A Comparative Study on the Effects of 0.1% Bupivacaine and 0.15% Ropivacaine for Epidural Analgesia During Labour

Snehal Shrikant Shenvi[1], Ashutosh Vijay Jaiswal[2]

ABSTRACT

Introduction: Epidural analgesia is the most versatile method of labour analgesia commonly administered. Bupivacaine is the most commonly used drug because of its long duration of action, limited placental transfer. However it is associated with cardiotoxicity and motor blockade at higher concentrations which led to the discovery of Ropivacaine. Additives, like Fentanyl, improve the analgesic potency and reduce the dose of local anesthetics. According to minimum local analgesic concentration (MLAC), Ropivacaine was 40% less potent than Bupivacaine. Hence, this study was conducted to compare equianalgesic concentrations of 0.1% Bupivacaine and 0.15% Ropivacaine for labour analgesia.

Material and Methods: This study was carried out on 80 ASA grade I and II nulliparous patients, between 37 to 42 weeks of gestation with cervical dilatation between 3-6 cm, singleton pregnancy with cephalic presentation requesting epidural labour analgesia. They were randomly divided in the Bupivacaine Group and Ropivacaine Group. Intraoperative and postoperative analgesic parameters were observed.

Results: The onset of analgesia was faster in the Ropivacaine Group than the Bupivacaine Group. Rest all the parameters were comparable. One case of Grade I motor blockade was observed in the Bupivacaine Group but the difference was statistically insignificant. The percentage of instrumental delivery was more in Ropivacaine Group.

Conclusion: Both drugs are safe and provide equivalent analgesia in equianalgesic concentration. But Ropivacaine provides faster onset of epidural analgesia during labour and also leads to increased incidence of instrumental deliveries.

Keywords: Epidural Analgesia in Labour, Bupivacaine, Ropivacaine, Instrumental Deliveries, Motor Blockade

INTRODUCTION

Pain relief in labour has always been surrounded by myths and controversies. Labour pain is not only distressing to the mother but also to the baby, hence labour analgesia is a well-accepted component of comprehensive anaesthetic care. Thus, providing safe and effective analgesia during labour has remained an ongoing challenge. An ideal labour analgesic method demands the safety of mother and foetus, simplicity of administration and maintenance of homeostasis of labour.

Historically, the era of obstetric analgesia began with Ether and Chloroform. Central neuraxial analgesia, developed in 1950, is the most versatile method of labour analgesia and the gold standard for pain control in obstetrics.[1] It is the most flexible, effective, and least depressant option when compared with parenteral and inhalational techniques.

Regional analgesia does not produce drug-induced depression in the mother or foetus. The benefits of epidural analgesia include effective pain relief without appreciable motor block, reduction in maternal catecholamines, and a means to rapidly achieve surgical anesthesia when required.

For many years, Bupivacaine has been used for labour analgesia because of its long duration of action, limited placental transfer and minimal neonatal effects.[2,3] Bupivacaine is an amide local anaesthetic which consists of two stereoisomers, S^- and R^+, and is marketed as a racemic mixture of these isomers.[4] However, Bupivacaine is more cardiotoxic than other local anesthetics and is associated with motor blockade especially at higher concentrations.[5] When separated, the R^+ component was found to contribute to Bupivacaine's unwanted toxicity.[6]

Ropivacaine is a homolog of Mepivacaine and Bupivacaine. It was the first S^- (levo) isomer of a local anesthetic to be marketed. Ropivacaine is less lipid soluble than Bupivacaine; therefore, it may be less potent. Although clinical evidence suggests that the two drugs might be similar in potency[7], minimum local anesthetic concentration (MLAC) studies have found that the analgesic potency of Ropivacaine was 0.60 (0.47 to 0.75) relative to Bupivacaine. This difference is responsible for reduced toxicity and motor block.[8]

An additive, like Fentanyl which is a highly lipid soluble synthetic opioid is added to Ropivacaine and Bupivacaine to provide better analgesia. Opioids act in synergism with local anaesthetics thereby decreasing the requirement of higher concentration of local anaesthetic. Low doses of local anaesthetic and opioid combinations are administered (usually by infusion) to provide a continuous T_{10}-L_1 sensory block during the first stage and S_2-S_4 sensory block during second stage of labour.

