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0.5% ropivacaine with fentanyl in combined spinal epidural for labor analgesia: Comparison with 0.25% ropivacaine with fentanyl and 0.25% bupivacaine with fentanyl

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Abstract

Background: The pains of labor result in a maternal stress response, which is neither beneficial for the fetus nor the mother [1]. Hence, maternal pain relief not only benefits the parturient, but her neonate also [2]. Studies have also shown that the newer, low-dose regimes do not have a statistically significant impact on the duration of labor and breast feeding and also that these reduce the instrumental delivery rates thus improving maternal and foetal safety [3]. Central neuraxial analgesia is the most versatile method of labour analgesia and the gold standard technique for pain control in obstetrics that is currently available [5]. The availability of newer local anaesthetics like ropivacaine and levo-bupivacaine have contributed towards the increased maternal safety in terms of being less cardiotoxic after an inadvertent IV injection.

Materials and method: This Prospective, randomised comparative study was conducted in 60 ASA physical status I or II women with term pregnancy, single, vertex presentation in active labour (cervical dilatation 3-4 cm) requesting labour analgesia.

Result: VAS pain scores were significantly lower in group 3 than in group I and II at 5 min, 60 min and 90 min of the study period, $P < 0.001$. Parturient and anesthesiologists graded acceptance rate as either excellent or "good" in all groups. Neonatal outcome was favorable in both the groups (APGAR scores >7 at 1 and 5 min) with no side-effect.

Conclusion: The results from our study support that intra-thecal 5mg ropivacaine with fentanyl and ropivacaine epidural top-up is a suitable choice for labour analgesia. The addition of opiods is always necessary to achieve good analgesia, high maternal satisfaction and acceptable motor blockade.

Keywords: labor analgesia, parturient, ropivacaine, VAS score, motor blockade, sensory level.

1. Introduction

Advances in the field of labour analgesia have tread a long journey from the days of ether and chloroform in 1847 to the present day practice of comprehensive programme of labor pain management using evidence-based medicine. The pains of labor result in a maternal stress response, which is neither beneficial for the fetus nor the mother [1]. Evidence is suggestive that labor disorders including maternal hypertension, dystocia, meconium staining, and fetal distress are stress related. Hence, maternal pain relief not only benefits the parturient, but her neonate also [2]. Newer advances include introduction of newer techniques like combined spinal epidurals(CSE), low-dose epidurals facilitating ambulation, pharmacological advances like introduction of fentanyl, patient-controlled epidural analgesia pumps (PCEA), newer local anaesthetics ropivacaine, levobupivacaine., all have revolutionized the practice of pain management in labouring parturient. Recent randomized controlled trials and Cochrane studies have concluded that the association of epidurals with increased caesarean section and long-term backache remains only a myth [4]. Studies have also shown that the newer, low-dose regimes do not have a statistically significant impact on the duration of labour and breast feeding and also that these reduce the instrumental delivery rates thus improving maternal and foetal safety [3]. Modern neuraxial labour analgesia reflects a shift in obstetrical anaesthesia, thinking away from a simple focus on pain relief towards a focus on the overall quality of analgesia. Increasing knowledge of the physiology and pharmacotherapy of pain and the development of obstetric anaesthesia as a subspecialty has improved the training in obstetric anaesthesia, leading to an overall improvement in the quality of labour pain relief [4]. With the evolution of sequential "needle-through-needle" combined spinal epidural technique, it can be safely used to provide labour analgesia. It combines the rapid, reliable onset of profound analgesia resulting from spinal injection with the flexibility and longer duration of epidural techniques [4]. The availability of newer local anaesthetics like ropivacaine and levo-bupivacaine have contributed towards the increased maternal safety in terms of being less cardiotoxic after an inadvertent intravenous injection. Fentanyl is a highly lipid-soluble synthetic opioid with analgesic potency 100-times that of morphine and 800-times that of pethidine [5]. Its rapid onset of action with short duration of action and with no major metabolites makes it superior for labour analgesia. A review of the complications has concluded that CSEA is as safe a technique as a conventional epidural technique and is associated with greater patient satisfaction. Central neuraxial analgesia is the most versatile method of labour analgesia and the gold standard technique for pain control in obstetrics that is currently available [5]. Reducing the dose of local anesthetics significantly reduces the incidence and severity of maternal motor neural blockade [6]. Increased mobility during epidural analgesia has been associated with greater maternal satisfaction. The objective of this study was to compare different concentration of ropivacine and bupivacaine, with fentanyl in combined spinal epidural labor analgesia, regarding

