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A Comparison of Continuous Infusion and Intermittent Bolus Administration of 0.1% Ropivacaine with Fentanyl for Combined Spinal Epidural Labor Analgesia: A Randomized Prospective Study.

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KEYWORDS

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

ABSTRACT:

Background: To reduce maternal and perinatal morbidity arising due to pain-induced maternal sympathetic activation, maternal pain relief is essential, it not only benefits the parturient, but her neonate also. The availability of newer local anesthetics like ropivacaine and levo-bupivacaine has made Central neuraxial labor analgesia as the gold standard technique for pain control in obstetrics that is currently available, leading to higher maternal safety and satisfaction with better cardiovascular and pulmonary physiology. This study aims to investigate whether there are any differences exist between CEI and IEB analgesia for the parturients undergoing spontaneous delivery and the safety of these techniques in parturients and neonates.

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

Result: To achieve similar lower VAS, the mean total dose of ropivacaine was 19.33 ± 0.88 mg in Group I(IEB) and 24.66 ± 1.3 mg in Group B(CEI), the difference being statistically significant (P = 0.04). 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 study results support that intra-thecal 5mg ropivacaine with fentanyl and 0.1% ropivacaine of intermittent bolus through epidural is a ideal choice for labor analgesia. Intermittent bolus administration provides a more efficacious drug delivery route when compared to continuous infusion by decreasing the total amount of local anesthetic significantly without affecting patient safety or maternal satisfaction.

INTRODUCTION

Advances in the field of labor 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 labor pain results in a maternal stress response, which is neither beneficial for the mother nor the fetus [1]. Labor disorders like maternal hypertension, dystocia, meconium staining, and fetal distress are all stress related. Hence, maternal pain relief through labor analgesia benefits both the parturient,and her neonate [2]. Newer advances include pharmacological advances like introduction of fentanyl, newer local anaesthetics levobupivacaine, ropivacaine, low-dose epidurals facilitating ambulation, newer techniques like combined spinal epidurals(CSE), patient-controlled epidural analgesia pumps (PCEA), all have revolutionized pain management in laboring parturient. Studies have also

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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 fetal safety [3]. Increasing knowledge of the physiology and pharmacotherapy of pain and the development of obstetric anaesthesia as a subspecialty has improved the training in obstetric anesthesia, leading to an overall improvement in the quality of labor pain relief [4]. With the evolution of sequential "needle-through-needle" combined spinal epidural technique, it can be safely used to provide labor 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 anesthetics 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 synthetic opioid, high lipid-solubility with analgesic potency 800-times that of pethidine and100-times that of morphine [5]. Its rapid onset of action with short duration of action and with no major metabolites makes it superior for labor analgesia. A review of the adverse effects and complications has concluded that CSEA is safer technique as a conventional epidural technique and with greater patient satisfaction. We hypothesized that intermittent bolus of low concentration local anesthetic (0.1% ropivacaine) after intra thecal dministration of 5 mg ropivacaine with 25 mcg fentanyl, would offer safe and superior quality labor analgesia by decreasing total dose of the drug combination. Central neuraxial analgesia is the most versatile method of labor 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]. Adequate dilution of local anesthetics and the method of administration, 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].

The objective of this study was to compare analgesic efficacy of different mode of epidural drug delivery technique in labor analgesia i.e., continuous infusion VS intermittent bolus administration of ropivacaine, in terms of visual analogue scale (VAS) score, total ropivacaine dose requirement and incidence of breakthrough pain that required top-up administration. The secondary outcomes were to measure the degree of motor blockade, neonatal and obstetric outcomes in combined spinal epidural labor anesthesia.

METHODS AND MATERIALS

After obtaining institutional ethical committee approval, this Prospective, randomized comparative study was conducted in 60 ASA physical status I or II women with term pregnancy, single, vertex presentation in active labor (cervical dilatation 3-4 cm) requesting labor analgesia. Exclusion criteria: weight > 120 kg, allergic towards local anesthetics, cervical dilatation > 5cm, ASA III or IV case, received IV or IM opiods (e.g IM pethidine) within 2 hours. The parturient were randomly allocated into 2 groups.

Group I – 30 patients. 5mg ropivacaine (1ml) with 25mcg fentanyl (0.5 ml) given intra-thecal and then if sensory blockade level regress to T10 and to maintain sensory level up to T6-T8, epidural top-up 10 ml of 0.1 % ropivacaine given as intermittent bolus through epidural catheter.

Group II – 30 patients. 5mg ropivacaine (1ml) with 25mcg fentanyl (0.5 ml) given intra-thecal and once sensory blockade level regress to T8 - T10 level, continous infusion of 0.1% ropivacaine, 10 ml/hour, started through epidural catheter to maintain sensory level up to T6-T8. If needed additional Top-up of 4 ml 0.1% ropivacaine given if sensory blockade level regress to T10 and to maintain sensory level upto T6-T8.

