Original Article

Combined Spinal Epidural Analgesia in Labour – Comparison between Levobupivacaine with Fentanyl and Fentanyl alone in Intrathecal Component

Md Mostafijur Rahaman[1], A K M Akhtaruzzaman[2], Mohammad Abul Kalam Azad[3] Mohammad Mizanoor Rahman[4], Ifthekhar Ahmed[5], Hasrat Jahan[6] Muinul Islam Shah[7], Lubna Marium[8]

[1]Assistant Professor,Institute of Child and Mother Health,Matuail,Dhaka, [2]Professor,BSMMU, [3]Medical Officer, BSMMU, [4]Associate Prpfessor,ICMH, [5]Associate Prpfessor,ICMH, [6]Associate Prpfessor,ICMH, [7]Anaesthesiologist, SSMCH. [8]Consultant BSMMU

Corresponding Author: drmostafijicmh@gmail.com.

Abstract

Background: *The combined-spinal epidural analgesia (CSEA) technique using intrathecal administration of low dose local anaesthetic drug with opioid to provide analgesia is a routinely practiced method of labour analgesia now-a-days. Levobupivacaine is a local anaesthetic which is very popular by virtue of the safety and fentanyl is an opioid which causes rapid onset and longer duration of 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 combined spinal-epidural technique of labour analgesia.*

Objective: *Evaluate the effect of Intrathecal Levobupivacaine with Fentanyl versus Fentanyl only for Combined Spinal - Epidural Analgesia in Labour.*

Method: *This randomized controlled trial was conducted at labour suit of Department of Obstetrics and Gynaecology, Institute of Child and Mother Health (ICMH). A total of 50 primiparous parturients, 18-35 years old, ASA status I and II, full-term women admitted for labour analgesia were selected according to eligible criteria. Those who gave consent for the procedure were underwent a thorough pre-anaesthetic check up 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 -100 mm visual analogue scale. Adverse effects such as hypotension, bradycardia, pruritus, urinary retention, nausea and vomiting were noted. All information was recorded in a preformed data sheet and statistical analysis was done by SPSS.22.0*

Results: *Onset of analgesia was significantly faster in group A (1.85 ± 0.49) than group B (5.57± 0.34) (p = 0.000) 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 Combined Spinal - Epidural Analgesia 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 an unique pain for parturients. The pain of labour results in a maternal stress response, which is neither beneficial for the foetus nor the mother. Evidence is suggestive that labour disorders including maternal hypertension, dystocia, meconium staining, and foetal distress are stress related. Hence, maternal pain relief not only benefits the parturient, but her neonate also.

The combined-spinal epidural technique combines the advantages of speed of onset and reliability of block achieved by the subarachnoid analgesia with flexibility of extending analgesia, provided by the presence of an epidural catheter and avoids their individual disadvantages.

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 (Polley LS et al.2004, p. 336) or local anaesthetic only or a combination of local anaesthetic and opioid.

Fentanyl is used extensively now a days as an intrathecal agent for labour analgesia in combined spinal-epidural technique. Advantages of using fentanyl intrathecally include the ease of use, low cost, rapid onset and longer duration of profound analgesia. 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.

Neuraxial labour analgesia using new local anaesthetics such as levobupivacaine has become very popular by virtue of its safety and lesser motor blockade. Levobupivacaine is thought to be a good alternative to racemic bupivacaine for labour analgesia because the S(-) enantiomer has less affinity for the sodium channels and thus has fewer depressant effects on cardiovascular and central nervous system than the R(+) enantiomer (Gristwood R et al.1994;3:1209–12)

The combined-spinal epidural analgesia (CSEA) technique using the intrathecal administration of low dose local anaesthetics with opioid to parturient is a routinely practiced method of labour analgesia nowadays .The addition of lipophilic opioids to local anaesthetic for neuraxial analgesia increases the duration of sensory block, but still there is a chance of having motor block and maternal hypotension.

The purpose of this study is to compare 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.

Materials and 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 who fulfilled the inclusions and exclusions criteria. Demographic and clinical data including age, weight, height, gestational age and cervical dilatation were recorded for all parturients A total of 50 parturients admitted of 18-35 years old, 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 check up and were randomized into two groups, group A (BF group) and B (F group) according to the intrathecal drug delivery in combined-spinal epidural analgesia technique. Group A were received 2.5mg (0.5ml) isobaric levobupivacaine with 25μg (0.5ml) fentanyl(total1.0ml) intrathecally and Goup B were received only 25μg(0.5ml) fentanyl with 0.5 ml of distilled water (total 1ml) intrathecally. Both group 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 (Mousa, Al-Metwalli and Mostafa 2010).

Assessment of neonate was done by APGAR score in 1st and 5th minute after delivery as more or less than seven (Akhtaruzzaman et al. 1997). If APGAR score was below 7 and initial management failed, then the neonates were transferred to the neonatal intensive care unit.