their sensory and motor block characteristics as well as the feto-maternal outcomes.

2. Materials and Methods

After obtaining institutional ethical committee approval, this Prospective, randomised comparative study was conducted in 60 ASA physical status I or II women with term pregnancy, single, vertex presentation in active labour (cervical dilatation 3-4 cm) requesting labour analgesia. Exclusion criteria included weight more than 120 kg, allergy to local anesthetics, cervical dilatation more than 5cm, ASA III or IV patients, received parental opiods (e.g i.m pethidine) within 2 hours. The parturient were randomly allocated into 3 groups.

Group I – 20 patients. 5mg ropivacaine (1ml) with 25mcg fentanyl (0.5 ml) given intra-thecal and for each top-up 8-12 mg ropivacaine (10-12 ml) given through epidural catheter.

Group II – 20 patients. 2.5mg ropivacaine (1ml) with 25mcg fentanyl (0.5 ml) given intra-thecal and for each top-up 8-12 mg ropivacaine (10-12 ml) given through epidural catheter.

Group III – 20 patients. 2.5mg bupivacaine (1ml) with 25 mcg fentanyl (0.5 ml) given intra-thecal and for each top-up 8-12 mg bupivacaine (10 -12 ml) given through epidural catheter.

2.1 Equipments Required

- Multimonitor for recording mothers vital parameter
- External Cardio-tocogram.

Each parturient received an initial infusion of intra-venous 500 mL of Ringer's lactate solution for hydration. Baseline pain scores on a 0-10 visual analogue scale (VAS, 0-no pain and 10-severe pain) were obtained before CSE. Systolic blood pressure (SBP), which was measured non-invasively with the parturient supine and with left uterine displacement was also recorded pre-block. The fetal heart rate was monitored via external cardio-tocogram throughout the study period and obstetrician consulted when necessary.

For CSE administration, patients either in the sitting or right lateral position, with 25G quincke spinal needle, drugs allotted to each group is injected into sub-arachnoid space at L2 – L3 level and with 18 G touhy epidural needle, multi-port catheter inserted and threaded caudally 4-5cm in L3 – L4 epidural space and a initial bolus dose of 10 ml of distilled water injected in the epidural catheter to compress the subarachnoid space so that injecting small volume of local anesthetics intra-thecally, more sensory level could be blocked without much hemodynamic changes. Patient placed supine with a 15° left tilt. The following data were collected at 5, 10 minutes and thereafter each 15 minute till study is completed.

1 Blood pressure and pulse rate of the mother.
2 Pain scores using the VAS.
3 Highest dermatomal sensory block (loss of sensation to pin prick).
4 The maximum motor block of either lower limb based on the modified Bromage scale (0 – no impairment, 1- unable to raise extended legs but able to move knees and ankles, 2 - unable to raise extended legs as well as flex knees, able to move feet, 3- not able to flex ankle, feet, or knees).
5 Fetal heart rate.

