

A Comparative Study of Efficacy of Bupivacaine and Ropivacaine with Fentanyl in Epidural Labour Analgesia

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Abstract

Introduction: Labour is a highly complex and personal process for every woman. Analgesic intervention is a matter of personal choice for delivery. Local anesthesia given as an epidural injection along with an opioid gives quicker analgesia without impeding motor activity. Bupivacaine and Ropivacaine are commonly employed drugs to provide efficient epidural analgesia in labour. **Aims:** To compare the efficacy of ropivacaine with fentanyl and bupivacaine with fentanyl given as continuous infusion in labour epidural analgesia. **Materials and Methods:** This was a prospective randomized control trial wherein 70 women in labour were studied. These 70 parturients were randomly put into two groups. Group A (n=35) received 12 ml of 0.125% ropivacaine as the initial bolus followed by 8 ml/hour infusion of 0.125% ropivacaine with 2 µg/ml fentanyl. Group B (n=35) received 12 ml of 0.125% bupivacaine as initial bolus followed by 8ml/hour infusion of 0.125% bupivacaine with 2 µg/ml fentanyl. Various parameters like duration of labour, mode of delivery, neonatal outcome and complications were noted and compared for both the groups. **Results:** Both the groups showed minimal fluctuations in pain that were clinically and statistically insignificant. The spontaneous deliveries were similar in both groups. The rate of instrument assisted delivery and caesarean delivery was similar in both groups. No adverse neonatal outcome (because of the drugs used) in the form of low APGAR scores or admission to NICU were noticed in both the groups. Motor block was not statistically significant. The incidence of complications was minimal and comparable in both groups. **Conclusion:** Ropivacaine used at lower concentration (0.125%) offers good pain relief equivalent to that of bupivacaine. Both the drugs give similar results as regards the duration of labour, mode of delivery, neonatal outcome and complications. Though ropivacaine is less potent than bupivacaine, its safety and efficacy is equivalent to bupivacaine.

Keywords: Epidural analgesia, Ropivacaine, Bupivacaine, Motor blockade

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Introduction

Labour is a natural and physiologic process with a happy outcome for most of the women. But it can be a very painful and unpleasant experience for some. Analgesic intervention during delivery is a matter of personal choice for an individual.

All the antenatal women should be provided with information regarding the process of labour and the means available to ease the process. Whether a woman opts for analgesia during labour is her own decision. Many religious and cultural factors influence the patient's thought process regarding analgesia during labour. An ideal analgesic should

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be safe for the mother and newborn, should not affect the progress of labour, and should be adaptable to changing conditions.

The analgesia should last for a sufficient time period, should be titratable as per patient requirements, without any undue adverse effects in the mother or new-born. Also it should be physician and cost friendly. At present to achieve this end, many modalities are available. Extensive research has made way for use of neuraxial techniques that are safe and effective.

Current neuraxial labour analgesia focusses not only on pain relief but also on the overall quality of analgesia [1].

Central neuraxial analgesia is considered the gold standard method for pain control in the present day practice of obstetrics. This method also gives a better and satisfying birth experience to women [2]. This technique can be used as a subarachnoid or as an epidural block. Between the two, epidural block is considered to be better for labour as it can provide continuous analgesia for longer time period and also is amenable to conversion to anesthesia if at all a surgical intervention is required.

Epidural injection of a local anaesthetic combined with an opioid provides a more rapid onset of analgesia with little motor blockade. The onset of pain relief is faster and also lasts longer if both the drugs are used. As two drugs are being used each has a lower concentration, which reduces the risk of systemic toxicity by local anesthetic and also reduces the side effects of opioids [3]. Bupivacaine and Ropivacaine are widely used to provide efficient epidural analgesia in labour. Bupivacaine has increased risk of motor blockade thereby leading to increased rates of forceps/instrument use and also it has some cardiac toxicity. On the other hand, Ropivacaine is advantageous in having more sensory motor differential blockade and also less systemic toxicity. Various authors have reported contrasting results of ropivacaine and bupivacaine for labour analgesia [1]. Some studies observed less motor block by ropivacaine as compared to bupivacaine while others observed no difference between the two. To prevent or lessen unwanted motor block, dilute solutions of epidural local anesthetics combined with opioids have been recommended.

