Original Article

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Epidural infusion of Ropivacaine versus Bupivacaine for labor analgesia - A prospective, randomized, double blind study of obstetric outcome

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Abstract:

Background: Conventional high doses of bupivacaine (0.25%), used for epidural labor analgesia result in increased operative delivery which is undesirable. Lower concentrations of local anesthetics and drugs like ropivacaine with high sensory motor block ratio may cause lesser motor blockade and result in lesser operative delivery. Opioids are added for its synergetic analgesic effect. This is a prospective, randomized, double blind study to assess the obstetric outcome following epidural infusion of ropivacaine (0.1%) and bupivacaine (0.0625%) both with fentanyl (0.001%) and to substantiate if there is any outcome advantage with ropivacaine over bupivacaine. **Method:** 350 ASA I primigravidae with singleton cephalic presentation were randomized to two groups to receive either of the study drugs. Initial bolus of 10ml drug was followed by infusion at 5ml/hour. Five ml top ups were given for break through pain and for perineal analgesia in the second stage of labor. Besides obstetric outcome, (the primary end point of the study) motor block, quality of analgesia, maternal and neonatal safety were considered. Analysis of variables of interest is compared using independent sample t-test (SPSS 22 version). A p-value of <0.05 was considered significant. **Results:** Total of 340 patients (ropivacaine-169 and bupivacaine-171) completed the study. Operative delivery was similar in both the groups [51.48% (ropivacaine) and 46.78% (bupivacaine)]. There was no motor block (as per modified Bromage scale) in any of the parturients. The safety of the mother and neonate was ensured. Subjective score of quality of analgesia was 'excellent to good' in 80% of the parturients. **Conclusion:** We concluded that both ropivacaine and bupivacaine in weak concentration with fentanyl confer adequate analgesia, maternal and fetal safety and that the choice of drug does not influence the mode of delivery.

Key words: Epidural, Ropivacaine, Bupivacaine, Fentanyl, Analgesia labor

Introduction:

Ropivacaine with high sensory motor block ratio was introduced into obstetric analgesia with the proposed advantage of causing less motor block when given epiduraly and therefore less operative deliveries compared to conventional doses of local anesthetics like bupivacaine [1,2]. Writer et al.[3] published a meta-analysis showing less operative deliveries with ropivacaine 0.25% compared to bupivacaine 0.25%. The search for the ideal type and concentration of local anesthetic which provides good analgesia with minimum risk of operative delivery assuring maternal and fetal well-being is continuing. This study was designed to document obstetric outcome and effectiveness of analgesia in primigravidae receiving very low concentrations of ropivacaine and bupivacaine with fentanyl for epidural labor analgesia and to substantiate if there was any outcome advantage with ropivacaine over bupivacaine.

Materials and Methods

Duration of study: Over a period of two years from 2010 to 2012.

This is a prospective, randomized, double blind study to assess the obstetric outcome following epidural infusion of ropivacaine (0.1%) and bupivacaine (0.0625%) both with fentanyl (0.001%).

Inclusion criteria: ASA I physical status, primiparous, laboring women with term cephalic singleton pregnancy.

Exclusion criteria: Patients were excluded if they had pre-eclampsia, gestational diabetes mellitus, infection at the site of injection, coagulopathies, any

spinal deformities, previous spinal surgeries or any medical contraindication to epidural analgesia.

Considering mode of delivery as the primary outcome, based on a pilot study with matched controls, alpha error of 5% and power of study 80%, the number of cases required was 165 in each group. To allow for a drop out of 5%, we increased the sample size to 175 per group.

All parturients were counseled when they were first admitted to the labor ward. If patients requested epidural analgesia, eligibility for recruitment was confirmed before enrolling in the study. With the approval of the Clinical Research Ethics Committee of the institution and written informed consent from patients, 350 Parturients were randomly allocated to either the ropivacaine group (n = 175) or bupivacaine group (n = 175) by drawing of sequentially numbered, opaque sealed envelopes, each containing a code based on a computer-generated random number list. The patient, obstetrician, anesthesiologist and the neonatologist were unaware of group assignment. Study drug was prepared by an anesthesiologist who was not involved in patient management or assessment.

