this study.

Sixty multiparous parturientswho are in the active phase of labor belonging to AMERICAN SOCIETY OF ANAESTHESIOLOGISTS (ASA) grade I and II physical status consenting for labor analgesia were randomly assigned to two groups- bupivacaine group (group B) and levobupivacaine group (group LB). (n= 30 patients/group)

Bupivacaine group :Received Intrathecal 1.25 mg of 0.5% Hyperbaric Bupivacaine + 25mcg Fentanyl followed by epidural top-ups on demand using 10mlsolution containing 0.125% Bupivacaine + 2 ug/ml of Fentanyl.

Levobupivacaine group:receivedintrathecal2.5mg of 0.25% isobaric bupivacaine + 25mg fentanyl followed by epidural top-ups on demand using 10mlsolution containing 0.125% levobupivacaine + 2mg/ml fentanyl.

The onset of spinal analgesia, duration of spinal analgesia, Mode of delivery, fetomaternal outcomes, maternal satisfaction, and incidence of complications were assessed in both the groups.

Inclusion Criteria: Healthy parturients at term, belonging to the age group of 18-35 years, having a singleton pregnancy with vertex presentation, who are in active labor with a cervical dilatation of >4cms, requesting for labor analgesia were included in this study.

Exclusion Criteria: Parturients belonging to ASA grade III and above, with a BMI >/= 35, those having a bleeding diathesis, or on anticoagulant therapy were excluded in the study. Likewise, women with nonsingleton pregnancy, non-vertex presentation, preterm gestation, cephalopelvic disproportion, were excluded. Parturients with a raised ICP, having vertebral column deformities like kyphosis or scoliosis, pre-existing neurological deficits in the lower extremities, or having any sign of infection at the puncture site, or having a history of cardiac arrhythmias, or history of anaphylaxis to local anesthetics were excluded in this study.

Methodology

A detailed history, complete physical examination, and routine investigations were done for all patients. An intravenous line was secured with an 18G cannula.

Before labor analgesia was initiated, several baseline variables like maternal age, height, weight, gestational age, cervical dilatation were recorded.

Every parturient was preloaded with 10ml/kg of lactated Ringers solution.

The baseline severity of pain was assessed by using a visual analog scale.

The extremes are marked "NO PAIN" at one end and "PAIN AS BAD AS EVER CAN BE" at the other end.

VAS 0 indicates NO PAIN, VAS 10 indicates SEVERE PAIN.

In this study, CSE was performed by **SINGLE SPACE NEEDLE THROUGH NEEDLE TECHNIQUE**. The parturient was positioned in left lateral. L3-L4 intervertebral space was identified, and local wheal was raised with one cc of 2% lignocaine by using 26 gauge needle.

Epidural space was identified with 18-gauge Tuohy's needle using the loss of resistance technique. A 25-gauge Whittacre spinal needle was then passed in the same space through the epidural needle. The accurate positioning of the spinal needle was confirmed by the dribbling of CSF. Then the prefilled drug mixture was administered intrathecally. The spinal needle was then removed, and an epidural catheter was threaded through the Tuohy needle. Aspiration was done to ensure that there was no blood or CSF. Test dose was not administered because it may cause undesirable loss of proprioceptive and motor functions. The parturient was then turned supine, and a wedge was placed under the right buttock to prevent aortocaval compression.

Maternal blood pressure, heart rate, respiratory rate, oxygen saturation were noted every 5 minutes for the first 30 minutes, every 15 minutes for the next 60 minutes, every 30 minutes for the next 120 minutes or baby delivery whichever is earlier.

Time of spinal analgesic onset was taken as the time between intrathecal injection till the time when the VAS score of the parturient was less than 3 or 4. (comfortable state).

Fetomaternalhemodynamics were monitored regularly. Maternal hypotension was considered when there a fall in systolic blood pressure of >20% from the baseline value. It was treated by giving i.v. fluid boluses and, if necessary, i.v.Mephentermine was given.

Fetal heart rate monitoring was done regularly with cardiotocography.

The epidural catheter was activated with the loaded epidural drug mixture when the parturient first complains of mild pain VAS > 3. The time period between the onset of spinal analgesia and the activation of the epidural catheter was considered as the duration of spinal analgesia.