In this study, the equianalgesic potencies of epidural Bupivacaine 0.1% and Ropivacaine 0.15% were compared for labour analgesia by continuous infusion technique,

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by assessing the parameters of onset of action, sensory and motor blockade, neonatal outcome by APGAR Score, maternal satisfaction and maternal hemodynamics.

MATERIAL AND METHODS

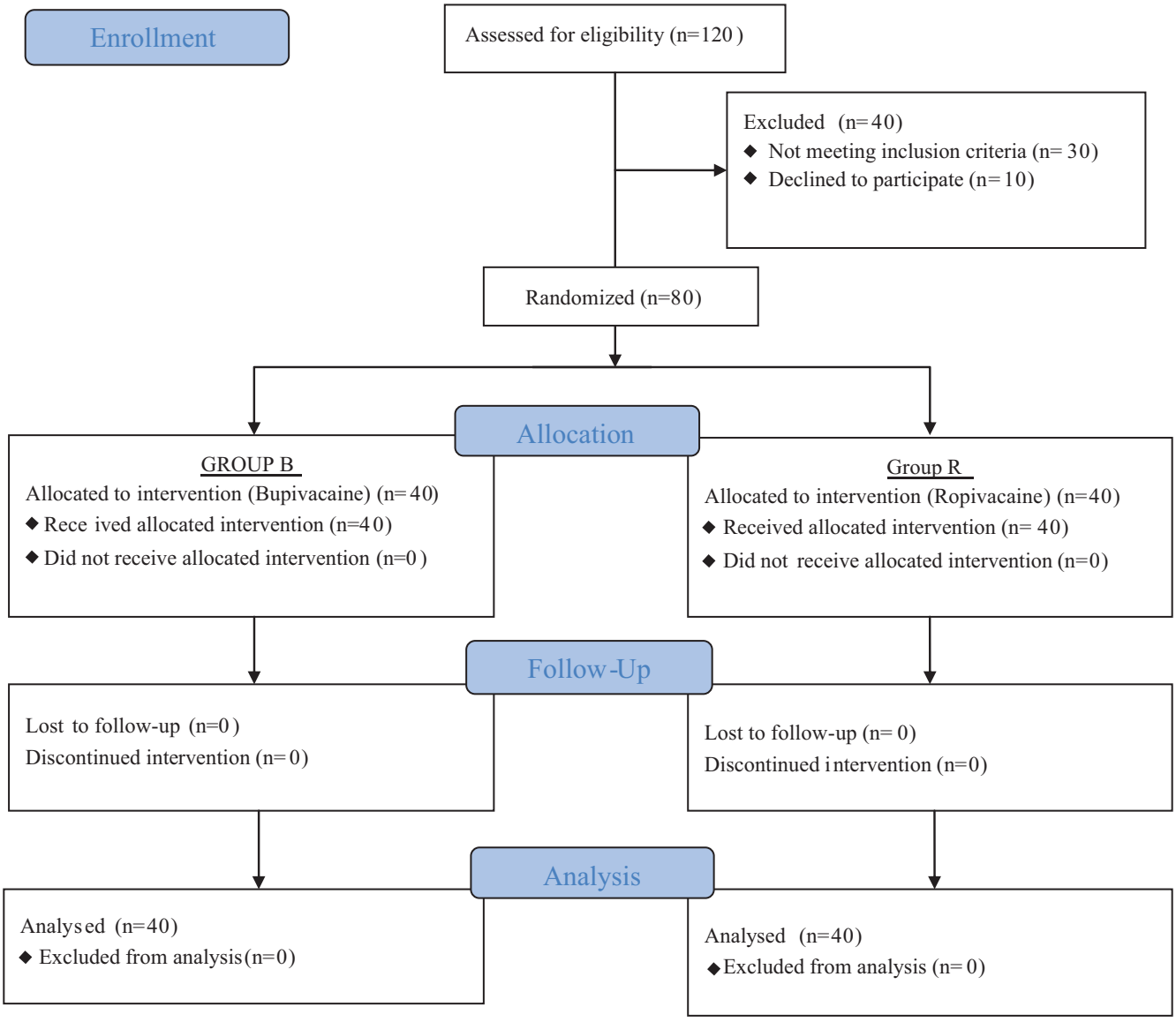
This was a randomized, prospective, single – blind (patients), non-crossover type study conducted in Deenanath Mangeshkar Hospital, after obtaining clearance from the Institutional Ethics Committee. It was carried out on American Society of Anaesthesiologists (ASA) Grade I and II nulliparous patients, between 37 to 42 weeks of gestation, in active labour (with cervical dilatation between 3-6 cm), singleton pregnancy with cephalic presentation requesting epidural labour analgesia. The patients refusing to participate or with any of the maternal factors (severe coagulopathy, infection at the needle site, severe aortic stenosis, haemodynamic instability, allergy to local anaesthetics, severe pregnancy induced hypertension [Blood pressure >160/100 mm Hg] or parturients receiving intravenous opioid or other analgesic within 1 hour of epidural request) or foetal factors (major anomalies, intrauterine growth retardation, foetal distress, or non-vertex presentation) were excluded from the study.

