Original Article

Intrathecal Fentanyl Versus Fentanyl with Levobupivacaine For Combined Spinal Epidural Analgesia in Labour

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ABSTRACT

Background: The combined-spinal epidural analgesia (CSEA) technique, which involves administering a low dose of local anesthetic drug with an opioid via intrathecal route. Currently, this method of labor analgesia is commonly and routinely utilized. Levobupivacaine, a local anesthetic, is widely recognized for its safety profile, while fentanyl, an opioid, is renowned for its ability to induce rapid and long-lasting profound analgesia. It can also be done with intrathecal fentanyl alone. This study compared the effect of intrathecal two drug regimen (Levobupivacaine with fentanyl and fentanyl alone) in CESA in labour.

Methods: This randomized controlled trial was conducted at labour room of Department of Obstetrics and Gynaecology, Institute of Child and Mother Health (ICMH). A total of 50 parturients admitted of 18-35 years old, American Society of Anaesthesiologists- ASA status I and II, full-term, primiparous women admitted for labour analgesia were selected according to eligible criteria. Those who gave consent for the procedure were underwent a thorough pre-anaesthetic checkup and were randomized into two groups, group A (LF group) and B (F group) according to the intrathecal drug delivery in combined-spinal epidural analgesia technique. Pain was measured using a 0 -10 mm visual analogue scale. Adverse effects such as hypotension, bradycardia, pruritus, urinary retention, nausea and vomiting were noted.

Results: Onset of analgesia was significantly faster in group A (mean= 1.85 minutes, SD= 0.49) than group B (mean= 5.57minutes, SD= 0.34) ($p < 0.001$) and pain intensity was less in group A than group B for first 30 mins. Parturients of group A developed some lower limb weakness but that was resolved later and there was no such weakness in group B. Maternal hypotension occurred significantly in group A with no such in group B. Seven out of 25 parturients in group A had instrumental delivery which was significantly higher than group B (no instrumental delivery) ($p=0.001$).More parturients in group A were satisfied of good quality of pain relief than group B ($p =0.003$).

Conclusion: Intrathecal Levobupivacaine with Fentanyl produces adequate analgesia than Fentanyl only for CESA in labour with more maternal satisfaction and with some non-significant maternal side effects like lower limb motor block and hypotension.

Keyword: Combined-spinal epidural analgesia, Labour analgesia, VAS, Levobupivacaine, Fentanyl.

INTRODUCTION

Labour pain is a unique pain for parturient. The pain triggers a stress response in the mother, which is detrimental both to the fetus and the mother.[1] Evidence is suggestive that labour disorders including maternal hypertension, dystocia, meconium staining, and foetal distress are stress related. Therefore, providing pain relief to the mother during childbirth not only benefits her but also has a positive impact on her newborn.[2]

The Combined-Spinal Epidural Analgesia (CESA) technique offers the benefits of both subarachnoid analgesia, such as rapid onset and reliable block, and the flexibility of

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extended analgesia through the presence of an epidural catheter. This approach effectively avoids the drawbacks associated with each technique individually. Several different drugs and combinations have been described for combined spinal-epidur alanalgesia in labour. The analgesia in the intrathecal component can be provided by opioid only or local anaesthetic only or a combination of local anaesthetic and opioid.[3]

Due to its rapid and dependable onset of analgesia, lower anaesthetic dosage requirement, minimal motor blockade, and the ability to extend the duration of pain relief according to the length of labor, the CSE technique is increasingly being favored as an alternative to traditional epidural analgesia. As a result, it is gaining popularity among healthcare professionals and patients alike.[4]

Using Intrathecal levobupivacaine with fentayl is an established and reliable technique of labour analgesia .Yvonne Lim et al described that the addition of 25 µg intrathecal fentanyl to 2.5 mg levobupivacaine as part of CSE for labour analgesia decreased the incidence of labour breakthrough pain and resulted in a longer duration of labour pain relief.[5] As a result, there is a potential reduction in the requirement for additional pain relief during labor and a potential decrease in the workload of anesthesiologists in the delivery suite.