The duration of analgesia was documented from the beginning of intra-thecal injection to the time of regression of sensory level to T 10 level. A reduction of SBP - 20% from the baseline was promptly treated with 6 mg boluses of IV ephedrine. Nausea and vomiting were treated with metaclopramide. Fetal heart rate (from a continuous external cardiotocogram) was assessed by the attending obstetrician. New changes suggestive of an abnormal (nonreassuring) fetal heart pattern within 0.5 h after CSE resulted in appropriate obstetric intervention. These included left uterine displacement, supplemental oxygen via face mask, and tocolytic drugs if uterine hyperactivity was suspected. The pain score using the VAS, cervical dilation, and use of oxytocin were also recorded. Quality of maternal expulsive efforts was assessed by an obstetrician as Grade 0 – Failure, 1 –Incomplete, 2 – Good, 3 – Excellent. Quality of analgesia was assessed by an anesthesiologist as Grade 0 – Failure, 1–Incomplete, 2 – Good, 3- Excellent, 4 – Not possible to evaluate (NPE) if delivered by caesarean section.

The mode of delivery and overall satisfaction with neuraxial analgesia were assessed and documented within 24 h of delivery on a 0–10 scale (0 -very dissatisfied and 10 – extremely satisfied).

Statistical Analysis for categorical variables (presented as number [proportions]), the proportions of variances in the two groups were compared using the Chi squared test with calculation of the $\chi 2$ statistic value and *P* value. For quantitative variables (data presented as mean ± standard deviation [SD] measurements), the groups were compared using Student's t-test for independent samples.

3. Results

Demographic data, obstetric data, and injection delivery interval were comparable between the groups, $P > 0.05$ (Table: 2). Before initiation of analgesia mean VAS score was 9.33 ± 0.38 in group 1 and 9.42 ± 0.23 in group II and 9.60 +_ 0.63 in group III ($P > 0.05$). All the groups produced effective analgesia (defined by VAS <3) after intra thecal injection and 95 % of parturient, VAS <3 maintained till the delivery of the baby. VAS scores were significantly lower in group 3 than in group I and II at 5 min, 60 min and 90 min of the study period, $P < 0.001$. (Table 1)

Group III had the most frequent incidence of lower limb motor block (bromage score 1 or 2, 8 of 20 subjects had a score of 1). 2 of 20 subjects in group I had a Bromage score of 1 versus 1 of 20 in group II, respectively, $P > 0.05$). All the parturient in the groups attained a sensory blockade level of T6 – T 8 after intra-thecal injection and none of the patients in both the groups showed a sensory block higher than T6. Duration of analgesia of initial bolus dose, defined as the time of onset of analgesia upto T10 until sensory blockade level regress to T 10. 8 (40%) subjects in group 2 needed 3 epidural top ups but all the subjects in group 1 and III delivered within 1 or 2 epidural top ups. Mean duration of intra-thecal injection are 63 minutes for group I, 49 minutes in group II and 73 minutes for group III.

Spontaneous vaginal delivery occurred in 19 (95%) parturient in group I ,18 parturient (90%) in group II and 15 parturient 75% in group III . 2 parturient in group III and none in group I and group II had caesarean delivery. 1 parturient in group I, 3 parturient in group III and none in group II had forceps delivery. (Fig 4). Obstetrician's graded maternal expulsive efforts as excellent in group I and group II parturient (P> 0.05). 2 subject were graded as incomplete in group III. Parturient and anesthesiologist graded acceptance rate as either excellent or "good" in all groups (Table 3). However, significantly higher number of cases (97.5%) reported acceptance rate as

excellent in group I and II, by both parturient and anaesthesiologist (P< 0.001). Neonatal outcome was favourable in both the groups (Apgar scores >7 at 1 and 5 min) with no side-effect.