The progress of labor was recorded by serial pervaginum examinations by the obstetrician. The mode of delivery in terms of vaginal,instrumental, or cesareansection was noted. Complications like hypotension, pruritis, motor blockade, nausea, and vomiting were observed.

Motor blockade was assessed by using **MODIFIED BROMAGE SCALE**.

Table 1. Modified bromage scale to assess the motor blockade

score	GRADING	
1.	COMPLETE BLOCK	Unable to move feet or knees
2.	ALMOST COMPLETE BLOCK	Above to move feet only
3.	PARTIAL BLOCK	Just able to move knees
4.		Detectable weakness of hip flexion
5.	NO MOTOR BLOCK	Able to fully flex the knees
6.		Able to perform knee bend

Motor blockade was considered when the Bromage score was </= 4.

APGAR scores at 1 min and 5 min after baby delivery was noted, which denotes the neonatal outcome.

TABLE 2: APGAR scoring system for the assessment of neonatal outcome.

SCORE	0 points	1 point	2 points
Appearance - Skin colour	Cyanotic/ Pale all over	Peripheral cyanosis only	Pink
Pulse (Heart rate)	0	<100	100-140
Grimace - Reflex irritability)	No response to stimulation	Grimace (facial movement)/ weak cry when stimulated	Cry when stimulated
Activity - Tone	Floppy	Some flexion	Well flexed and resisting extension
Respiration	Apnoeic	Slow, irregular breathing	Strong cry

Parturient was monitored for 2 hours postoperatively, and then the epidural catheter was removed. Parturient was enquired about the satisfaction during the course of labor and delivery and noted on a **maternal satisfaction grading scale** as follows

Table 3: Showing maternal satisfaction grading scale

Grade 1	Excellent
Grade 2	Good
Grade 3	Fair
Geade 4	Poor

Statistical Analysis

The collected data was consolidated in a master sheet using Microsoft Excel software, and this data was used for statistical analysis. The relevant data was analyzed using Microsoft Excel and medcalc calculator software.

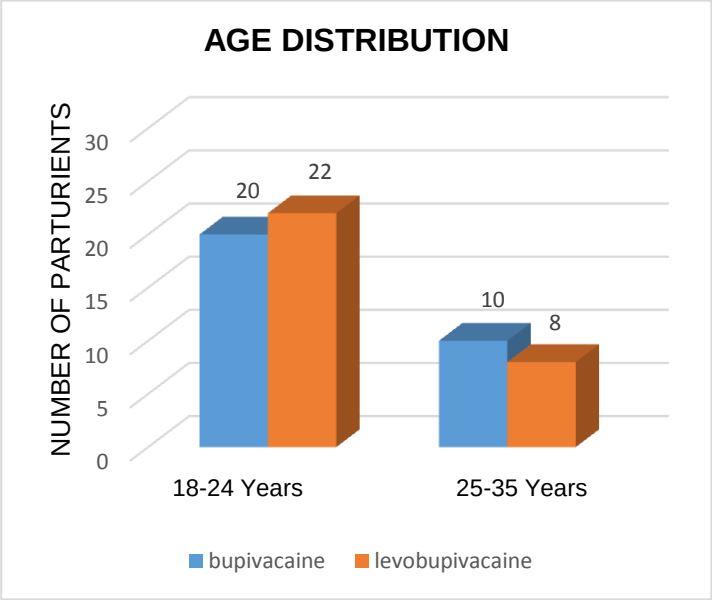
Non-categorical data such as onset, duration were represented as MEAN ± SD and wereanalyzed using the unpaired t-test.

Categorical data such as maternal satisfaction were expressed as proportions and were analyzed using the Chi-Square test.

A p-value of < 0.05 was considered to be statistically significant.

