ORIGINAL RESEARCH PAPER

Volume-8 | Issue-8 | August - 2019 | PRINT ISSN No. 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A COMPARATIVE STUDY ON EQUIPOTENT DOSES OF BUPIVACAINE AND ROPIVACAINE WITH FENTANYL ON EPIDURAL LABOUR ANALGESIA

Anaesthesiology

Dr. Azeem Davul Assistant Professor in Anaesthesiology, KMCT Medical College Hospital, Kozhikode, Kerala.

ABSTRACT

Pain in labour is an extremely agonizing experience for most women. Unrelieved labour pain produces many physiological changes which are detrimental to both the mother and the foetus. Various methods have been used to alleviate this pain. It is now well recognized that the only consistently effective method of pain in labour is lumbar epidural analgesia. Using a higher concentration of local anaesthetic agent to produce analgesia can be associated with undesirable side effects such as motor block, haemodynamic disturbances or interference with the progress of labour. Hence, various adjuvants like adrenaline, clonidine and particularly opioids have been used to reduce the amount of local anaesthetic used and yet provide satisfactory analgesia. Two commonly used local anaesthetics for the purpose are bupivacaine and ropivacaine. Here, equipotent doses of bupivacaine and ropivacaine with equal amounts of fentanyl as adjuvant are compared.

KEYWORDS

INTRODUCTION

Labour and delivery though physiological, is very different from other physiological conditions. These are not only associated with changed physiological parameters, but also it is the only physiological state associated with pain. The pain though temporary and resolves spontaneously is one of the most painful condition experienced by a person.

Pathophysiological changes occur in the body in response to pain. In respiratory system pain causes hyperventilation[1], leading to hypocapnia[2] reducing uteroplacental circulation by 25% and also causing respiratory alkalosis and subsequent metabolic acidosis. This shifts oxygen dissociation curve to left and foetal PaO_2 may fall up to 23%[2]. Unrelieved labour pain increases release of catecholamines and cortisol further decreasing uteroplacental flow[3] up to 35 -70%.These all causes foetal acidosis. Catecholamines also increase peripheral resistance and cardiac output. Excessive sympathetic activity results in uncoordinated uterine contraction and causes prolonged labour. Activation of autonomic nervous system also delays gastric emptying and reduces intestinal peristalsis[1]. There is an increase in glucagon, growth hormone, renin and ADH levels while testosterone and insulin decreases.

Epidural analgesia has been gold standard for labour pain for decades. Epidural analgesia effectively tackles all the fore mentioned adverse effects of labour pain, offers excellent analgesia and while causing least side effects. Still epidural at higher doses produce unwanted motor weakness confining the activity of the person and even producing foetal depression. Attempts were taken to reduce the dose of local anaesthetic while offering good analgesia using various adjuvants. Two commonly used local anaesthetics for the purpose are bupivacaine and ropivacaine. Several authors attempted to use and compare low doses of these drugs to find the better. But considering the fact both drugs defer in potency, attempts to compare similar strength of the drugs are not rational. Here we tried to compare equipotent doses of bupivacaine and ropivacaine at low concentrations.

The current study was designed to compare the analgesic efficacy and degree of motor block produced by epidurally given 0.0625% bupivacaine with 1 mcg/ml fentanyl and 0.1% ropivacaine with 1 mcg/ml fentanyl, following bolus doses of 0.125% bupivacaine or 0.2% ropivacaine with 25 mcg fentanyl, respectively.

METHODOLOGY

This randomized prospective clinical study was conducted in Department of Anesthesiology in association with Department of Obstetrics and Gynecology at Government Medical College, Kozhikode from October 2011 to March 2013. Clearance was obtained from hospital ethics committee for the study, written informed consent was obtained from all the patients.

The exclusion Criteria were as follows: History of allergy to local anaesthetics, contraindications to central neuraxial blockade, patients' refusal, parturients with multiple pregnancies, hypertensive disorders of pregnancy, severe anemia, cephalopelvic disproportion, previous LSCS , history of ante partum hemorrhage, history of CVS/RS disease, history of bleeding disorders, diabetes mellitus, history of psychiatric/neurologic disease.