Table 1: Dose and duration characteristics

parameters	Group I	Group II	Group III	P Value
VAS score (mean±SD)				
Before bolus dose	9.33±0.38	9.42±0.23	9.60±0.63	P >0.05
5 min after bolus dose	1.24±0.64	2.33±0.45	0.68±0.23	P<0.001
15 min after bolus dose	0.33±0.67	0.45±0.67	0.12±0.25	P >0.05
30 min after bolus dose	0.66±0.23	0.92±0.45	0.14±0.45	P <0.001
15 min after first top up dose	1.34±0.53	1.67±0.34	0.45±0.34	P<0.001
No of doses required				
Bolus dose only	0	0	1	P<0.001
Bolus dose + 1 top-up	6	3	2	P<0.001
Bolus dose + 2 top-up	14	8	15	P<0.001
Bolus dose + 3top-up	0	9	1	P<0.001
Duration of analgesia of bolus dose	62.45±04.55	48.23±05.66	71.48±02.34	P<0.001

P < 0.001 Highly Significant *P* > 0.005 Not Significant

Table 2: Demographic and obstetric data

variable	Group I (n=20) %	Group I (n=20) %	Group III (n=20) %	P value
Age (Years)	25.13 ± 4.06	24.35 ± 3.06	23.87 ± 4.56	NS
Weight (Kg)	59.56 ± 4.87	57.67 ± 3.65	55.38 ± 3.89	NS
Height (Ft. In)	5.07 ± 0.46	5.06 ± 0.54	5.04 ± 0.43	NS
Parity				
Primi	14 (70%)	13 (65%)	15 (70%)	NS
Multiparous	06 (30%)	07 (35%)	05 (25%)	NS
Obstetric Data				
Dilatation Of Cervix (Cm)	3.34 ± 0.54	3.41 ± 0.32	3.23 ± 0.72	NS
Station Of Vertex	2.07 ± 0.87	2.21 ± 0.65	2.45 ± 0.54	NS
Effacement Of Cervix (%)	76 ± 1 2	75 ± 14	78 ± 08	NS
Presence of Membrane				
Present	19 (95%)	18 (90%)	18 (90%)	NS
Absent	01 (5%)	02 (10%)	02 (10%)	NS