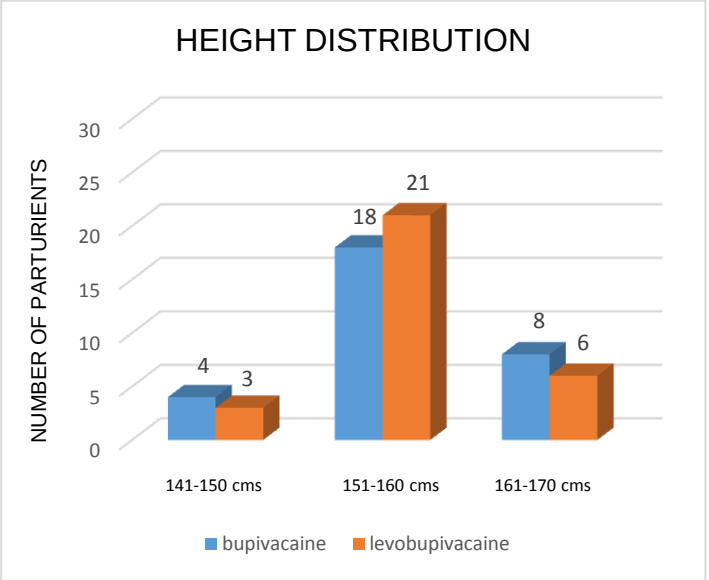
Results

Figure depicting age distribution



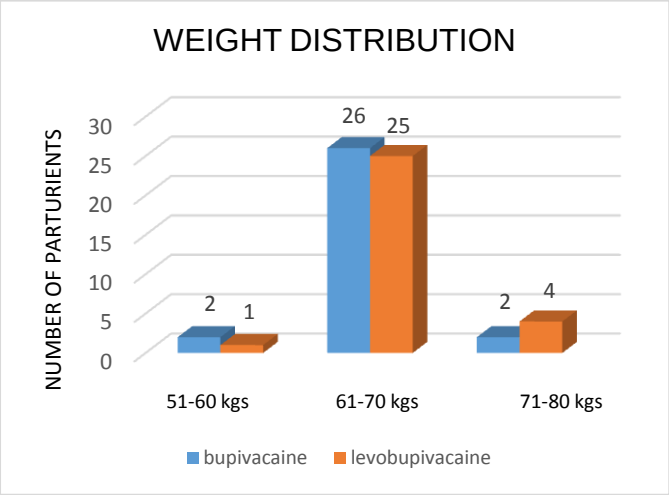
P value= 0.597 = Not Significant

Figure depicting height distribution



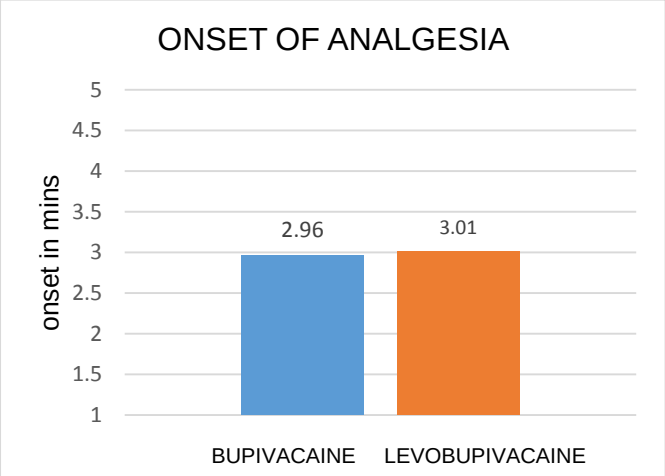
P value >0.05 so statistically not significant.

Figure depicting weight distribution



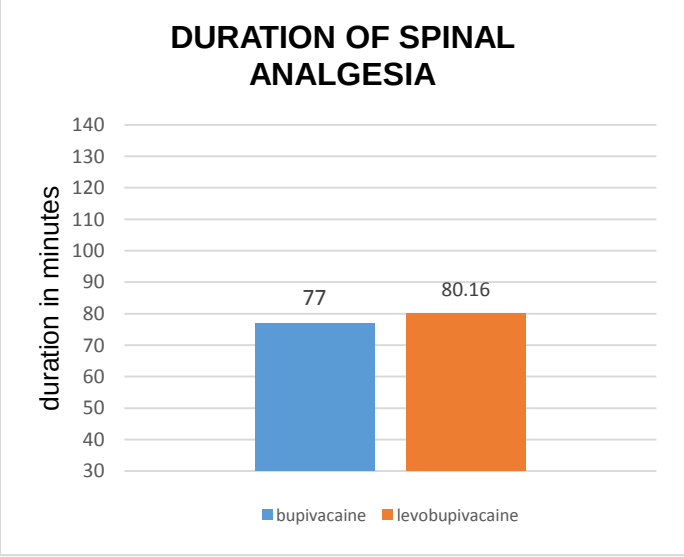
P-0.11 (>0.05 = Not Significant)