Fentanyl is used extensively now a days as an intrathecal agent for labour analgesia in CESA technique. Advantages of using fentanyl intrathecally include the ease of use, low cost, rapid onset and longer duration of profound analgesia.[6] But there are some drawback also as nausea, vomiting, pruritus, fetal bradycardia and maternal respiratory depression. But using a low dose of fentanyl the incidence of such side effects are not so high.

The utilization of newer local anesthetics, such as levobupivacaine, in neuraxial labor analgesia has gained significant popularity due to its enhanced safety profile and reduced motor blockade. Levobupivacaine is considered a favorable option for labor analgesia as it serves as an alternative to racemic bupivacaine. This preference is attributed to the fact that the S(-) enantiomer in levobupivacaine exhibits lower affinity for sodium channels, resulting in fewer depressive effects on the cardiovascular and central nervous systems compared to the R(+) enantiomer.[7]

The CSEA technique involves administering a low dose of local anesthetics with opioids to the parturient via intrathecal route, is commonly and routinely utilized for labor analgesia.[8] Incorporating lipophilic opioids with local anesthetics for neuraxial analgesia extends the duration of sensory block; however, there is still a possibility of experiencing motor block and maternal hypotension.

In this study is we compared intrathecal use of fentanyl with levobupivacaine and fentanyl alone in CSEA in terms of rapid onset of analgesia, duration of analgesia, incidence of motor blocked and frequency of the adverse foetomaternal outcome.

METHODS

This randomized controlled trial was conducted at labour suit of Institute of Child and Mother Health (ICMH). After receiving the approval from Institutional Review Board (IRB) of BSMMU and obtaining informed written consent from each individual patient was enrolled in this study. Demographic and clinical data including age, weight, height, gestational age and cervical dilatation were recorded for all parturients.

A total of 50 parturients were enrolled for this study. Those who gave consent for the procedure were underwent a thorough pre-anaesthetic checkup and were randomized into two groups, group A (LF group) and B (F group) according to the intrathecal drug delivery in combined-spinal epidural analgesia technique. The randomization was performed by an independent staff. The staff used fifty (50) opaque sealed envelopes inside which there was a token contains group name (A or B) and a code number of the patients (01 to 25). Each group has 25 tokens. When parturients admitted at labour ward for vaginal delivery and gave consent for study, they were asked to pick up an envelope by lottery. And in each group had 25 parturients. Group A were received 2.5mg (0.5ml) isobaric levobupivacaine with 25μg (0.5ml) fentanyl (total1.0ml) intrathecally (also named as LF group) and group B were received only 25μg(0.5ml) fentanyl with 0.5 ml of distilled water (total 1ml) intrathecally (also named as F group). Both groups received epidural infusion of 0.0625% levobupivacaine and 2μg /ml fentanyl at a rate of (10-15) ml/hr as infusion.

Study Procedure:

All parturients had the standard monitoring including noninvasive blood pressure, pulse oximetry and cardiotocography for foetal monitoring. Intravenous (IV) access with 18G cannula connected with a Hartmann's solution was established on the upper limb. Before performing the CSEA procedure, baseline measurement of pain intensity was made using a visual analog scale VAS (0= no pain, 10= worst imaginable pain) at the peak of uterine contraction, baseline arterial pressure (BP), heart rate (HR) and foetal heart rate (FHR) were measured. After IV preload with Hartmann's solution at the rate of 10-15ml/kg, CSE was performed at the L3-4 or L4-5 intervertebral space with the patient in sitting position. Then the epidural catheter was inserted 3-5 cm into epidural space and was secured without a test dose.

The parturient was then positioned supine with left lateral displacement and the head end of the bed was elevated to 15-20 degree. After 20 minutes of intrathecal dose, the level of sensory blockade was checked to ensure the sensory level at least reached at the level of T10. Then continuous epidural infusion of 0.0625% levobupivacaine with fentanyl 2μgm/ml @ 10ml/hr through epidural catheter was started via syringe pump and continued till the delivery of the baby. With the time noted 'zero' all the patients received intrathecal injection according to the lottery and asked to indicate pain intensity using the VAS scale.