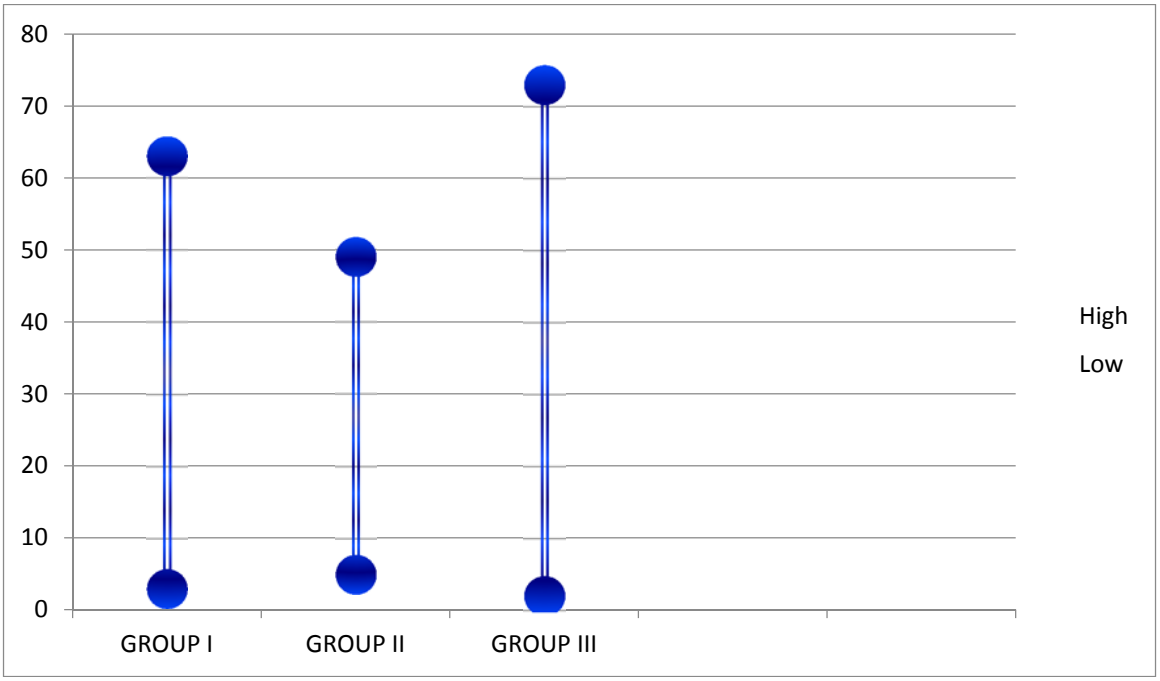

Fig 3: Duration of intra-thecal dose in minutes

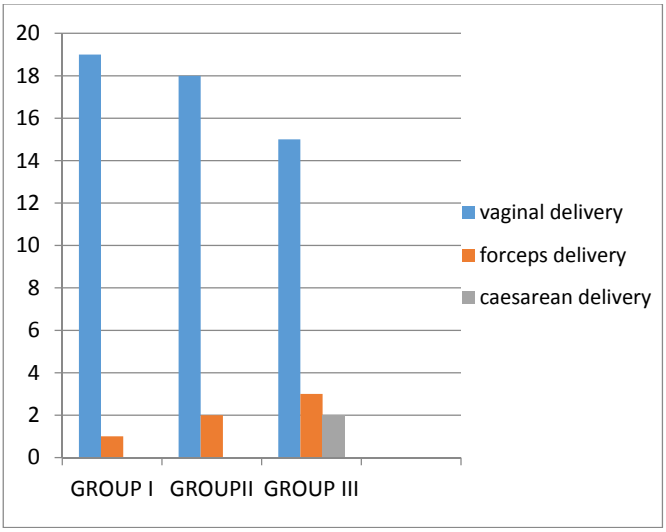

Fig 4: Mode of delivery in the parturients

Table 3: Assessment by obstetrician, parturients and anesthesiologist

	Group I	Group II	Group III
Maternal expulsive efforts			
Grade 0 – Failure	Nil	Nil	Nil
Grade 1 – Incomplete	Nil	Nil	2
Grade 2 – Good	Nil	2	6
Grade3 – Excellent	20	18	12
Parturient's acceptance			
Grade 0 – Failure	Nil	Nil	Nil
Grade 1 – Incomplete	Nil	Nil	2
Grade 2 – Good	2	4	5
Grade 3 – Excellent	18	16	13
Anesthesiologist's grading			
Grade 0 – Failure	Nil	Nil	Nil
Grade 1 – Incomplete	Nil	Nil	2
Grade 2 – Good	3	5	6
Grade 3 – Excellent	17	15	12