A written informed consent was obtained. A total of 80 parturients were included in this study which were randomly divided into two groups, Group B and Group R, based on computer generated randomization code.

They were demonstrated the use of 10 cm Visual Analogue Scale, for quantification of their pain at the peak of uterine contraction. A full medical, obstetric and anaesthetic history was taken on admission, followed by a detailed general and obstetric examination. Basic investigations were done.

Emergency resuscitation kit was kept ready. Preloading was done with 500 ml Ringer lactate. Premedications (Inj. Ranitidine 50 mg and Inj. Metoclopramide 10 mg IV) were given. Baseline fetal heart rate, maternal pulse, non invasive blood pressure (supine position with left lateral tilt) and SpO_2 were measured. Under all aseptic precautions, epidural space was identified at the level of L_3-L_4 interspace in sitting position using 18 G Tuohy's epidural needle and by loss of resistance to saline technique. A closed end multi-orifice 20

CONSORT 2010 Flow Diagram



	Number of patients	Onset of action(min) (Mean ± SD)	P value	Significance (*P*-value < 0.05)
Group B	40	19.88 ± 3.07	0.006	Significant
Group R	40	17.65 ± 3.85		

Table-1: Comparison of onset of analgesia between Group B and Group R

Bromage grade	Groups	
	Group B	Group R
0	39	40
1	1	0
Total	40	40

Table-2a: Comparison of degree of motor blockade between Group B and Group R Using Modified Bromage Scale

Groups	Median Bromage grade	*P*-value	Significance (*P*-value < 0.05)
Group B	0	0.317	Not significant
Group R	0		

Table-2b: Comparison of degree of motor blockade between Group B and Group R Using Modified Bromage Scale

G epidural catheter was inserted 5 cm into epidural space cephalad and aspirated to test for inadvertent intrathecal or intravascular placement. The catheter was then secured and the parturient was placed in supine position with left uterine displacement. Epidural test dose was not given. Epidural anesthesia was given as

Group B - loading dose of 15 ml of 0.1% Bupivacaine with 2 µgm Fentanyl/ml of 0.1% Bupivacaine followed by continuous epidural infusion of 0.1% Bupivacaine only (using 0.9% normal saline for dilution) at 6-8 ml/hr to be started 30 minutes after loading dose.

Group R - loading dose of 15ml of 0.15% Ropivacaine with 2 µgm Fentanyl/ml of 0.15% Ropivacaine followed by continuous epidural infusion of 0.15% Ropivacaine only (using 0.9% normal saline for dilution) at 6-8 ml/hr to be started 30 minutes after loading dose.

The epidural infusion to maintain analgesia did not contain Fentanyl or any other additive.

The following parameters were assessed:

1. Pain intensity was evaluated during contraction using Visual Analogue Pain Scale [0-10; 0: no pain and 10: worst pain] every 5 minutes for first 30 minutes followed by every 30 minutes thereafter. A reduction in pain score to less than 3 was considered to represent onset of analgesia.
2. Maternal haemodynamics (pulse, blood pressure, SpO_2) was measured every 5min for first 30 minutes followed by every 30 minutes later on. Maternal hypotension (systolic blood pressure <100 mmHg or fall by 20% of baseline values) was treated by IV fluid bolus, left uterine displacement, maternal oxygen supplementation and Inj. Mephentermine.
3. Sensory block was assessed by loss of cold sensation to ice pack in midclavicular line, every 5 minutes for first 30 minutes followed by every 30 minutes later. The peak sensory level achieved during study was noted.
4. Motor blockade was assessed bilaterally using Modified Bromage scale.
5. Breakthrough pain was treated with 8-10 ml bolus of either 0.1% Bupivacaine or 0.15% of Ropivacaine depending upon the group. Patients were excluded from data analysis if they had persistent inadequate analgesia (requiring more than 2 sequential supplemental doses), or delivery within 2 hours of epidural catheter insertion.
6. Labour was managed as per institutional obstetric protocol, and all parturients were given oxytocin post delivery. Any instrumental deliveries like forceps or ventouse were noted.
7. Neonatal welfare was assessed at 1st min, 5th min by Virginia APGAR score, any abnormality detected was noted down.
8. Maternal side effects like nausea, vomiting, pruritus, respiratory depression were assessed.
9. Infusion was stopped after delivery of the baby and the catheter was removed with tip intact.
10. Maternal satisfaction was assessed by interrogating the parturients post delivery day after 24 hours.