In the present study, we attempted to evaluate whether ropivacaine offers any significant advantage over bupivacaine with regard to obstetrical outcome and whether changing over from bupivacaine to ropivacaine is warranted. Both

the drugs were evaluated and compared for pain relief, motor block, and labour characteristics.

Materials and Methods

This was a prospective randomized control trial carried out in the Department of Obstetrics and Gynaecology, Dr. PSIMS and RF, Chinnaoutpalli over a period of 13 months from 1st October 2012 to 31st October 2013. Approval was taken from Institutional ethics committee and scientific committee.

The study had 70 women who were due for labour. They were informed and counselled regarding facility of labour analgesia. The procedure was explained to all the patients and informed consent was obtained from willing patients. Complete clinical history of the patient was recorded. Routine investigations like blood grouping and typing, hemoglobin estimation, and platelet count were done as per our hospital labour protocol. Only those patients who fulfilled the inclusion criteria and who gave consent were selected and were then randomly allocated to one of the study groups.

Inclusion Criteria

1. Normal singleton pregnancies.
2. Age between 18 to 35 years
3. ASA status: I and II
4. Patients in active labour with cervical dilatation of 3-5 cm.

Exclusion Criteria

1. Contraindications to epidural block
2. Pre-term pregnancy
3. Multiple gestations.
4. Previous cesarean section.

The patients were cannulated with 18G IV cannula and infused with Ringer lactate solution. The patient was asked to be in sitting position with the back aligned with the edge of the bed. Under all aseptic precautions, cleaning and draping of the skin in the lower thoracic and lumbar region was done. The best interlumbal space between L₂ and L₄ was selected and infiltrated with 2 ml of 2% lignocaine.

Epidural catheterization was done and a length of 5 cm of catheter was kept in the epidural space. Care was taken not to aspirate CSF or blood at any time during the procedure.

After the catheter was satisfactorily in situ, the puncture site was cleaned and an occlusion dressing was applied. A bacterial filter was attached to the hub of the catheter. The catheter was secured by adhesive tape by fixing it against the dorsum. First a small test dose of local anaesthetic (3 ml of 2% Lignocaine with Adrenaline) was given through the catheter to rule out intravascular or intrathecal placement of catheter. Signs of motor block suggest intrathecal placement and tachycardia suggests intravascular placement so these were looked for. In absence of these signs (after 5 minutes) the patient was put in a supine position. Then the test drug was given as bolus dose followed by the infusion.

If there was any breakthrough pain then patient was given 6 ml of either 0.125% Ropivacaine or 0.125% Bupivacaine based on the subject's study group. Various maternal parameters were continuously monitored and noted every 15 minutes in the first hour, every 30 minutes in the second hour and every hourly thereafter. Continuous fetal heart monitoring was also done. Duration of first stage of labour was taken from insertion of epidural catheter (3-5 cm of cervical dilatation) to full dilatation of cervix.

Parameters monitored: Maternal Heart rate, Maternal Blood pressure, Maternal respiratory rate and oxygen saturation, Pain relief by 11 point verbal numerical rating scale (VNRS) and Motor block by Bromage score (0-3).

Clinical outcome studied: The following parameters were noted: Pain relief, Motor block, Duration of labour, Mode of delivery and Neonatal outcome.

The statistical analysis was performed using SPSS (Statistical package for social sciences) version 17 for windows. The profile of the cases was compared with the treatment allocation in order to check if there was any significant imbalance. Descriptive statistics are presented as mean \pm SD. Chi-square test for association was used to compare categorical variables between treatment allocations

Results

Total number of cases was 70.