Figure depicting onset of spinal analgesia



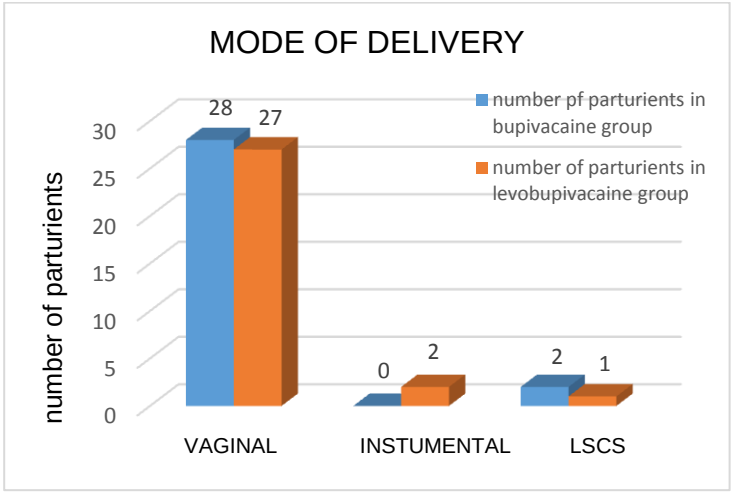
P Value- 0.65(> 0.05) =Not Significant

Figure depicting duration of spinal analgesia



P value is > 0.05 = Not Signficant

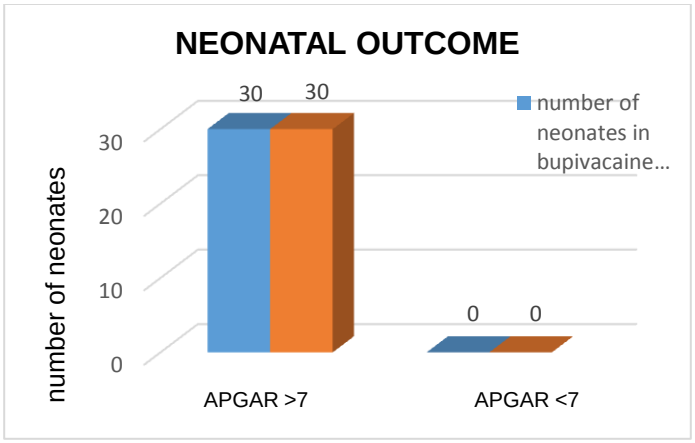
Figure depicting mode of delivery



P value is > 0.05, [Not Significant]

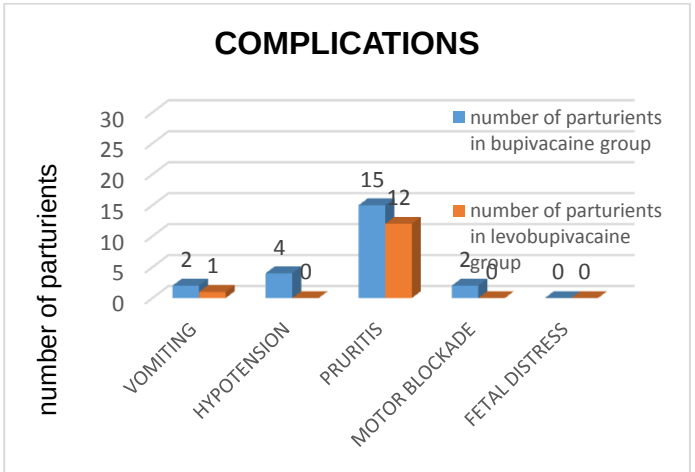
The statistical analysis was done using Chi-Square test. The P value is >0.05, so the difference was statistically not significant.