60 parturients with ASA II in established labour with cervical dilatation 3 to 4 cm were randomly selected. A detailed history, complete physical examination and routine investigations for complete blood count and screening were done for all patients. IV line was secured with 18G cannula. Patients were divided into 2 groups of 30 each. IV line was secured with 18 G cannula; patient was preloaded with 500ml normal saline. Pulse, NIBP, SPO2, respiratory rate were recorded. Foetal heart rate is also documented. The patient was positioned in a left lateral position with the help of an assistant. Back of the patient was prepared with 5% povidine iodine solution, spirit and area was draped. L3-L4 interspace was identified; skin and deeper tissues were infiltrated with 2ml of 2% lignocaine, 18G Tuohy needle was introduced using loss of resistance technique and 18 G epidural catheter was threaded into epidural space and fixed with 4 cm length of the catheter in the epidural space.

Group B was given 8 ml 0.125% bupivacaine and Group R 8 ml 0.2% ropivacaine with 25 mcg fentanyl in 2 divided doses of 4 ml each at 10 minute interval. Adrenaline was not used as test dose. Cohen et al[4] showed addition of lignocaine-epinephrine test doses increase motor weakness in the parturient receiving 0.125% bupivacaine epidural bolus to degrees where person was not able to walk for more than 1 hour. It is suggested in low dose regimens a test dose is not required.

Patient is monitored for hemodynamic changes, sensory block, motor block and subjective symptoms of intravenous local anaesthetic administration like circumoral numbness. Foetal heart rate is rechecked. After ascertaining epidural catheter placement, patient is started on maintenance solution of the corresponding group; 0.0625% bupivacaine for Group B and 0.1% ropivacaine for Group R, with 1 mcg/ml fentanyl at 10 ml/hr.

Mother's vital parameters, progress of labour, efficacy of analgesia and foetal welfare were watched in coordination with attending obstetrician. Pulse, NIBP, SPO2, respiratory rate were recorded every 5 min for first 30 minutes and then every 10 minutes thereafter. If bradycardia were to occur at any time (<60 beats/min) Inj. glycopyrolate 0.2mg was given. If hypotension occurred, i.e. systolic BP less than 100 mm Hg, it was treated appropriately with IV normal saline and inj. Ephedrine 6 mg IV. If pruritis occurred it was treated with chlorpheniramine maleate, 20 mg IV.

If the upper end of sensory block is less than T10 at 30 minutes after the bolus dose administration or in case of unilateral or segmental blockade, the patient is excluded from the study and the epidural catheter is repositioned. Patients who undergo unforeseen complications such as bloody tap or dural puncture during institution of block are treated as necessary and are also excluded. Epidural catheter is removed when the patient is shifted from labour room.

Assessment of analgesic efficacy: Verbal numeric rating scale of 0 to 10 was used. Patient is familiarized with VNS before procedure. Score ≤3 is considered acceptable. Whenever patient complains of pain score is >3, 5 ml of the maintenance solution is administered. Up to 3 rescue doses are given 30 minutes at 10 minutes interval before the patient is excluded from the study.

Assessment of motor block: Motor blockade was assessed by Modified Bromage scale[5]. Grades 0,1,2,3 and 4 were awarded to responses complete motor block, able to move feet only, able to move knees, detectable weakness in hip flexion and no detectable weakness in hip flexion respectively.

Neonatal outcome was assessed using APGAR score: Assessed at 1 and 5 minutes. Score less than 7 indicate a depressed neonate. Foetal heart rate is monitored; a foetal heart rate of < 110/minute is counted as an episode of foetal bradycardia.

Duration of labour, i.e. the time from start of labour pain till delivery and epidural- delivery time also noted .The patients were carefully monitored for any untoward effects like inadequate block, hypotension, bradycardia, respiratory distress, nausea, vomiting, restlessness, pruritis, shivering, anaphylactic reaction. Bladder was evacuated intermittently by temporary catheterization by the obstetrician. Onset of spontaneous micturition was noted as the time need for micturition after the delivery. Patient satisfaction was assessed under the headings satisfied, benefitted, and no benefit. Satisfied patient is the one who does not want any more improvement. A benefitted patient while agreeing that there was some good with the procedure but agrees there is room for improvement.

In the present study, results are given as mean ± standard deviation and range values for continuous data. Students 't' test was used to compare the two groups, categorical data are expressed as number and percentages and difference between the groups was compared by chi-square test. A p value of 0.05 or less was set for statistical significance.

RESULTS

Demographic data for the 60 patients who participated in the study are shown in Table 1. Mean age for Group B was 23.2 +/- 3 and for Group R was 22.8 +/- 3.3.With a P value of 0.65 the groups showed no statistically significant difference in age distribution. Majority of the parturients belonged to weight class 60-69 kg. The P value was 0.12, and the groups are comparable.