STATISTICAL ANALYSIS

Analysis was done using Unpaired t-test (for numeric data), Mann Whitney test and Pearson Chi Square test (for ordinal data), considering statistically significant if *P value< 0.05*.

RESULTS

There was no statistically significant difference between the mean age and height of both the groups. The baseline maternal hemodynamics (pulse rate, systolic blood pressure and diastolic blood pressure) was comparable between the two groups. The initial fall in pulse rate is attributed to the onset of analgesia (faster onset in Group R than Group B, Table 1). The VAS score was comparable throughout the study, indicating good analgesia and better maternal satisfaction with equivalent analgesia in both the groups. The sensory level at T10 was comparable. Grade 1 motor blockade was seen in 1 case in Group B and the difference was statistically insignificant (*P* value of 0.317, Mann Whitney test, Tables 2a and 2b). Though some parturients required rescue top-up (7 in Group B and 6 in Group R), this difference was statistically insignificant (Pearson Chi square test). There was higher percentage of instrumental delivery in Group R, but the difference was statistically insignificant.

The APGAR score at 5 min (*P* value: 0.174, Mann Whitney test), the duration of labour (Group B: 218.35±65.17 min and Group R: 198.75±53.27 min; *P* value: 0.145, Unpaired t test), adverse effects and degree of maternal satisfaction

were comparable with no significant difference between the Groups.

DISCUSSION

Epidural labour analgesia is the most effective method of pain relief during childbirth. An ideal local anaesthetic drug for extradural use in labour should produce effective and controllable sensory block of rapid onset and long duration with minimal motor block. It should also have a high therapeutic index and minimal placental transfer.[9] The search for ideal local anesthetic led to the investigation of newer agents.

Lignocaine is not a popular drug for labour analgesia because of its motor block, shorter duration of action and repeated doses resulting in cumulative toxicity and tachyphylaxis.[10]

Bupivacaine is the most commonly used local anaesthetic drug in epidural analgesia for labour, although this drug provided excellent sensory analgesia, some patients experienced unacceptable motor block especially when higher concentrations (0.25% or 0.5% more) were used.[11,12] Various reports suggest that decrease in muscle power and relaxed pelvic diaphragm which results from concomitant motor block may lead to increased incidence of instrumental delivery and caesarean section.[5,13] Motor block also reduce maternal satisfaction by limiting mobility of parturient.[14]

Motor block from local anesthetic can be minimized either by reducing the concentration of local anesthetic or by choosing a local anesthetic with a high differential sensory: motor block ratio such as Ropivacaine.[15]

Large doses of Bupivacaine are also associated with cardiac and central nervous system toxicity when accidentally injected intravenously.[11] It is more difficult to resuscitate patients from Bupivacaine-induced cardiac arrest compared with other local anaesthetic drugs.

Ropivacaine was released for clinical use in 1996. It has been shown to have an increased therapeutic index (ratio between local anaesthetic drug and toxic effects) in laboratory, animal and human volunteer studies. (40) and greater margin of safety with accidental intravenous injection.[11] It was found to be safer in pregnant sheeps compared to Bupivacaine.[12,16]

Lipophilic opioids, like Fentanyl and Sufentanyl, are frequently been added to local anaesthetic solutions. They reduce local anaesthetic requirements by 19% to 31%.[17] However, they may result in dose dependent pruritus, thus lowest, clinically effective, concentration of lipophilic opioid should be added to avoid excessive pruritus.[18]

Studies using the up-down sequential allocation design to estimate 50% effective dose (ED50) suggest that Ropivacaine is 40% less potent than Bupivacaine for initiating labour analgesia, and that this difference may account for decreased toxicity and motor block when equal drug concentrations are compared. If Ropivacaine is less potent than Bupivacaine, then larger concentration or a larger volume of Ropivacaine is required to produce the same degree of analgesia.[8,19]

This study was done by the technique of continuous epidural infusion of study solution because it allows continuous level of comfort to the parturients rather than waxing and waning that occurs with intermittent epidural top-ups. At the concentrations used, they are equipotent[8,19] producing effective analgesia without excessive side-effects.