Figure depicting neonatal outcome



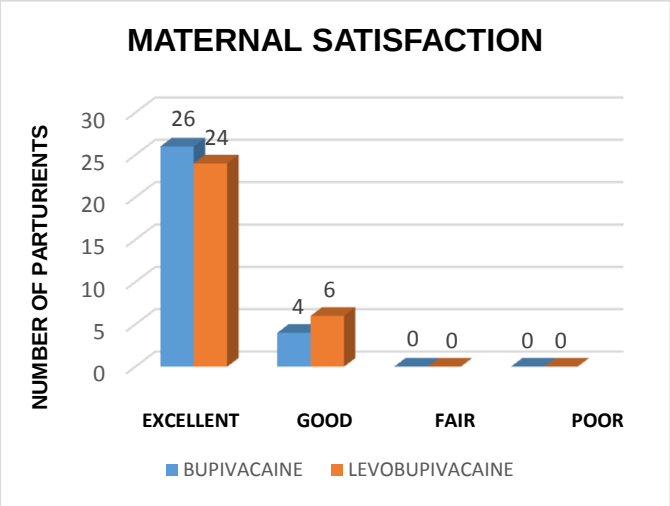
P value- Not Significant

Figure depicting incidence of complications



P value- > 0.05- not significant -Analysed by using CHI Sqaure Test

Figure depicting maternal satisfaction:



P value is > 0.05, so statistically not significant

Discussion

Although neuraxial analgesia provides excellent satisfaction during labor, it may affect the progress and outcome in terms of increased incidence of instrumental deliveries. Diminished fergusons reflex, reduced motor efforts due to weak abdominal muscles, inadequate rotation of fetal head secondary to weak pelvic floor musculature remain the predisposing factors[10]. In an attempt to overcome this situation, walking epidural is preferred for labor analgesia as ambulation increases the intensity of uterine contractions, and therefore result in effective progression of labor[11]. Levobupivacaine has a lesser propensity for motor block, as compared to bupivacaine and hence, it is preffered for labor analgesia in the recent years.

The present study compared bupivacaine and levobupivacaine in CSE technique in 60 healthy multiparous parturients in the active phase of labor, who consented for labor analgesia. Both groups were standardized with respect to drug dosages of the epidural component and the local anesthetic used intrathecally.

The demographic variables like age, weight, height, were similar between the two groups. Baseline variables like cervical dilatation, and VAS scores were similar between both the groups.

The onset of spinal analgesia was measured in minutes and was assessed by using a visual analog scale. The mean time of onset of analgesia in bupivacaine group (n=30) was 2.96 mins (S.D=0.47) and that levobupivacaine group (n=30) was 3.01 mins (S.D=0.40). This data was statistically analyzed by using the standard error of the difference between means, and the P-value obtained is >0.05, indicating there is no statistical significance between the two groups. Both groups had a rapid analgesic onset.The mean duration of spinal analgesia in the bupivacaine group was 77+8.05 mins, and in the levobupivacaine group was 80.16+10.54 mins. This difference is not significant statistically.

VeenaChatrath et al[12] in their similar study comparing fentanyl and tramadol as adjuvants with levobupivacaine, observed a rapid analgesic onset with fentanyl and levobupivacaine in 1.85 + 0.49 mins. When compared to the present study, this onset is more rapid, though not clinically significant. The duration of spinal analgesia observed in their study was 95.67+7.96 mins, which is almost similar to the present study. Similarly, Chuttani p etal,[13] in their study administered 0.1% levobupivacaine with fentanyl as patient controlled epidural analgesia and stated that it provided excellent satisfaction. Kyung Kim et al[14] in their study compared 3mg intrathecal levobupovacaine with 20mcg fentanyl and 3mg intrathecalropivacaine with fentanyl and concluded that at clinically relavant doses, intrathecallevobupivacaine offered more effective analgesia compared to ropivacaine. Similarly, LIM et al[15] administered 2.5mg intrathecal levobupivacaine with fentanyl and stated that addition of fentanyl to intrathecallevobupivacaine provided satisfactory ambulatory labor analgesia with less incidence of break through pain.

Previous studies have also quoted that the minimum local analgesic dose for intrathecal levobupivacaine as 2.73-3.16 mg[16]. So, in the present study, 2.5mg of levobupivacaine was administered intrathecally.