Table 1: Demographic details and profile of the cases

Mean	Group A (Ropivacaine with Fentanyl)	Group B (Bupivacaine with Fentanyl)
Age (in years)	25.37	25.23
Weight (in Kgs)	68	64.29

<i>Gravida and parity</i>		
Gravida 1	19	26
Gravida 2	15	8
Gravida 3	1	1
Parity 0	21	27
Parity 1	14	4.4
<i>ASA Grade</i>		
ASA Grade I	94.3	91.4
ASA Grade II	5.7	8.6
<i>Mode of delivery</i>		
Cesarean	11.4	8.6
Vaginal Assisted	25.7	37.1
Vaginal Spontaneous	62.9	54.3
<i>Level of epidural catheter placement</i>		
L2-L3	22.9	40
L3-L4	68.6	51.4
L4-L5	8.6	8.6

The patient demographics of age (p=0.874), weight (p=0.843), Gravida (p=0.200) and parity (p=0.122) were statistically insignificant between the two groups.

Also the ASA grade II distribution of patients was statistically insignificant. (p=0.643).

There were more spontaneous vaginal deliveries in Group-A (62.9%) compared to group-B (54.3%). Assisted vaginal deliveries were less in group- A (25.7%) compared to group-B (37.1%). Four patients in group-A (11.4%) and three patients in group-B (8.6%) had cesarean deliveries.

More than 50% of the patients in both the groups received epidural in the L3-4 interspace. The distribution of level of epidural catheter placement among both the groups did not have any statistical significance. (p=0.287).

Comorbid conditions

Gestational diabetes mellitus (GDM) was present in one woman (2.9% in each group). PIH Pregnancy Induced Hypertension (PIH) was present in one woman (2.9%) in group-A and in two (5.8%) women in group-B. Their distribution among groups was statistically insignificant. (p=0.840).

Vaginal dilatation

The average vaginal dilatation of all 70 subjects was 3.44 \pm 0.65 cm. The mean for group-A was 3.37 \pm 0.54 cm and for group-B it was 3.51 \pm 0.74 cm. The difference was statistically insignificant. (p=0.206)

Outcome measured

Hemodynamics

All the 70 patients had continuous monitoring of their hemodynamic parameters. The baseline values were noted before giving epidural analgesia, then at 15 minutes, at 30 minutes, at 45 minutes, and at the end of 1, 1.5, 2, 3, 4, 5, 6, 7 hours. All 70 individuals had minimum monitoring time around 3 hours.