Progress of labour, cervical dilatation and foetal monitoring of all parturients were followed up until delivery on a partograph by an obstetrician along with assessment of pain, sensory and motor block, hemodynamic parameters and foetal monitoring.

Degrees of analgesia, motor block, foetal heart rate and blood pressure were assessed at 5, 15 and 30 minutes after the intrathecal dose and then hourly interval of throughout the labour. Intensity of pain was assessed by VAS score (0= no pain, 10= worst imaginable pain). After 30 minutes of intrathecal dose, if VAS is less than or equal to 3, then it was considered as adequate analgesia, If VAS is >3 then the parturient was excluded from study. Any breakthrough pain was managed by 5ml bolus epidural infusion of 0.0625% levobupivacaine with fentanyl 2μgm/ml. Motor block was bilaterally evaluated according to Bromage scale. Cephalad level of the sensory block was determined by perceived temperature difference to alcohol

swab. Parturients' haemodynamic parameters including arterial blood pressure and heart rate were monitored at regular intervals throughout the labour. Maternal hypotension was defined as systolic blood pressure < 90 mm of Hg or > 20% decrease from baseline. It was treated by turning parturients to the left lateral position, and administration of maternal oxygen, intravenous fluid infusion, or vasopressor (ephedrine 5mg bolus) as indicated. Maternal bradycardia (heart rate less than 50 beats / min) was treated with atropine 0.6 mg increments. Mode of delivery was assessed as normal vaginal delivery, instrumental delivery-ventouse or forcep delivery and caesarean section delivery.

Assessment of neonate was done by APGAR score in 1st and 5th minute after delivery as more or less than seven[1]. If APGAR score was below 7 and initial management failed, then the neonates were transferred to the neonatal intensive care unit.

The parturients were asked a question which was formulated as – "how would you describe the quality of your pain relief since the epidural bolus was given?" The answers were graded as excellent, good, fair and poor.

Statistical Analysis:

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Qualitative variables of this study are expressed as percentage. Quantitative variables are expressed as mean ± standard deviation. Fisher exact test is used to analyze the categorical variables, Student t-test is used for continuous variables. P values <0.05 is considered as statistically significant.

RESULTS

There was significant differences in pain intensity measured by VAS score among group A and group B at 5, 10, 20, 30 and 60 minutes (Figure-1). Motor blockade was more in group A compared to group B in first half hour (Table- 1). Analgesic action of these drugs starts three times faster in levobupivacaine with fentayl group than the fentanyl only group (p<0.001). Number of patients need to treat in case of levobupivacaine with fentayl group is 1 and fentanyl only group is 8, that is statistically significant (p= 0.04). (Table 2). No differences of fetal heart rate are observed among groups except 5 and 60 minutes (Table- 3). Normal vaginal delivery rate was higher in group B than group A. No caesarean section delivery was required in any group. In group A instrumental delivery rate is higher than group B. (Figure- 2). There is no differences in APGAR score in between the groups in 1st and 5th minute. (Table- 4). There is no significant maternal side effects observed between the groups except hypotension, which was higher in group A (12%) (p=0.031) **(**Table-5). Higher maternal satisfaction was achieved in group A than group B (Table-6).

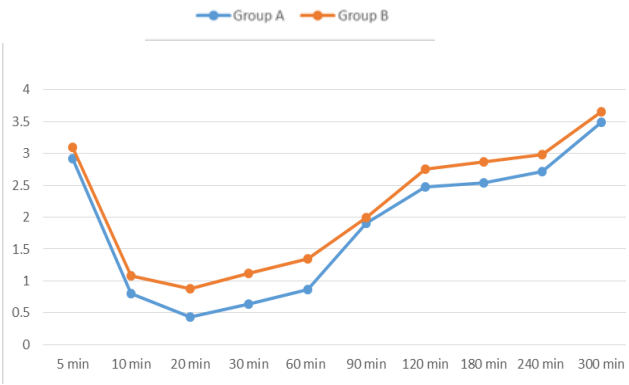

Figure 1: Visual analogue scale between two groups.