None of the parturients in the levobupivacaine group present study had a motor block, while two of the women in bupivacaine have complained of

slight weakness for half an hour after the intrathecal block. Several studies on intrathecal levobupivacaine conducted by Chuttani p et al, Kim et al, Lim et al also concluded that levobupivacaine did not cause any motor weakness when administered for labor analgesia supporting the present study. On the contrary, M.T.Atienzar et al who compared bupivacaine, levobupivacaine and ropivacaine for labor analgesia have stated that the incidence of motor block was high in bupivacaine and levobupivacaine groups, though they administered these drugs in a continuous epidural infusion which may have altered the observations[17]. Almost all the women in the present study had a normal vaginal delivery except for two women in bupivacaine group and three women in levobupivacaine group who had an instrumental delivery and cesarean section due to obstretic indications. The incidence of pruritis was found to be similar in both the groups which is transient and self limiting. Several supporting reviews have shown that the incidence of pruritus after intrathecal administration of opioids varies from 30% to 100 %. The incidence among the commonly used intrathecal opioids (morphine, fentanyl, sufentanil) has been reported to be similarly frequent, and the exact underlying mechanism of neuraxial opioid-induced pruritus remained unclear.

Krause L et al.[18] have stated that naloxone's reversibility of opioid-induced pruritis supported the basis of an opioid receptor-mediated centrally mediated mechanism.

In the present study, the neonatal outcome was assessed using the APGAR score. APGAR scores immediately after delivery and after 5 minutes were> 7 in both the groups (100%).

Cardiotocography monitoring was done during the course of labor, and fetal bradycardia was not observed in both groups similar to all the above quoted studies.

Maternal satisfaction was found to be excellent in both the groups.

Summary

After obtaining the informed consent of 60 healthy multiparous parturients in labor, aged between 18 to 35 years were selected and motivated for labor analgesia. This study population were randomly divided into two equal groups of 30 parturients in each group, and Combined spinal-epidural (CSE) technique of labor analgesia was administered in all the parturients

Bupivacaine group received Intrathecal 1.25 mg of 0.5% Hyperbaric Bupivacaine + 25mcg Fentanyl followed by epidural top-ups on-demand using 10mlsolution containing 0.125% Bupivacaine + 2 ug/ml of Fentanyl, while

Levobupivacaine group received intrathecal 2.25mg of 0.25% isobaric levobupivacaine + 25mcg Fentanyl followed by epidural top-ups on-demand using 10mlsolution containing 0.125% bupivacaine + 2mg/ml fentanyl. The onset of analgesia, duration of analgesia, mode of delivery, neonatal

outcome, maternal and fetal side effects and maternal satisfaction were observed, compared and analyzed statistically.

Demographic and baseline variables were comparable in both the groups.

Both groups had a rapid analgesic onset.

Onset in bupivacaine group (n=30) was 2.96 mins (S.D=0.47) and that levobupivacaine group (n=30) was 3.01 mins(S.D=0.40). This difference is not statistically significant.

The mean duration of spinal analgesia was similar in both the groups- bupivacaine group- (77$\pm$8.05) minutes when compared to that in levobupivacaine group (80.16$\pm$10.54) minutes. This difference is not statistically significant.

Mode of deliveryandneonatal outcomes were comparable in both the groups.

28 parturients in bupivacaine group and 27 parturients in tramadol group delivered vaginally. All the neonates in both the groups had an APGAR > 7 at the end of 5th minute of delivery. Complications in both groups were compared.

Both groups have a significant incidence ofpruritis (~50%) but it was selflimiting.

2 of the parturients in bupivacaine group had a mild motor blockade (bromage 4) but this resolved within 20 minutes of block. None of the parturients in levobupivacaine group had motor block and all were ambulatory.

Maternal satisfaction was excellent in both groups.

Conclusion

The newer S- enantiomer of bupivacaine-levobupivacaine had similar analgesic properties compared to bupivacaine with no adverse fetomaternaloutcomes.owing to its less cardiovascular and neurological side effects and better sensory block propensity at low concentrations, it can be a safe alternative to bupivacaine in CSE technique of labor analgesia.

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