TABLE 1 : PATIENT DEMOGRAPHICS, LABOUR DURATION

Variable	GROUP B				GROUP R			
	Min	Max	Mean	SD	Min	Max	Mean	SD
Age(yrs)	18	30	23.2	3	19	30	22.8	3.3
Weight(Kg)	51	74	62	5.9	53	70	59.9	4.4
Duration of labour(minutes)	320	720	476	120.8	270	650	445	88.7
Epidural- delivery time(minutes)	200	450	311	71.5	150	450	298.3	77.3

There were 19(63.3%) primigravida and 11(36.7%) second gravida in group B and 20(66.7%) primigravida and 10(33.3%) second gravida in group R. The P value based on Chi-square test is 0.79.The two groups were comparable with respect to parity.

76.7% in Group B and 60% in Group R had onset of analgesia in 10 to 15 minutes, with Pearson Chi-square P value is 0.29, hence groups were comparable. Mean duration of labour was 476+/- 120.8 and 445+/-88.7 minutes respectively. With P value of 0.26 the groups are comparable. Mean epidural-delivery time for Group B and Group R were 311+/-71.5 and 298.3+/-77.3 minutes respectively with p value 0.5 (Table 1).

Verbal numerical scores before procedure were comparable, but during procedure ropivacaine group showed a better pain relief with p value being 0.02. 70% parturients in Group B needed at least one rescue dose but in Group R only 30% needed rescue doses and a P value of 0.03 was significant. Amount of ropivacaine is adjusted to the equipotent dose of bupivacaine using the potency ratio of 0.6. (Table 2) and with P value being 0.03 Group B had a higher dose requirement.

TABLE 2 :AMOUNT OF LOCAL ANAESTHETIC USED

	Group B	Group R
Amount of drug in mg	42	37.7
SD	7	7.4

With a p value of 0.07, modified Bromage score was comparable among the groups. One patient in Group B had partial motor weakness with Bromage score 3 but rest showed afull score of 4.

None of the patients had any side effects and all the deliveries were normal expect for two vacuum assistant ones in Group R with full APGAR scores.

DISCUSSION

Labour is one of the most agonizing events experienced by majority of women.Several different drug combinations have been described for epidural analgesia in labour. Synergism has been demonstrated for a local anaesthetic opioid combination, the addition of local anaesthetic significantly improves analgesia with faster time of onset, greater efficacy and longer duration of analgesia[6].

Bupivacaine and ropivacaine are two common local anaesthetics used for epidural labour analgesia. These drugs are time tested in different concentrations and are found to be extremely safe whilst providing good analgesia. Eddleston et al[7] in 1996 has proven using even 0.25% ropivacaine and 0.25% bupivacaine for continuous epidural does not cause foetal depression. But comparing equal concentrations of the drugs is not rational as they have different potencies. So we attempted to compare equipotent doses of each drug. Equipotent dose is calculated by up-down sequential allocation method by Polley et al[8].

Epidural analgesia was given to 60 parturients admitted in Government medical college, Kozhikode after randomly dividing into 2 groups of 30 each. Each group received 8 ml bolus; 0.125% bupivacaine or 0.2% ropivacaine with 25 mcg fentanyl, in two 4ml increments. For maintenance the patients received 0.0625% bupivacaine or 0.1% ropivacaine respectively at 10 ml/hr. with added fentanyl 1 mcg/ml. The dosing is justified by Bee B. Lee[9] study where the authors compared ropivacaine 0.1% with fentanyl 0.0002% and bupivacaine 0.1% with fentanyl 0.0002% as epidural infusion and Jaime Ferna´ndez-Guisasola et al[5], 2001 who compared 0.0625% bupivacaine with 2mcg/ml fentanyl and 0.1%ropivacaine with 2mcg/ml fentanyl. G.Lyons et al[10] compared varying concentrations of fentanyl with bupivacaine. They found higher concentrations of fentanyl (>4 mcg/ml) resulted in itching. Though lower concentrations showed a linear increase in requirement of local anaesthetic, adding of 1 mcg/ml of fentanyl was found to be satisfactory.

Primi and second gravida of uneventful antenatal period were selected. Choice of mixing primi and second gravida was based on the theory that parity alone does not appear to be an independent influence on outcome as it is common for obstetric units to use same epidural regimens for nullipara and multipara. Capogna G et al[11] have suggested acceptability of same epidural regimens for nullipara and multipara.