Equipments Required

- Multimonitor for recording mother 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 26G quincke spinal needle,

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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 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 T10 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 was assessed by the attending obstetrician from a continuous external cardio-tocogram. New changes suggestive of an abnormal (non-reassuring) fetal heart pattern within 0.5 h after CSE resulted in appropriate obstetric intervention, included oxygen via face mask, left uterine displacement, and tocolytic drugs to be given if uterine hyperactivity was suspected. The pain score using the VAS, cervical dilation, and use of oxytocin were also recorded. Maternal expulsive efforts was assessed by an obstetrician (Grade 0 – Failure, 1 – Incomplete, 2 – Good, 3 – Excellent). Analgesia effect was assessed by an anesthesiologist (Grade 0 – Failure, 1–Incomplete, 2 – Good, 3- Excellent, 4 – Not able to evaluate (NAE) if delivery 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 □2 statistic value and *P* value. Statistical Analysis for quantitative variables i.e 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 ($P > 0.05$). 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 both group at 5 min, 60 min and 90 min of the study period, $P < 0.001$. (Table 1). 1 of 30 subjects in group I had a Bromage score of 1 versus 2 of 30 in group II, respectively, $P > 0.05$. All the parturient in the group I and II, 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 T6-T8 until sensory blockade level regress to T10. Mean duration of intra-thecal injection are 64 minutes for group I and II. The total dose requirement of ropivacaine in Group I was 580 mg and mean dose was 19.33mg and 740 mg and mean dose 24.86 mg in Group II. To achieve similar VAS, this dose requirement was significantly higher in Group II ($P = 0.04$). 6 (20%) subjects in group 1 needed 3 epidural top ups but 24 (80%)subjects in group I delivered baby within 1 or 2 epidural top up. 5 (17%) subjects in group 2 needed additional 4 mL boluses of ropivacaine 0.1% but all the subjects in group II delivered within 3 hours of infusion. Spontaneous vaginal delivery occurred in 27 (90%) parturient in group I, 24 parturient (80%) in group II. 1 parturient in group I and 1 in group II had caesarean delivery. 2 parturient in group I, and 5 in group II had forceps delivery. (Fig 4). Obstetrician's graded maternal expulsive efforts as excellent in group I and group II

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parturient (P> 0.05). Acceptance rate was graded as either excellent or "good" in all groups (Table 3) by Parturient and anesthesiologist. However, significantly higher number of cases (98.5%) reported acceptance rate 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	P Value
VAS score (mean±SD)			
Before Intrathecal dose	9.33±0.38	9.42±0.23	P >0.005
15 min after Intrathecal dose	1.24±0.64	1.33±0.45	P<0.001
30 min after Intrathecal dose	0.33±0.67	0.45±0.67	P >0.05
30 min after EPIDUARL dose	0.66±0.23	0.92±0.45	P <0.001
1 hr after first EPIDUARL dose	1.34±0.53	1.67±0.34	P<0.001
Total Ropivacaine given through Epidural catheter	580 mg Mean 19.33	740 mg 24.66	P >0.05
Duration of analgesia after Intrathecal dose	65.45±04.55	64.23±05.66	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 II (n=20) %	P value
Age (Years)	25.13 ± 4.06	24.35 ± 3.06	NS
Weight (Kg)	59.56 ± 4.87	57.67 ± 3.65	NS
Height (Ft. In)	5.07 ± 0.46	5.06 ± 0.54	NS
Parity			
Primi	21 (70%)	20 (66%)	NS
Multiparous	09 (30%)	10 (34%)	NS
Obstetric Data			
Dilatation Of Cervix (Cm)	3.34 ± 0.54	3.41 ± 0.32	NS
Station Of Vertex	2.07 ± 0.87	2.21 ± 0.65	NS
Effacement Of Cervix (%)	76 ± 1 2	75 ± 14	NS
Presence of Membrane			
Present	29 (97%)	28 (93%)	NS
Absent	01 (3%)	03 (07%)	NS

Table 3: Assessment by obstetrician, parturients and anesthesiologis

	Group I	Group II
Maternal expulsive efforts		
Grade 0 – Failure	1	1
Grade 1 – Incomplete	2	5
Grade 2 – Good	2	3
Grade3 – Excellent	25	21
Parturient's acceptance		