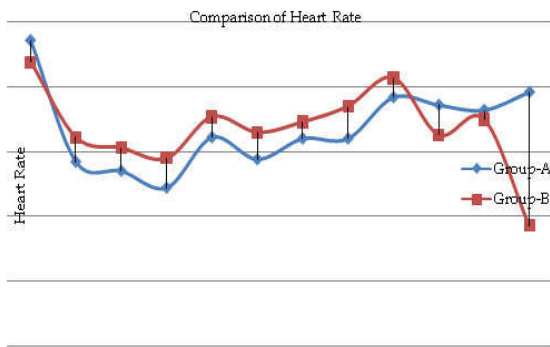


Fig. 1: Comparison of heart rate in both groups

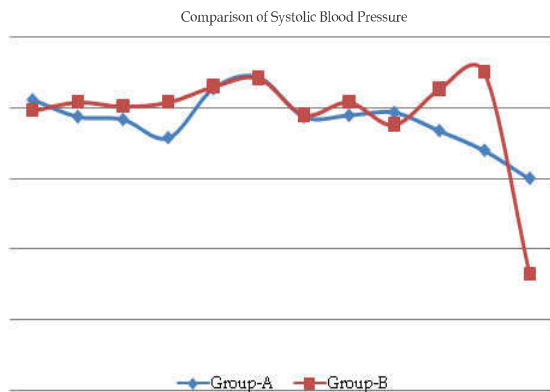


Fig. 2: Comparison of systolic blood pressure in both groups

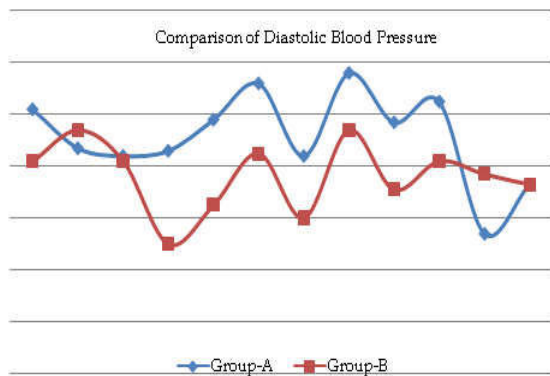


Fig. 3: Comparison of diastolic blood pressure in both groups

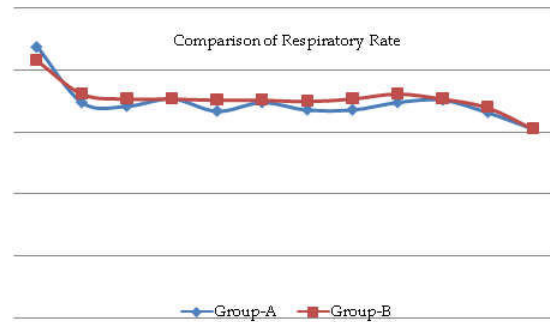


Fig. 4: Comparison of respiratory rate in both groups

The hemodynamic parameters did not show any statistically significant difference between the two groups. The oxygen saturation (SpO₂) among both groups also did not vary significantly.

Table 2: Comparison of pain score in both groups

Time	Group-A	Group-B	t Value	p Value
Baseline	7.88 ± 0.7	7.65 ± 0.8	1.170	0.246
15 mins	0.31 ± 0.4	0.17 ± 0.3	1.393	0.168
30 mins	0.02 ± 0.1	0.08 ± 0.2	-1.023	0.310
45 mins	0.02 ± 0.1	0.05 ± 0.2	-0.583	0.562
1 hr	0.02 ± 0.1	0.08 ± 0.2	-1.023	0.310
1.5 hr	0.11 ± 0.5	0.05 ± 0.2	-1.358	0.179
2 hr	0.08 ± 0.2	0.02 ± 0.1	1.023	0.310
3 hr	0.20 ± 0.6	0.08 ± 0.3	1.041	0.302
4 hr	0.28 ± 0.8	0.09 ± 0.3	1.235	0.221
5 hr	0.42 ± 0.9	0.52 ± -.2	-0.289	0.774
6 hr	0.00 ± 0	0.38 ± 1.1	-1.127	0.276
7 hr	0.00 ± 0	0.00 ± 0		

The pain levels immediately after bolus were reduced. The pain levels did not go above VNRS (verbal numerical rating scale) of 3 during infusion in both the groups. Most of the increase in pain scores occurred during the second stage of labour. But the pain score variation was statistically insignificant.

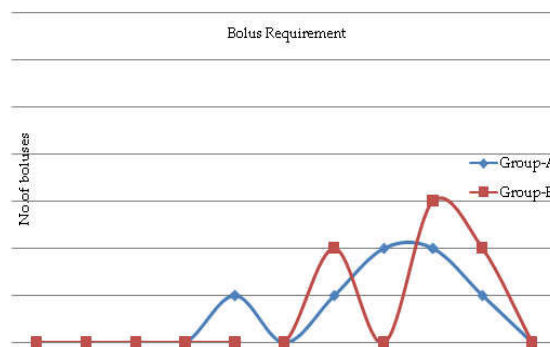


Fig. 5: Bolus Requirement for both groups

For both the groups an equal number of patients (7 women in each group) required boluses during their labour.

Table 3: Duration of labour for both groups

Duration (in minutes)	Group-A	Group-B	t Value	P Value
Stage-I	467.4 ± 95.8	467.6 ± 87.8	-0.007	0.995
Stage-II	33.5 ± 8.5	31.1 ± 8.9	1.116	0.269
Stage-III	6.8 ± 1.7	6.1 ± 1.2	1.769	0.082

All 3 stages of labour were comparable for both groups without much variation.