4. Discussion

The last few years have been marked by the arrival of new local anesthetics; ropivacaine and levo-bupivacaine, with reduced systemic toxicity and a better preservation of motor function. Toxicity is not an issue when low concentrations of local anesthetics are used as is the case in modern neuraxial labor analgesia [6]. It seems evident that the adequate dilution of local anesthetics and the strategies aiming to reduce their consumption are more important than the choice of the local anesthetic by itself when the goal is to provide optimal neuraxial labor analgesia [7]. There are controversial data regarding minimum effective concentration of ropivacaine for initiation of epidural labor analgesia. Using up and down sequential allocation MLAC of ropivacaine for epidural labor analgesia was reported to be 0.111% w/v (95% confidence interval [CI], 0.100-0.112) [7]. In another study MLAC of ropivacaine alone was 0.13% (95% CI, 0.12-0.13) compared to 0.09% (95% CI, 0.08-0.1) with sufentanil, $P < 0.01$. [15]. On the other hand, many authors [16] found that ropivacaine 0.2% offers adequate analgesia more often than either 0.15% or 0.1% and the resultant motor blocks and hemodynamic effects are minimal. Addition of fentanyl 2 mcg/ml to 0.1% ropivacaine improved analgesia to a quality similar to 0.2% ropivacaine. In the present study, epidural labor analgesia with ropivacaine 5mg or 2.5 mg both combined with fentanyl (25mcg) produced adequate labor analgesia in all the 40 parturients in group I and II showing a 100% success rate of both concentrations. However, we observed that the onset of analgesia was significantly faster when labor analgesia was initiated with 5mg ropivacaine than 2.5 mg ropivacine as reported earlier that a decrease in time for onset occurs with increasing concentrations of epidural bupivacaine. [8]. Duration of analgesia of initial bolus dose was also significantly more with 5mg ropivacaine in our study as observed by others [8]. Addition of adjuvant opioids leads to further increase in duration of analgesia. Number of top ups was also less frequent in 5 mg group than 2.5 mg ropivacaine group , which is in concordance to other studies [9]. The recent trend in practitioners of labor analgesia is to use the least possible concentration of local anesthetic and adjuvant for the purpose of attaining analgesia. The undesirable side-effects with ropivacaine analgesia are hypotension, bradycardia, nausea, paresthesia, and urinary retention, which are considered mild and transient. Even, the side-effects observed with opioids are also mild and transient. (Nausea, pruritus, respiratory depression, lower Apgar scores in the neonate). In the present study, no motor block was observed in both Groups 1 and II, which is in concordance to others. [7, 13, 16]. However, higher incidence of motor block in group III shows bupivacaine even in minimal concentration can also cause motor blockade . In a Cochrane systematic review of epidural versus no analgesic in labor that included 38 studies involving 9658 women; 13 of the studies reported hypotension as an adverse effect [11]. We also observed slight fall in the MAP and heart rate, but none of the patients had episodes of hypotension and bradycardia requiring treatment as was also noted earlier that changes in maternal pulse rate (PR) and blood pressure are not related to change in the dose of local anesthetic [12]. Injection delivery interval was comparable in both groups, but it was shorter as compared to others. [10, 13] The reason for this difference is probably because other studies included only nulliparous parturients, whereas we studied both nullipara and multipara parturients and a significant correlation between parity and duration of labor has been found in earlier studies. In our study, maternal expulsive effort, instrumental delivery, and neonatal status were comparable between groups as observed by others. [7, 13, 14] Authors of the Cochrane systematic review (2011) [9] opined that epidural analgesia appeared to be effective in reducing pain during labor. However, women who used this form of pain relief were at increased risk of having an instrumental delivery [12]. Epidural analgesia had no statistically significant impact on the risk of caesarean section, maternal satisfaction with pain relief and long-term backache and did not appear to have an immediate effect on neonatal status as determined by Apgar scores. However, they also stated that further research would be helpful to evaluate rare but potentially severe adverse effects of epidural analgesia on women in labor and long-term neonatal outcomes [14]. No parturient had hypotension, hypersensitivity reaction, pruritus, nausea, urinary retention, vomiting, respiratory depression, weakness in the limbs or shivering, though cases of pruritus, hypotension, have been reported with epidural labor analgesia [16]. All groups produced maternal expulsive efforts, parturient and anaesthesiologist acceptance grades in excellent or good range similar to Beilin (92% satisfaction) [11] and Lee who reported a satisfaction grade of 8 on a scale of 10 for all concentrations. However, in our study parturient and anesthesiologist acceptance was

significantly in group I, which could be attributable to less breakthrough pain that caused significantly less number of top-up requirement and VAS also remained significantly low at various time intervals.

5. Conclusion

- Ropivacine at either concentration has less motor blockade than bupivacine
- Ropivacine at higher concentration has faster onset and prolonged duration .than its lower concentration.
- Ropivacine at higher concentration with opiods have excellent maternal effort and patient satisfaction, have insignificant hemodynamic changes in both mother and fetus.
- The addition of opiod has no changes in neonatal outcome.

In summary, the results from our study support that intra-thecal 5mg ropivacaine with fentanyl and ropivacaine epidural top-up is a suitable choice for labour analgesia. The addition of opiods is always necessary to achieve good analgesia, high maternal satisfaction and acceptable motor blockade.

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