Table 1: Motor block assessed by Bromage scale between two groups after CSE

Bromage scale	Group A (n = 25)	Group B (n = 25)	p value
5 min	2.92 ± 0.82	4.00 ± 0.00	<0.001
15 min	3.23 ± 0.43	4.00 ± 0.00	<0.002
30 min	3.55 ± 0.50	4.00 ± 0.00	<0.001
60 min	4.00 ± 0.00	4.00 ± 0.00	-
120 min	4.00 ± 0.00	4.00 ± 0.00	-
180 min	4.00 ± 0.00	4.00 ± 0.00	-
240 min	4.00 ± 0.00	4.00 ± 0.00	-
300 min	4.00 ± 0.00	4.00 ± 0.00	-

Table 2: Parturient analgesic quality

Analgesic quality	Group A (n = 25)	Group B (n = 25)	p value
Onset of analgesia (in minutes)	1.75±0.33	5.57±0.34	<0.001
Time to reach highest dermatome (in minutes)	10.40±1.07	19.54±1.43	<0.001
Duration of first stage of labour after CSE (in minutes)	209.36±3.05	207.92±2.08	0.06
Duration of second stage of labour (in minutes)	58.24±1.50	57.36±1.16	0.04
Spinal to delivery interval (in minutes)	231±35.38	215±37.03	0.09
Number of patients that required epidural top up (%)	1(4%)	8(32%)	0.04

Table 3: Comparison of mean foetal heart rate between two groups at different time intervals.

Foetal heart rate	Group A (n = 25)	Group B (n = 25)	p value
5 min	139.58 ± 4.78	143.27 ± 4.95	0.002
15 min	139.17 ± 6.35	140.80 ± 5.59	0.414
30 min	140.00 ± 4.34	141.18 ± 3.75	0.221
60 min	139.79 ± 4.90	141.97 ± 3.66	0.037
120 min	141.05 ± 5.03	141.51 ± 4.33	0.684
180 min	140.87 ± 3.12	141.18 ± 4.89	0.756
240min	145.43±4.56	142.56±4.67	0.342
300min	137.43±4.76	139.53±3.43	0.231

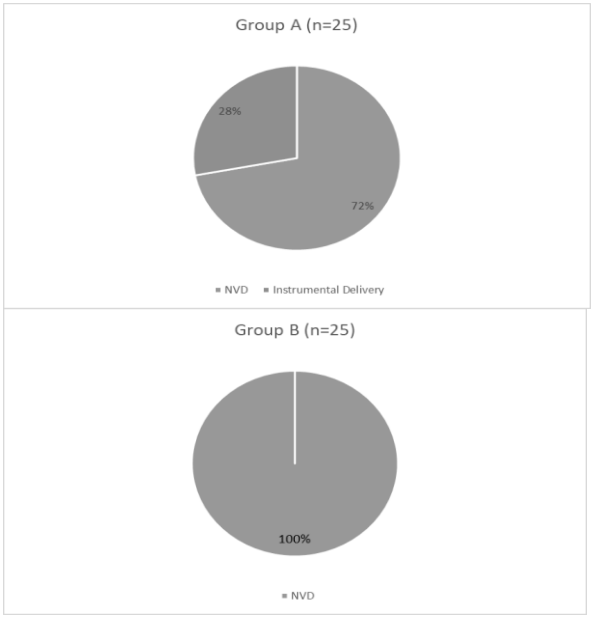

Figure 2: Distribution of mode of delivery in two groups.