Duration of labour as measured from onset of labour pain to the delivery of placenta was 476 minutes for bupivacaine and 445 minutes for ropivacaine, which is statistically comparable. It was also similar to the findings of Jaime Ferna´ndez-Guisasola et al[5], where the bupivacaine had average duration of 457 minutes and ropivacaine 412 minutes. This also shows neuraxial administration of opioids doesn't prolong labour and neither does a combination of local anaesthetic and opioid.

The verbal pain score was similar in the two groups at the start of the procedure. Before epidural injection, the mean scores were 7.06 for bupivacaine and 7.13 for ropivacaine (P value 0.75). Jaime Ferna´ndez-Guisasola et al[5], had similar observations; 7.9 for bupivacaine and 8.2 for ropivacaine (P value 0.4).

Analgesic efficacy assessed by verbal numeric score during procedure showed ropivacaine as better; verbal numeric score for bupivacaine was 2 +/- 0.45 and ropivacaine was 1.7+/- 0.6 and P value is 0.02. This value is the highest pain level patient reported after successful initiation as acceptable, i.e. ≤ 3. Higher pain levels are controlled with rescue doses and reassessed till they are acceptable. Also bupivacaine

group needed more rescue doses (0.87 +/- 0.7) than ropivacaine (0.43 +/- 0.8) with a P value of 0.03. Most of the rescue doses were needed in the first one hour into the procedure. Finally average amount of bupivacaine needed was 42 mg and ropivacaine was 62.8 mg which is equivalent to 37.7 mg of bupivacaine, showing bupivacaine group did require more amount of drug.(P value is 0.03). This is similar to observations by M. Dresner et al[12] in 2000, authors found 0.2% ropivacaine with 2mcg/ml fentanyl required lesser initial and top-ups compared to 0.1% bupivacaine with 2mcg/ml fentanyl and better first stage analgesia. This may be due to longer duration of action for ropivacaine. Though the authors found both groups comparable, the observed difference from our study may be due to the confounding effects of double dose of fentanyl used.

There was no incidence of significant motor blockade. Studies of Ferna´ndez-Guisasola et al[5], Bee B. Lee[9], showed no incidence of motor blocks. Bleyaert et al[13] found even 0.125% bupivacaine caused no discernable motor blockade. But in our study there was a single incidence of motor blockade in bupivacaine group, where the patient was only partial able to flex at hip. In focused review by Yaakov Beilin[14], 2010, the authors states ―Ropivacaine seems to cause less motor block, particularly in long labors, but this finding may be attributable to differences in drug potency rather than intrinsic differences between drugs.

Wong CA et al[15] showed that neuraxial analgesia in labour does not increase the rate of cesarean delivery but provides better analgesia and decreases the duration of labour than systemic analgesia. In our study there was only 2 incidences of vacuum assisted deliveries, both in ropivacaine group, but the results were concurrent with institutional norm. There was no incidence of caesarean section throughout the study.
Neonatal outcome in either group were comparable. All the neonates had an APGAR score of 9 at 1 minute and 5 minutes, except one in bupivacaine group with an APAGR of 6 at 1 minute which was readily corrected with stimulation and suction. No neonate needed opioid reversal. The study proves low dose fentanyl is extremely safe for epidural analgesia. Breast feeding was initiated within half hour.

None of the cases showed any of the side effects such as shivering, nausea, vomiting, itching, urinary retention, hypotension or bradycardia. This is safety is attributed to low concentrations of local anaesthetics and opioids. Bee B. Lee[9] compared ropivacaine 0.1% with fentanyl 0.0002% and bupivacaine 0.1% with fentanyl 0.0002% there were no differences in other outcomes including analgesia, sensory or motor block, drug consumption, and maternal satisfaction. From these observations it's safe to say further lowering concentrations should offer even better side effect profile.

Patient satisfaction was excellent and similar in both groups and all the parturient not undergoing post-partum sterilization expressed an interest in future epidural analgesia. The results were consistent with finding of Jaime Ferna´ndez-Guisasola[5].

Cost of the Local Anesthetics

Ropivacaine is more costly than bupivacaine. Ropivacaine is approximately 10 times more expensive on a milligram basis than bupivacaine in US. D'Angelo[16] estimated that the cost to switch from bupivacaine to ropivacaine for all deliveries in the United States would be $15,000,000/year.