We demonstrated the use of 100mm Visual Analogue Pain Scale (VAPS) for quantification of pain at the peak of uterine contractions (0 mm = no pain and 100 mm = worst pain). Patient's age, height, weight, gestational age of the fetus, cervical dilatation, and the VAPS score at the time of initiation of epidural analgesia were noted. Motor block in the lower extremities was assessed using modified Bromage score (0= no motor block, 1= unable to raise extended leg, able to move knees and foot, 2= unable to raise extended leg or knees, able to move foot, 3= complete motor block of lower limbs). The time of initial drug injection to first painless contraction was recorded as onset of analgesia. ECG, SpO2 (peripheral oxygen saturation) & noninvasive blood pressure (NIBP) were monitored using multichannel monitors (Philips Intellivue MP20) with trend facilities.

Hypotension was defined as systolic blood pressure less than 100 mm Hg or 80% of baseline values and bradycardia as heart rate less than 60/min. Oxygen saturation below 94% in room air was considered abnormal and oxygen was supplemented. Hypotension was managed by rapid infusion of lactated Ringer's solution and, or intravenous boluses of ephedrine 6 mg and bradycardia by intravenous atropine. Ondasetron 4 mg was given intravenously at 8 hourly intervals. Oxytocin was administered if required in titrated doses to augment labor till regular contractions occurred at 2-3 minutes interval. Continuous tococardiography monitoring evaluated uterine contractions and fetal heart rate.

Obstetrical decisions were made according to the obstetric department protocol. The occurrence of late or recurrent variable decelerations were recorded as significant for fetal distress. In the second stage of labor, the mother was encouraged to 'bear down' during contractions. Prolonged second stage was defined as failure to deliver the fetus after actively pushing for 2 hours. Delivery was then assisted by either vacuum extraction or forceps or by caesarean delivery if criteria for instrumental delivery have not been fulfilled. If the decision for caesarean delivery was made, anesthesia was achieved by a bolus of 2% xylocaine with adrenaline 15 ml and titrating with 2 ml increments if found necessary.

Patients were followed up on the day after delivery. Subjective score of patient satisfaction for analgesia was obtained on a four-point scale (1 = excellent, 2 = good, 3 = fair, and 4 = poor). Any complications such as fever, dizziness, headache, back pain, nausea, vomiting, itching, weakness of lower limbs, post-partum hemorrhage and urinary retention were recorded.

Epidural analgesia was initiated when there were regular contractions at least at 5 minute intervals. Patients were preloaded with 500 ml of lactated Ringer's solution. In lateral position, an epidural catheter was inserted at L2-3 or L3-4 inter vertebral space using loss of resistance to air technique and fixed at 2 to 3 cm in the epidural space.

Epidural test dose was omitted for the purpose of the study. After confirming negative aspiration for blood and CSF, analgesia was initiated with either 10 ml bolus of 0.1% ropivacaine or 0.0625% bupivacaine with 50mcg fentanyl. If adequate analgesia was not achieved (VAPS score > 30) with this bolus dose, a subsequent dose of 5 ml of the drug (0.1% ropivacaine or 0.0625% bupivacaine with 50mcg fentanyl) was administered.

In our study design, we used continuous epidural infusion as that is the standard technique practiced in our institution. Either 0.1% ropivacaine or 0.0625% bupivacaine with fentanyl .001% (1 μg/ml) was instituted as an infusion at the rate of 5 ml per hour using a syringe pump (B Braun) after half hour of the initial bolus dose. For break through pain, further boluses of 5 ml of the test drug were given from the allocated syringes. At full cervical dilatation, a bolus of 5 ml of the test drug was given maintaining sitting up position for 5 minutes to achieve perineal analgesia during delivery of the fetus. Parturients were nursed in supine position

maintaining a 15° lateral tilt alternating between the left and right side. The attending obstetrician, who was blinded to the study group, managed the second stage of labor according to the standard labor ward practice, which remained unchanged for the study. Patients were shifted out to the ward from the labor suite after voiding.

ECG, NIBP, pulse rate, oxygen saturation, motor block and VAPS score at the peak of uterine contraction were recorded every 5 minutes till establishment of analgesia and each time a bolus dose was given and thereafter, it was repeated every 30 minutes.

Mode of delivery, duration of stages of labor, duration of analgesia, volume of test drug used per hour, neonatal Apgar scores at 1 minute and 5 minute post-delivery, umbilical venous blood gas values, quality of analgesia and maternal adverse events were noted.

Statistical analysis

SPSS – 22 version was used. Summary of continuous variables are presented as mean ± standard deviation. A p-value of <0.05 was considered as statistically significant in the study. Analysis of variables of interest is compared among the groups using independent sample t-test.