The standard APGAR score was used to rate the neonatal outcome which was taken at 1 and 5 minutes. At the end of 1 minute the average APGAR score was 7.65 ± 0.59 and 7.68 ± 0.47 in group-A and group-B respectively. At 5 minutes, the APGAR score was 8.94 ± 0.23 and 9 in group-A and B respectively. There was no statistically significant difference in the mean values 1 minute (p=0.460) and 5 minutes (0.221) for both groups.

NICU admission

NICU care and admission was required in 5 neonates (14.3%) in group-A and in 3 neonates (8.6%) in group-B. The difference was not statistically significant (p=0.845). The indications for admission in NICU in group-A, and group B were cord around the neck, respiratory distress and meconium stained liquor. The remaining two neonates in group A had IUGR.

Motor block

Motor blockade of Bromage score-1 was seen in 3 persons in group-B. This was observed during the 5th hour in all 3 patients. There was no clinically observable motor blockade in Group-A. However this statistically insignificant (p=0.071).

Numbness

In group-B, 2 patients had numbness that was seen in the 6th and 7th hour. In group A, no patient had numbness. The numbness rate was statistically insignificant.

Pruritus

No patient from either group complained of pruritus.

Discussion

In the recent Cochrane review it was concluded that epidural analgesia offered better pain relief as compared to non-epidural methods. Also it obviated the need for additional pain relief and had reduced risk of acidosis. In the present study we have compared bupivacaine and ropivacaine for labour epidural analgesia. Bupivacaine is an established drug and is often used for labour analgesia. We compared bupivacaine with ropivacaine, (levo-enantiomer) as ropivacaine gives better sensory-motor differentiation. Also it

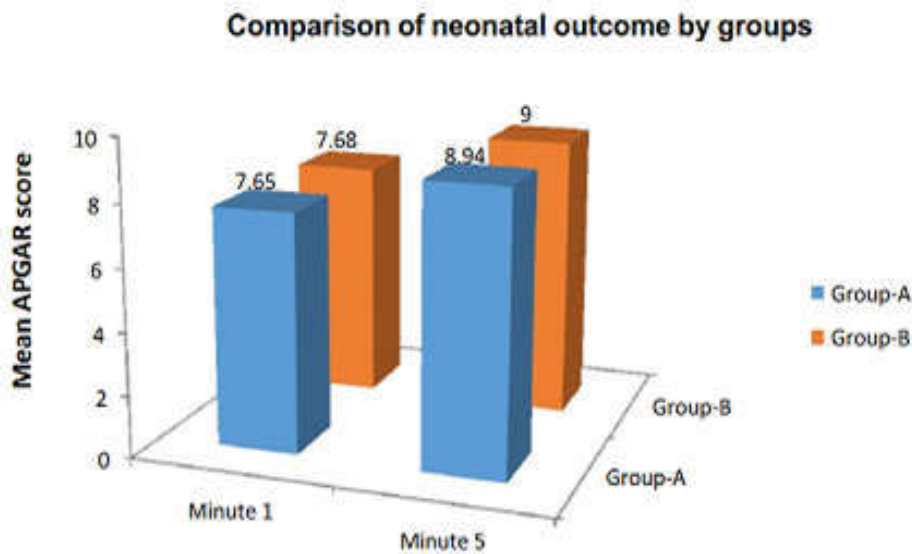


Fig. 6: Neonatal Outcome for both groups

has less cardiotoxic potential than bupivacaine.

Ropivacaine is only 60% potent as compared to bupivacaine [4]. Some of the studies have compared both drugs in equal concentrations [5] (i.e. 0.125% bupivacaine versus 0.125% ropivacaine) while some have compared equi-potent concentrations of both drugs [6] (i.e. 0.1% bupivacaine versus 0.15% ropivacaine). Most of the authors have concluded that both drugs are more or less equally effective and that ropivacaine has a slight advantage as it causes less motor block on prolonged infusion. The recommended dose of bupivacaine and ropivacaine in labour epidural analgesia is 0.0625%-0.125% (8-15 ml/hour) and 0.125%-0.25% (6-12 ml/hour) respectively [7].