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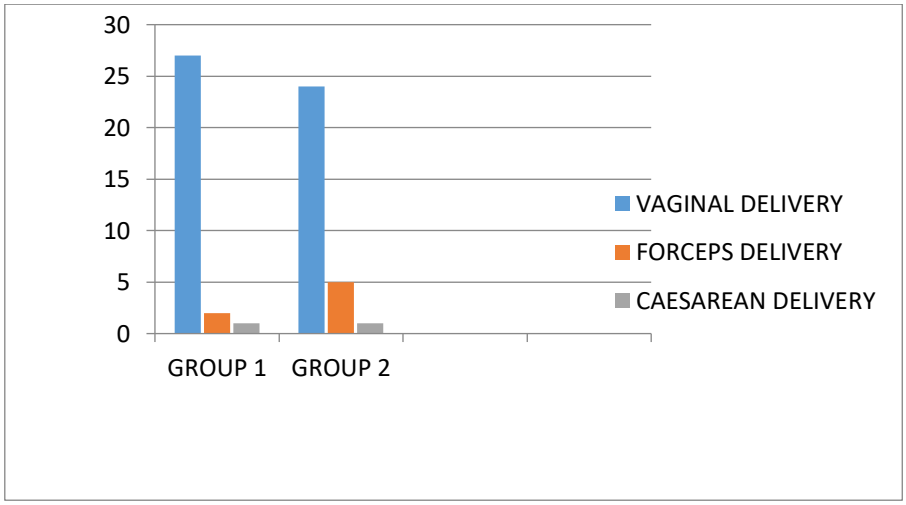
Grade 0 – Failure	1	1
Grade 1 – Incomplete	2	4
Grade 2 – Good	1	4
Grade 3 – Excellent	26	21
Anesthesiologist's grading		
Grade 0 – Failure	1	1
Grade 1 – Incomplete	1	2
Grade 2 – Good	2	5
Grade 3 – Excellent	26	22

Fig 4: Mode of delivery in the parturients



DISCUSSION

The introduction of combined spinal-epidural blockade for labor analgesia has gained popularity as an option for conventional epidural blockade due to its rapid onset of analgesia and may reduce subsequent epidural top up requirements with minimal motor blockade, compared with an epidural-only technique. A cochrane review in 2007 looked at 19 randomized trials involving 2658 women. The authors concluded that CSE had a slightly faster onset of effective pain relief than epidurals, but with no difference in the women's overall satisfaction between the two techniques [15]. 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. It seems evident that the adequate dilution of local anesthetics and the method of administration, 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]. Our most significant findings were the reduction in number of boluses and overall reduction in local anesthetic use in the intermittent group. We attribute it to a more uniform spread occurs with high injectate pressure and correspondingly large volumes of anesthetic solution in the intermittent group as compared to continuous group. An in vitro study done with the help of the computer-aided design and drafting (CADD) pump proved that peak pressure was directly related with the delivery speed of a solution [14]. This longitudinal and uniform spread of drug by the intermittent route leads to a more extensive blockade as compared to the limited, localized degree of blockade by the continuous infusion technique. Lim *et al*. Remarked that in addition to the volume of injectate, the delivery speed of the bolus dose and the pressure created in the epidural space affects dispersion.[16].

During continuous infusion under low pressure, the infusate discharges predominantly in the proximal hole of catheter with minimal flow in the distal hole. When injected as a bolus through a multi-orifice epidural catheter, the solution exits the distal end of the epidural

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catheter[17]. This suggests that an epidural bolus through a multi-orifice epidural catheter could result in more sensory blockage thereby improving the quality of analgesia compared with continuous infusion with the same volume. We found that the rate of instrumental delivery is high in group II without any significant motor blockade. The reasons cited that intermittent bolus (hourly bolus) group resulted in less epidural drug use and reduction in motor blockade. The degree of motor blockade during epidural analgesia depends not only on the drug used but also on the cumulative dose of local anesthetic[10]. Motor blockade in the lumbo-sacral area leads to lax pelvic floor muscles, this might delay the fetal head rotation and increase the chance for assisted vaginal delivery. A meta-analysis of nine RCTS comparing PIEB and CEI also demonstrated a reduction in motor block from 16% (CEI 28/175) to 2.8% (PIEB 5/180). The marked reduction in the incidence of motor blockade observed by our study is related with the consistent marked reduction in hourly and total dose of local anaesthetic agent. We found statistically significant reductions in the rates of instrumental delivery in Group I when compared with Group II this is consistent with the meta-analysis of nine RCTS comparing PIEB and CEI finding difference in the rates of LSCS (OR 0.87, 95% CI: 0.56–1.35) or instrumental delivery (OR 0.59, 95% CI: 0.35–1.00). The point estimates of the rates observed in our study and previous RCTS demonstrate a consistent trend toward reduced incidence of instrumental delivery in intermittent bolus group I. [7]

The undesirable side-effects of ropivacaine (hypotension, bradycardia, nausea, paresthesia, and urinary retention) and fentanyl (Nausea, pruritus, respiratory depression, lower Apgar scores in the neonate) are considered mild and transient. 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 observed mild fall in the heart rate and MAP, but none of the parturient had bradycardia and hypotension episode 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]. 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 significant statistical impact on maternal satisfaction with pain relief, on the risk of caesarean section, 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]. All groups produced maternal expulsive efforts, parturient and anesthesiologist 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 dose requirement and VAS also remained significantly low at various time intervals.

CONCLUSION

In conclusion, in our study the intermittent bolus group I required significantly less total drug and less rescue medication than the continuous infusion group II, to maintain similar sensory, motor block and pain scores. Duration of analgesia as indicated by time to first rescue bolus was also longer in the intermittent group. This represents a more efficacious mode of analgesia and should lead to a reduction in workload for the anaesthetist. These findings are consistent with current understanding of the nature of spread of solution within the epidural space. It is thought that intermittent boluses of local anaesthetic solution result in more uniform spread, therefore giving more reliable analgesia than infused solution.

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