Result

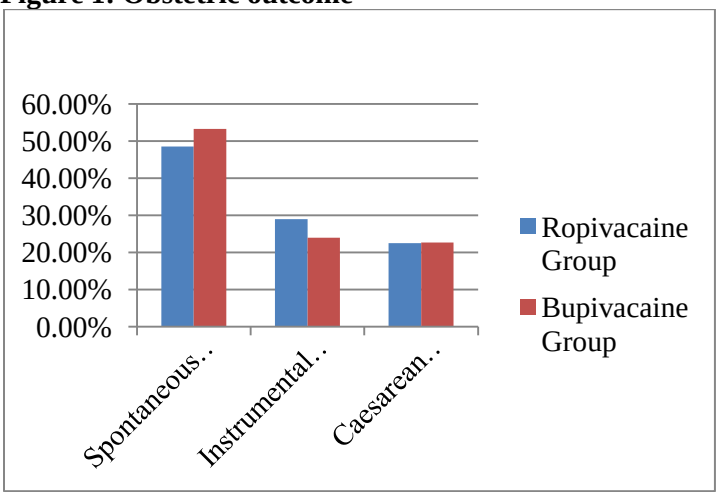
Patient recruitment and data collection occurred over a period of 2 consecutive years. A total of 350 patients participated in the study. 2 from the ropivacaine group and 2 from the bupivacaine group were excluded from the study as epidural analgesia was not fully effective and systemic opioids had to be depended on for analgesia. 4 from the ropivacaine group and 2 from the bupivacaine group had to be taken off from the study as the data was incomplete.

Table: 1 – Patient characteristics (Mean ± SD)

Patient data	Rop. gp. (n = 169)	Bup. gp. (n = 171)	p-value
Age (yrs)	24.44±2.89	24.44±2.41	0.998
Weight (kgs)	62.41±6.96	62.72±7.46	0.695
Height (cm)	157.68±7.38	158.84±7.32	0.148
Gestation (wks)	38.61±1.21	38.40±1.01	0.087
Cervical dilatation at epidural (cm)	5.54±2.96	5.16±2.80	0.235
Baseline VAPS	47.99±11.47	48.30±11.22	0.798

Demographic details and patient observations were similar at the time of initiation of epidural analgesia (Table I)

Figure 1: Obstetric outcome



Mode of delivery

The primary study outcome, mode of delivery was similar between the groups (Fig. 1). The spontaneous vaginal delivery rate was similar among the groups 48.52 % in the ropivacaine group and 53.23% in the bupivacaine group (p=0.387). Caesarean delivery rate [22.49% in ropivacaine group and 22.65% in bupivacaine group (p=0.943)] and Instrumental vaginal delivery rate [28.99% in ropivacaine group and 23.98% in bupivacaine group (p=0.294)] were comparable.

Subgroup analysis was done on patients who eventually delivered by operative delivery (87 in ropivacaine and 80 in bupivacaine group) on factors which could contribute to it like the degree of motor block, duration of analgesia, duration of first stage, volume of local anesthetics consumed per hour and the weight of the baby more than 3.5kgs. These factors were equally distributed among groups. There was no motor block recorded at any time in any of the patients in either group. (Table 2)

Table 2: Factors contributing to operative delivery

Parameters	Rop. gp. (n=87)	Bup. gp. (n=80)	p-value
Duration of labour analgesia (min)	257.54 ±95.91	253.69±97.76	0.799
Duration of first stage (min)	356.17 ±97.71	354±70.44	0.869
Epidural drug ml/h	7.08±1.05	6.94±0.48	0.266
Birth weight > 3.5 kgs (n)	18	18	0.776
Motor block	Nil	Nil	-

Neonatal outcome

Neonatal outcome was satisfactory. Mean Apgar scores at 1 minute and 5 minutes were comparable between groups. All neonates had an Apgar score of 9 or 10 at 5 minutes. Umbilical venous blood gas values were within normal limits (Table 3). 3 neonates in the ropivacaine group and 2 in the bupivacaine group needed observation in the ICU for 24 hours.

Table 3: Neonatal outcome

Neonatal outcome		Rop.gp (n=169)	Bup. gp (n=171)	p-value
Apgar scores	1 min	8.44±0.93	8.50±0.86	0.544
	5 min	9.91±0.29	9.88±0.32	0.506
Umbilical venous blood gas	pH	7.35±0.02	7.35±0.03	0.156
	pO2 (mmHg)	26.09±2.58	26.01±2.15	0.765
	pCO2 (mmHg)	39.21±3.37	39.23±2.39	0.947
	HCO3 (mmol/L)	20.01±1.77	20.24±1.18	0.153
	BE	-5.74±0.89	-5.88±0.97	0.156

Quality of analgesia

The quality of analgesia was good in most of the parturients, as judged by the subjective score (Fig. 2). 80% of the parturients in both the groups considered the analgesia excellent or good and the VAP score recorded was consistently less than 30mm.