We used 12 ml of 0.125% ropivacaine for initiation and 8 ml/hour of 0.125% ropivacaine with 2 µg/ml fentanyl for maintenance. There is a synergistic action when neuraxial local anesthetics and opioids are used together and better neuraxial analgesia is achieved. This combination decreases the minimal local analgesic concentration (MLAC) of local anaesthetics used. We used fentanyl in a concentration of 2 µg/ml as many previous studies have used it at this concentration. We used ropivacaine at 0.125% concentration (with fentanyl) since it has less incidence of motor blockade at this concentration which is important during labour analgesia. Also as we wanted to compare the analgesic effect of two drugs it was reasonable to use them at same concentrations. The other factors like the age, weight, gravida, parity, vaginal dilatation were similar in both the groups.

Pain relief

It is difficult to measure pain as it is subjective and depends on the individual's pain perception. Various scales are in vogue to measure pain and the popular ones are verbal rating scale, numerical rating scale (NRS) and visual analog scale (VAS). We used the NRS in our study due to its ease and better patient compliance. We observed that the mean pain level was 7.8 ± 0.7 in ropivacaine group and 7.6 ± 0.8 in bupivacaine group. After epidural analgesia it came down to 0.31 in ropivacaine and 0.17 in bupivacaine group. At the end of 5 hours the pain score went up to 0.42 and 0.52 in ropivacaine and bupivacaine group respectively. The onset of pain relief was similar in both the groups. Our findings agree well with those of Meister *et al.* 2000 [5]. In their study, they compared equal concentrations of bupivacaine and ropivacaine (0.125%) along with fentanyl in both groups. They observed mean NRS scores of 9 in bupivacaine and

8 in ropivacaine group which came down to 0.4 and 0.3 post epidural analgesia. Similar observations were reported by Fernandez *et al.* 2001 [8] when they compared 0.0625% bupivacaine with fentanyl and 0.1% ropivacaine and fentanyl.

The onset of pain relief was similar in both groups. Also the patient satisfaction was more or less same in both groups. In spite of using a less potent ropivacaine, the pain relief was almost equal in both groups with insignificant statistical difference.

Motor blockade

Halpern *et al.* 2003 [9] did a meta-analysis and compared ropivacaine (0.05-0.2%) and bupivacaine (0.05-0.125%). In this meta-analysis 19 out of 23 studies concluded that ropivacaine has minimal motor block and 5 of these studies were statistically significant. In our study, only 2 patients in bupivacaine group had demonstrable Bromage score-I motor block. There was no clinically demonstrable motor block in the ropivacaine group. This difference was not clinically significant. In this study the incidence of motor block was low in bupivacaine and it was absent in ropivacaine group which is consistent with other studies [5].

Duration of labour

Duration of 1st stage of labour

The first stage of labour includes good uterine contractions, the dilatation of cervix and the descent of the presenting part of fetus. In our study the first stage of labour was taken from the insertion of epidural catheter (at 3-5 cms) of cervical dilatation to the full dilatation of cervix. The duration of first stage of labour was 467.7 ± 95.8 minutes in ropivacaine group and 467.6 ± 87.8 minutes in the bupivacaine group. The mean duration for both groups was not statistically significant. Various authors have compared varying concentrations of bupivacaine with ropivacaine. They observed similar duration of first stage of labour with both the drugs. (Feranandez 2001, Owen 2002, Boselli 2003) [8,10,11]. Our findings agree well with the above studies. In contrast, Lee *et al.* [12] in their study found longer first stage of labour in the bupivacaine group as compared to ropivacaine group. They felt that though this difference was statistically significant, it was clinically insignificant.

Duration of 2nd stage of labour

According to ACOG guidelines, if the second stage of labour takes more than 3 hours in case

of a primipara and more than 2 hours in case of a multipara with regional analgesia, then it is called prolonged second stage. Halpern *et al.* [9] did a meta-analysis which had 2400 parturients who received either epidural analgesia or parenteral opioid analgesia. He observed that those who received any medication had a slightly longer (14 minutes more) second stage of labour. A recent Cochrane review found that women in labour who had epidural analgesia had slightly longer second stage of labour [13].