Quality of pain relieved after CSEA was assessed by 4-point questions (Sheeba et al. 2018). The parturients were asked a question which was formulated as –"How would you describe the quality of your pain relief at the time of delivery?" Answer was rated as 0=No pain ,1=Awareness of contraction but no pain 2=Awareness of pressure but tolerable discomfort ,3=Distressing pressure or pain.Maternal satisfaction was assessed by 4 point questions (Akhtaruzzaman et al. 1997). 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). The mean values were calculated for continuous variables. 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 and Observations

This randomized clinical trial was conducted to find out an effective method of labour analgesia by CSEA techniqueusing intrathecallocal anaesthetic –opioid combination or opioid alone which does not affect the labour outcome. In this trial, 50 parturients were enrolled and in each group had 25 parturients as per inclusion and exclusion criteria. After 30 minutes of intrathecal dose, all parturients of both groups had Bromage scale more than 3 and sensory level below T6. No parturient was excluded from the study due to intense block or due to inadequate analgesia.Observations of the present study were

analyzed in the light of comparison among the subject groups.All results are expressed as mean ± SD or percentage as applicable.

There was significant differences in pain intensity measured by VAS score among group A and group B at 5,20,30,60,90,120,180,240and300 minutes(Table-I).

statistically significant differences in Bromage scale score were observed between two groups

at different time intervals. (Table- II).

significant differences were observedamong groups in Onset of analgesia(in minutes),Time to reach highest dermatome (in minutes),Duration of second stage of labor (in minutes), Number of patients that required epidural top up (%) .But in Duration of first stage of labor after CSE (in minutes),Spinal to delivery interval (in minutes)no significant difference is observed **(**Table III).

The foetal heart rate was significantly different among groups at 5 minute and 60 minute. But no significant differences are observed among groups at 15 minute, 30 minute , 120 minute , and 180 minute (Table-IV).Normal vaginal delivery rate was significantly 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. Among the instrumental delivery in group A forceps delivery are 2 and ventouse assisted are 5 in number(Table- V).

At the 1st minute, more neonate in group A had APGAR score > 7, which was not statistically different than group B . At 5th minute, >7 APGAR score was also higher in group A than the group B but the difference was not statistically significant . Two neonates in group B had APGAR score <7 at 1stminute but no neonate needed tracheal intubation. Only 1 neonate required facemask ventilation in group B(Table-VI).

Hypotension was significantly higher in group A (12%) than group B.Pruritus occurred more in group B than in group A but was not significant .Nausea/vomiting occurred more in group A than group B but was not significant.Shivering occurred more in group A than group B but not significant**(**Table VII).

Higher maternal satisfaction was achieved in group A than group B(Table-VIII).

Table-I: Pain intensity by visual analogue scale after CSEA

VAS	Group A (n = 25)	Group B (n = 25)	p value
5 min	2.92 ±0 .27	3.10 ± 0.78	0.005
10 min	0.8 ± 0.49	1.08 ±0.27	0.004
20 min	0.44± 0.49	0.88 ± 0.32	0.001
30 min	0.64±0.54	1.12±0.34	0.015
60 min	0.86 ± 1.05	1.35 ± 0.75	0.021
90 min	1.91 ± 0.842	02 ± 0.82	0.280
120min	2.48 ± 0.98	2.75 ± 1.09	0.279
180min	2.54±0.67	2.87±0.34	0.321
240min	2.72±0.34	2.98±0.44	0.332
300min	3.49±0.21	3.66±0.55	0.221

Table- II: 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	0.00001
15 min	3.23 ± 0.43	4.00 ± 0.00	0.00002
30 min	3.55 ± 0.50	4.00 ± 0.00	0.00001
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	-
240min	4.00 ± 0.00	4.00 ± 0.00	-
300min	4.00 ± 0.00	4.00 ± 0.00	-

TableIII :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	0.00002
Time to reach highest dermatome (in minutes)	10.40±1.07	19.54±1.43	0.00001
Duration of first stage of labour after CSE (in minutes)	209.36±3.05	207.92±2.08	0.061
Duration of second stage of labour (in minutes)	58.24±1.50	57.36±1.16	0.037
Spinal to delivery interval (in minutes)	231±35.38	215±37.03	0.090
Number of patients that required epidural top up (%)	1(4%)	8(32%)	0.039

Table-IV: 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

Table- V: Distribution of mode of delivery between two groups.