In this study, both the Groups were comparable with respect to demographic variables.

Hemodynamic Changes: There was no statistically significant difference in the pulse rate (baseline and fall due to onset of analgesia) and blood pressure. There was no development of bradycardia or hypotension.

This was comparable with the study by Fernandez-Guisasola et al[20] which found no difference with regard to haemodynamic stability in the parturients in both the groups. Thus, both the drugs are safe.

Onset of analgesia: A statistically significant difference was seen between the onset of analgesia in both the groups.

This is in contrast to the studies conducted by Clement et al[21] (Ropivacaine and Bupivacaine with Sufentanyl) and by Dresner et al[22] (Ropivacaine and Bupivacaine with Fentanyl), where no difference was found.

This difference may be attributed due to small sample size of the study and needs to be evaluated using large sample group.

Visual Analogue Score (VAS): The median VAS at the end of second stage was 2 in both the groups. The parturients remained pain free throughout the study and there was no statistical significant difference between the groups. Thus both the groups were comparable with respect to quality of analgesia.

This is in contrast to the studies by Mandell et al.[23] (Ropivacaine and Bupivacaine with Fentanyl: Lower VAS Scores with Ropivacaine) and by Celleno et al.[24] (Ropivacaine and Bupivacaine with Sufentanyl: longer analgesia with Ropivacaine)

SENSORY levels: Majority of the patients in both the groups had sensory level at T_{10} (65% in Group B and 62.5% in Group R). There was no significant difference in the sensory level.

This was comparable with studies by Fernandez-Guisasola et al[20] and Clement et al.[21]

Degree of motor blockade: One parturient in Bupivacaine group had a motor block of grade 1 assessed by Modified Bromage scale. None of the parturient in Ropivacaine group had motor block and Modified Bromage scale remained 0, but this difference was not statistically significant (p=0.317). This maybe because Ropivacaine is more selective for sensory fibers and is less lipid soluble (48), hence it has limited penetration of large myelinated nerve fibers, which convey motor impulse.[25]

This was comparable to the study by Fernandez-Guisasola et al[20] and by Dresner et al[22], where more parturients of Group B developed motor blockade than Group R.

Rescue Top-ups: 7 parturients in Bupivacaine group and 6 in Ropivacaine group required rescue top up, however this difference was statistically insignificant (*P* value: 0.99).

This was comparable to the study by Dresner et al.[22]

Modes of delivery: The percentage of instrumental delivery was higher in Ropivacaine group, though the difference was statistically not significant.
This was similar to the study by Dresner et al[22], but in contrast with the study by Clement et al[21], who found no difference in mode of delivery.

APGAR score: The APGAR score in neonates at 5 minutes in both groups was 9 which was comparable and statistically insignificant.
This was comparable with the studies by Clement et al[21] and Fernandez-Guisasola et al.[20]

Duration of labour: The duration of labour in Bupivacaine group was 218.35 ± 65.17 min and in Ropivacaine group was 198.75 ± 53.27 min, which was comparable and the difference was not statistically significant (p value = 0.145).
This was comparable with the studies by Campbell[26], Beilin et al[27], Dresner et al.[22]
This non-prolongation of labour maybe due to lower concentration of local anaesthetic drugs.

Profile of side effects: The side effects were comparable in both the groups, similar to the studies by Clement et al[21] and by Fernandez-Guisasola.[20]

Maternal satisfaction: There was no statistically significant difference between both the groups, similar to the studies by Clement et al[21] and Dresner et al.[22]

Limitations: This study was limited by the number of OPD attendance. Therefore, the results might not be generalized.

CONCLUSION

From the above study we conclude that, 0.1% Bupivacaine and 0.15% Ropivacaine provide equivalent analgesia in equianalgesic concentration. Both the drugs are safe and comparable in terms of maternal haemodynamics, duration of labour, quality of analgesia, sensory level achieved, neonatal outcome, maternal satisfaction and profile of side effect. Though the incidence of motor blockade and instrumental delivery was higher in Bupivacaine group but the difference was not statistically significant.

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