Table 4: Distribution of APGAR score of newborns between two groups

APGAR score		Group A (n = 25)	Group B (n = 25)	p value
At 1 min	≤7	1 (4%)	2 (8%)	1.00
	>7	24(96%)	23 (92%)	
At 5 min	≤7	0 (00)	1(4%)	1.00
	>7	25 (100%)	24 (96%)	

Table 5: Maternal side effects between two groups

	Group A (n = 25)(%)	Group B (n = 25)(%)	p value
Hypotension	6(12)	0	0.03
Pruritus	7(28)	12(48)	0.36
Nausea\vomiting	5(20)	4(16)	1.00
Respiratory depression	0	0	N/A
Shivering	7(28)	4(16)	0.548
Headache	0	0	N/A
Urinary retention	0	0	N/A

Table 6: Maternal satisfaction regarding pain relieve between two groups

Maternal satisfaction	Group A (n = 25)	Group B (n = 25)	p value
Excellent	18(56%)	7 (36%)	0.003
Very good	4(24%)	3 (12%)	
Good	2(16%)	10(32%)	
Poor	1 (4%)	5 (20%)	

DISCUSSION

The overall satisfaction of a parturient under labour analgesia depends on whether the onset of analgesia is rapid or not, whether she can move freely or not, whether duration of analgesia is long-lasting or not, whether she has any side effects or not and whether the condition of the baby is good or not. In our study the mean onset of analgesia of patients in group A was more rapid than that of group B. Veena Chatrath et al in their study also showed that levobuivacaine and fentanyl combination causes rapid onset of analgesia.[9] Time needed to reach highest dermatome was also short in group A than only group B which was also similar to Veena Chatrath et al. study. No significant difference was seen in terms of total duration of analgesia. But more parturients in F group (8/25) needed epidural top up doses than LF group (1/25).As every parturients of each group was given continuous epidural infusion of 0.0625% levobupivacaine with fentanyl 2µgm/ml @ 10ml/hr through epidural catheter immediately after spinal injections and continued till the delivery of the baby it was difficult to evaluate duration of spinal analgesia itself.

Parturients of each group experienced some degree of side effects and was managed accordingly. Hypotension was significantly higher in LF group than F group .Shivering occurred more in LF group than F group but was not significant .Pruritus occurred more in F group than LF group but was not significant .Nausea/vomiting occurred more in LF group than F group but was not significant.

Mode of delivery is an important determinant of the success of labour analgesia. In our study it was found that parturients of LF group had some degree of motor block at initial stage but it was not so

troublesome and was completely wear off after (30-60) minutes and no motor block was occurred in F group . In the present study a significantly increased rate of instrumental vaginal delivery was observed in the LF group than the F group. In the LF group 7 parturients had NVD (72%) and 25 parturients had NVD in the F group (100%). Intensity of motor block and instrumental delivery rate depends on the concentration of local anaesthetics and intrinsic motor blocking capacity of local anaesthetic. In this study as in F group only intrathecal fentanyl was used, no motor block was occurred initially but in LF group as 0.5% levobupivacaine was used in combination with fentanyl some degree of motor weakness was noted but it was wearied off quickly.

Pain perception is a subjective complex phenomenon which is undoubtedly influenced by physiological, psychological and cultural factors. Quantification of pain on a visual analogue scale is considered as the gold standard for assessment of pain.[6] In the context of our country, where people believe that labour pain is an eternal thing to bear, labour analgesia itself is a great challenge to accept as treatment modality. So, interpretation of maternal satisfaction in this regard is difficult. Rather from the experience of the current study, many parturients confuse increased pressure sensation during the second stage of labour as pain perception. In the present study, the quality of pain relief was compared after intrathecal injections and overall, after delivery. Quality of pain relieved was not similar in between two groups. More parturients in LF Group were satisfied regarding pain relief than those of F group.

In the present study, combination of levobupivacaine with fentanyl as intrathecal injection on the background of continuous epidural infusion seems to give satisfactory results. Giving fentanyl as a sole agent in intrathecal component however does not bring out any better result.

CONCLUSION

Intrathecal Levobupivacaine with Fentanyl for Combined Spinal-Epidural Analgesia in labour is the better option with more maternal satisfaction and with some nonsignificant maternal side effects (lower limb motor block and hypotension). In combined spinal epidural labour analgesia, intrathecal levobupivacaine (2.5mg) with fentanyl (25 microgram) can be safely practiced for pain free labour.

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