Future

Cynthia A. Wong et al[17] observed Programmed Intermittent Epidural Bolus (PIEB) ,i.e. administration of boluses at fixed intervals in addition to Patient Controlled Analgesia (PCA) was superior to Continuous Epidural Infusions (CEI).This technique not only improves patient satisfaction but also decreases mean anaesthetic volume. Rapid drug delivery during PIEB is attributed to the better spread of the drug and action. The authors showed total amount of drug used can reduced by the technique.

CONCLUSION

Ropivacaine seems to be the marginally better than an equipotent dose of bupivacaine with a better pain relief at lower dose. Still comparable safety profile and patient satisfaction does raise a question whether to use a costly drug to achieve almost similar results.

Financial support and sponsorship

Nil

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Holdcroft A. Regional Anaesthetic Techniques. Chapter – 15. In: Principles and practice of obstetric anaesthesia and analgesia, Black Well Science Publishers. 2000.;243-59.
2. Falconer AD, Powles AB. Plasma noradrenaline levels during labour –influence of elective lumbar epidural blockade. Anaesthesiology 1982;37:16-18.
3. Maltaujm, Eiclsen OV, Stokke KT. Effect of stress during labour on the concentrations of cortisol and estriol in maternal plasma. Am J. Obstet Gynecol 1979;134:681.
4. Cohen et al. ―Walkingl Epidural Anesthesia: Are Test Doses Necessary?. Anaesthesiology 2000 –volume 92 - pp. 5A-5A,299-634
5. Jaime Ferna´ndez-Guisasola, Marı´a L. Serrano, Bele´n Cobo, Lourdes Mun˜oz, et al. A Comparison of 0.0625% Bupivacaine with Fentanyl and 0.1% Ropivacaine with Fentanyl for Continuous Epidural Labor Analgesia . Anesth Analg 2001;92:1261–5
6. Lee BB, Kee WDN, Hung VYS , Wong ELY. Combined spinal epidural analgesia in labour: Comparison of two doses of intrathecal bupivacaine and fentanyl. Br. J. Anaesthesia 1999;83(6):868-74. 7. Breen TW. Optimal labour analgesia. CJA 1996;43(4):327-32.
7. Eddleston JM, Holland JJ, Griffin RP, Corbett A, Horsman EL, Reynolds F. A double-blind comparison of 0.25% ropivacaine and 0.25% bupivacaine for extradural analgesia in labour. Br. J. Anaesth. 1996;76:66-71.
8. Polley LS, Columb MO, Naughton NN, et al. Relative analgesic potencies of ropivacaine and bupivacaine for epidural analgesia in labour: implications for therapeutic indexes. Anesthesiology 1999;90:944 –50..
9. Bee B. Lee, Warwick D. Ngan Kee, Floria F. Ng , Tze K. Lau, , and Eliza L. Y. Wong; Epidural Infusions of Ropivacaine and Bupivacaine for Labor Analgesia: Anesth Analg 2004;98:1145–52
10. G Lyons, M Columb, L Hawthorne, and M Dresner. Extradural pain relief in labour: bupivacaine sparing by extradural fentanyl is dose dependent. Br. J. Anaesth.,1997 : 78(5): 493-7
11. G Capogna, D Celleno, G Lyons,M Columb et al. Minimum local analgesic concentration of extradural bupivacaine increases with progression of labour. Br. Journal 1998; 80(1): 11 -13
12. M.Dresner, J.Freeman,C. Calow,A Quinn et al. Ropivacaine 0.2% versus bupivacaine 0.1% with fentanyl: a double blind comparison for analgesia during labour , Br. J. Anaesth. 2000;85: 826-9
13. Bleyaert A, Soetens M, Vaes L, Van Steenberge AL, Van der Donck A.Anesthesiology 1979;51:435-8.
14. Beilin, Yaakov MD; Halpern, Stephen MD. Ropivacaine Versus Bupivacaine for Epidural Labor Analgesia. Anesth Analg 2010;111:482–7
15. Wong CA. Advances in labor analgesia. Int J Womens Health. 2010;1:139–54
16. D'Angelo R. Are the new local anesthetics worth their cost? Acta Anaesthesiologica Scandinavica 2000;44:639–41
17. Cynthia A. Wong, John T. Ratliff, John T. Sullivan, Barbara M. Scavone et al. A Randomized Comparison of Programmed Intermittent Epidural Bolus with Continuous Epidural Infusion for Labor Analgesia. Anesth Analg 2006;102:904 –9