Figure 2: Quality of analgesia

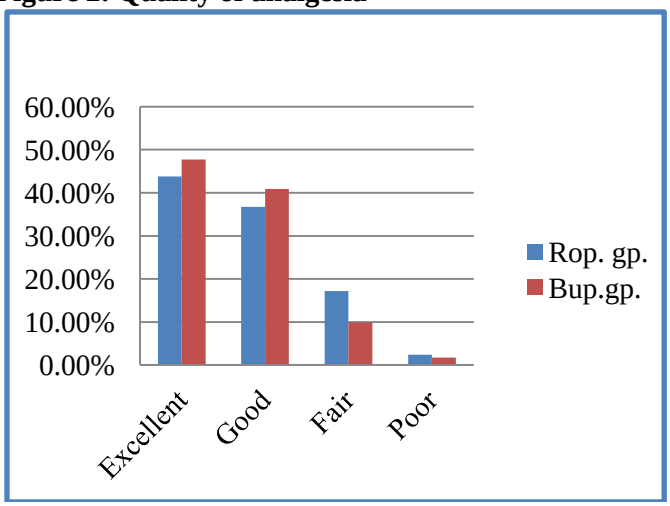


Table: 4 - Maternal adverse effects

Maternal effects	Rop. gp (n=169)	Bup. gp (n=171)	p-value
Nausea/Vomiting	4	4	0.987
Pruritus	29	24	0.427
Numbness	8	4	0.232
Shivering	6	2	0.148
Headache	3	6	0.319
Back pain	12	8	0.343
Fever ≥100^{o}	4	3	0.647

There was no fall in blood pressure, heart rate & oxygen saturation, respiratory depression, postpartum hemorrhage (PPH) or urinary retention in any of the patients in either group. Nausea, vomiting, pruritus, numbness, shivering, headache and back pain which occurred in small numbers were distributed equally between the groups (Table 4).

Discussion

As a result of superior analgesia, maternal-fetal benefits and improved safety, use of neuraxial techniques for labor analgesia has progressively increased over the past three decades. About 18% of primigravidae delivering in our institution utilize the epidural services. Whether epidural analgesia has adverse effects on the progress and outcome of labor resulting in more operative deliveries has been the topic of much debate [4]. One of the most significant factors implicated in increased rates of operative delivery (caesarean and instrumental vaginal delivery) with epidural analgesia is the motor block due to the local anesthetic.

The motor block may hamper maternal mobility, reduce maternal expulsive efforts in the

second stage, and may predispose to inadequate rotation of the fetal presenting part secondary to relaxation of pelvic floor muscles contributing to an increased requirement for operative delivery [5,6]. Hence local anesthetic that confers the least amount of motor block may be the best choice for epidural labor analgesia.

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. COMET trial [7] (using ropivacaine 0.1% with fentanyl 0.002% compared to traditional epidural regimen, bupivacaine 0.25%) demonstrated that the instrumental delivery rate was less when lower concentration of local anesthetic was used. Clinical studies by Writer et al. reported that ropivacaine (0.25%) provided analgesia with less motor block compared to bupivacaine (0.25%) and hence is superior to bupivacaine for labor analgesia [3]. This supports the in vitro data which showed ropivacaine to produce less block of motor A-fibers for a similar degree of block of nociceptive C-fibers [1]. The concentrations chosen for the present study were ropivacaine 0.1% and bupivacaine 0.0625% as the potency ratio of ropivacaine to bupivacaine is thought to be 0.6. [8,9]. The studies on potency ratio used up-down sequential allocation methodology, which is open and non-blinded, and the applicability of the results from these studies to small concentrations of local anesthetics has not been substantiated.

In the past, high concentration of local anesthetic for example 0.25 % of bupivacaine was used for epidural labor analgesia. Synergetic analgesic effect of lipophilic opioids when combined with local anesthetic improves analgesia and hence the concentrations of local anesthetic can be reduced with the possibility of reducing the intensity of motor block, there by achieving better obstetric outcome.