In our study there was no difference in the duration of second stage of labour in both groups. The mean duration was 33.5 min in ropivacaine group and 31.1 min in bupivacaine group. This difference was not statistically significant. Our result coincides well with the meta-analysis done by Halpern *et al.* in 2003 [9] which took into account 23 studies comparing ropivacaine and bupivacaine for labour epidural analgesia. They found that neither bupivacaine nor ropivacaine group had any difference in the duration of second stage of labour.

Mode of delivery

Instrumental vaginal delivery

Halpern *et al.* 1988 [9] in their meta-analysis found higher possibility of instrumental vaginal delivery in women who received epidural analgesia. Cambic and Wong 2010 [14] in their review also observed higher rate of instrumental vaginal delivery while using epidural analgesia. In our study we had an instrumental delivery rate of 25.7% and 37.1% in ropivacaine and bupivacaine group respectively, which was not statistically significant. In majority of cases, maternal failure was the cause of instrumental delivery. Finegold *et al.* [15] in their study reported instrumental vaginal delivery rate of 18% in ropivacaine and 28% in bupivacaine group respectively. In their study also the difference was statistically insignificant.

Halpern *et al.* [10] also did not find any difference in the mode of delivery between the two drugs. However a meta-analysis of 6 studies comparing 0.25% ropivacaine and 0.25% bupivacaine done by Writer *et al.* [16] in 1998 found that there were fewer instrumental vaginal deliveries in the ropivacaine group. This may be because of the higher concentration of bupivacaine used and difference in the motor blocking potency of ropivacaine.

Caesarean delivery

In general, the process of normal labour converting to caesarean delivery is never attributable

to epidural anaesthesia. In the present study, the ropivacaine group had a cesarean delivery rate of 11.4% and bupivacaine group had a rate of 8.6%. However, the indications for the cesarean delivery were failure to progress, cord around the neck and meconium stained liquor leading to fetal distress.

In the study done by Beilin *et al.* in 2007 [17] they observed a cesarean rate of 33% and 30% in bupivacaine and ropivacaine group respectively. Halpern *et al.* [10] also in their meta-analysis did not find any difference in cesarean delivery rates between the two groups when epidural analgesia was used.

Fetal and neonatal outcome

It was observed in the Cochrane review that women who had opted for epidural analgesia during labour, their new borns had less acidosis and lesser requirement for naloxone as compared to women who received inhalational and intravenous, mainly opioid analgesics [13]. In the present study, the fetal heart rate monitoring during labour analgesia was regular without much variations and post epidural fetal bradycardia was not evident. The mean APGAR scores were 7.65 and 7.68 in ropivacaine and bupivacaine groups respectively. At 5 minutes it averaged to 8.94 and 9 respectively. Both the groups had similar NICU admission rates. Beilin and Halpern in 2010 [9] in their review observed that there was no adverse outcome in neonates when the said drugs were used for labour analgesia.

Writer *et al.* [16] observed a difference in the neurologic and adaptive capacity score, favoring ropivacaine, at 24 hours after birth, but not at 2 hours after birth. However, a later study by Halpern SH *et al.* [9] suggested that these scores were unreliable. The incidence of low APGAR scores at 5 minutes is approximately 2% for both drugs. Also the umbilical artery and vein pH are well maintained irrespective of the drug used as observed by Lee BB *et al.* [12] Wang *et al.* [17] observed that the need for neonatal resuscitation is low and similar with both drugs. The incidences of complications were very minimal in both groups.

Conclusion

Obstetric analgesia aims at making childbirth a smooth and painless procedure. Epidural analgesia is one such method that bestows excellent analgesia that is safe for the mother and baby and also does not have any side effects. From this study we conclude

that ropivacaine used at lower concentration (0.125%) offers good pain relief equivalent to that of bupivacaine. Both the drugs give similar results as regards the duration of labour, mode of delivery, neonatal outcome and complications. Motor blockade was not seen with ropivacaine group. From this study it can be concluded that though ropivacaine is less potent than bupivacaine, its safety and efficacy is equivalent to bupivacaine.

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