In our study using very low concentration of ropivacaine and bupivacaine, there was no difference in the mode of delivery between groups. Operative delivery rate was near 50% in both the groups. Factors contributing to operative delivery like duration of analgesia, duration of first stage of labor, volume of local anesthetic infused, heavier neonates (birth weight more than 3.5kgs) and motor block were similar between groups and hence the choice of drug is the only variant criteria. We chose to measure lower extremity motor block as a surrogate for perineal muscle blockade. There was no motor block at any point of time in any of our patients in either group as assessed by modified Bromage scale. This suggests that at lower concentrations, the difference in motor block between ropivacaine and bupivacaine is negligible; the concentration or dose of local anesthetic may be more important than the choice of drug.

Majority (more than 80%) of patients in both the groups rated the analgesia as excellent or good and was keen on epidural analgesia for the subsequent deliveries. The very low concentration of local anesthetic provided effective analgesia. Neonatal safety was assured in all patients. Our results are consistent with the results of Halpern et al who found no difference in neonatal outcome with bupivacaine in comparison to ropivacaine [8].

Our study does not support any major obstetric outcome advantage between ropivacaine and bupivacaine at the concentration studied and our findings are consistent with those of Beilin Y et al [10]. There was no motor block in any of the parturients in either group at the low concentrations studied which might have been responsible for the lack of obstetric outcome advantage in the ropivacaine group. Both ropivacaine and bupivacaine in weak concentration conferred adequate analgesia while assuring maternal and fetal safety.

Conclusion

We conclude that both ropivacaine and bupivacaine in weak concentration confer adequate analgesia, maternal and neonatal safety and that the choice of the drug does not influence the mode of delivery. There was no motor block in any of the parturients in either group.

Strength

Large number of patients were studied during two consecutive years. This was a prospective, randomized, double blind study. Concentrations as low as 0.1% ropivacaine and 0.0625% bupivacaine was used for epidural analgesia and found effective.

Limitations

a) An ideal study should be prospective, randomized, double blind placebo controlled. There was difficulty in instituting a placebo controlled study as some form of analgesia is mandatory for all women in labor.

b) Continuous epidural infusions were set at pre-determined rates. With this design, in contrast to Patient Controlled Epidural Analgesia (PCEA), it is likely that some of the parturients received more local anesthetic than needed for pain relief.

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Conflicts of interest: Nil

References

1. Bader AM, Datta S, Flanagan H, Covino BG. Comparison of Bupivacaine– and Ropivacaine-induced conduction blockade in the isolated rabbit vagus nerve. Anesth Analg 1989; 68:724-7.
2. Stienstra R, jonker TA, Bourdrenz P, et al. ropivacaine 0.25% versus bupivacaine 0.25% for continuous epidural analgesia in labour: a double-blind comparison. anesth analg 1995;80:285-9.
3. Writer WD, Stienstra R, Eddleston JM, Gatt SP, Griffin R, Gutsche BB, et al. Neonatal outcomes and mode of delivery after epidural analgesia with ropivacaine and bupivacaine: A prospective meta-analysis. Br J Anaesth. 1998; 81:713–7.
4. Segal BS, Birmbach DJ. Epidurals and cesarean deliveries: a new look at an old problem. Anesth Analg 2000; 90:775-7
5. Gaiser RR, Venkateswaren P, Cheek TG, et al. Comparison of 0.25% Ropivacaine and Bupivacaine for epidural analgesia for labour and vaginal delivery. J Clin Anaesth 1997; 9:564-8.
6. Campbell DC, Zwack RM, Crone LL, Yip RW. Ambulatory labour epidural analgesia: Bupivacaine versus Ropivacaine. Anesth Analg 2000; 90:1384-9.
7. Comparative Obstetric Mobile Epidural Trial (COMET) Study Group UK. Effects of low-dose mobile versus traditional epidural techniques on mode of delivery: a randomised controlled trial. Lancet 2001; 358: 19–23.
8. Capogna G, Celleno D, Fusco P, Lyons G, Columb M. Relative potencies of bupivacaine and ropivacaine for analgesia in labour. Br J Anaesth. 1999; 82:371–373.
9. Polley LS, Columb MO, Naughton NN, Wagner DS, van de Ven CJ. Relative analgesic potencies of ropivacaine and bupivacaine for epidural analgesia in labor: implications for therapeutic indexes. Anesthesiology. 1999; 90:944–950.
10. Beilin Y, Guinn NR, Bernstein HH, Zahn J, Hossain S, Bodian CA. Local anesthetics and mode of delivery: Bupivacaine versus ropivacaine versus levobupivacaine. Anesth Analg 2007;105:756-63