Mode of delivery	Group A (n = 25)	Group B (n=25)	p value
NVD	18(72%)	25 (100%)	0.001
Instrumental Ventouse Forceps Caesarean section	7(28%) 5(11) 2(11) 0	0 0 0 0	

Table- VI: Distribution of APGAR score of newborns between two groups

APGAR score	Group A (n = 25)	Group B (n = 25)	p value
At 1 minute			
≤7	1 (4%)	2 (8%)	1.000
>7	24(96%)	23 (92%)	
At 5 minute			
≤7	0 (00)	1(4%)	1.000
>7	25 (100%)	24 (96%)	

Table VII: Maternal side effects between two groups

	Group A (n = 25)(%)	Group B (n = 25)(%)	p value
Hypotension	6(12)	0	0.031
Pruritus	7(28)	12(48)	0.359
Nausea\vomiting	5(20)	4(16)	1.000
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- VIII: 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 CSE technique is gaining popularity as an alternative of conventional EA because of its rapid and reliable onset of analgesia with lower dose of anaesthetic, minimal motor blockade and the flexibility to prolong the duration of analgesia as per the duration of labour and is therefore preferred.

Using Intrathecal levobupivacaine with fentayl is a established and reliable technique of labour analgesia .Yvonne Lim et al (2004) 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. This may decrease the need for supplemental labour pain relief and the anaesthetists' workload in the delivery suite.

As a sole agent, doses of intrathecal fentanyl reportedly used for labour analgesia range from 10–50 micro gram. So we used 25 microgram of fentanyl (Clarke VT et al.1994; 81:1083). Primary purpose with this study was to see if fentanyl can alone cause adequate analgesia as is fentanyl with levobupivacaine.

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 LF Group was more rapid than that of F Group. Veena Chatrath et al.(2015)in their study also showed that levobuivacaine and fentanyl combination causes rapid onset of analgesia. Time needed to reach highest dermatome was also short in LF group than only F group which was also similar to Veena Chatrath et al.(2015) 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 weared 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 (Hjermstad et al. 2011). 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 epiduralinfusion seems to give satisfactory results. Giving fentanyl as a sole agent in

intrathecal component however does not bring out any better result.

Limitation

The result of our study could have been more precise if the sample size of study group would have been large, but the patients willing for labour analgesia were limited in our institution. We had no control group of patients who received either i.v. labour analgesia or who did not receive any analgesia, so we could not comment on prolongation of the second stage of labour or overall duration of labour.

Conclusion

Under the condition of present study, it can be concluded that Intrathecal Fentanyl only does not produces adequate analgesia than Levobupivacaine with Fentanyl for Combined Spinal - Epidural Analgesia in labour. So 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).

Recommendation

In combined spinal epidural labour analgesia, intrathecal levobupivacaine (2.5mg) with fentanyl(25 microgram) can be safely practiced for pain free labour.

References

1. Akhtaruzzaman, AKM, Aziz Lutful, Islam, M, Iqbal, KM, Mustafa, MH, 1997; "Effect of continuous infusion epidural analgesia for labour-comparison between bupivacaine-fentanyl mixture or lignocaine at late second stage", Journal of the Bangladesh society of Anaesthesiology, vol.10, pp.10-19.
2. Cambic, C.R. and Wong, C.A.2010,"Labour analgesia and obstetric outcomes", British Journal of Anaesthesia;vol. 105, pp.50-60.
3. Clarke VT, Smiley RM, Finster M: Uterine hyperactivity after intrathecal injection of fentanyl for analgesia during labor: A cause of fetal bradycardia? Anesthesiology 1994; 81:1083.
4. de la Chapelle A, Carles M, Gleize V, Dellamonica J, Lallia A, Bongain A, 2006,Impact of walking epidural analgesia on obstetric outcome of nulliparous women in spontaneous labour. Int J Obstet Anesth;15:104- 8.
5. Gristwood R, Bardsley H, Baker H, Dickens J. Reduced cardiotoxicity of levobupivacaine compared with racemic bupivacaine (Marcaine): new clinical evidence. Exp Opin Investig Drugs. 1994;3:1209–12.
6. Hjermstad, M.J., Fayers, P.M., Haugen, D.F., Caraceni, A., Hanks, G.W., Loge, J.H. 2011, et al. "Studies comparing Numerical Rating Scales, Verbal Rating Scales, and Visual Analogue Scales for assessment of pain intensity in adults: a systematic literature review", Journal of pain and symptom management,;vol. 41, no.6, pp.1073-1093.
7. Kloosterman, G. J. 1982,"The universal aspects of childbirth: human birth as a socio-psychosomatic paradigm", Journal of Psychosomatic Obstetrics & Gynecology, vol.1, no.1, pp. 35–41.
8. Pandya ST. 2010 Labour analgesia: Recent advances. Indian J Anaesth. ;54:400–8.
9. Polley LS, GIosten B. 2004Epidural and spinal analgesia/anesthesia: Local anesthetic technique. In: Chestnut DH, editor. Obstetric Anaesthesia: Principles and Practice. St. Louis: Mosby;. p. 336.
10. Sheeba, A.J, Rani, P, Surya, R., Parthasarathy, S., Reddy, H.K.V. and Sivashanmugam, T. 2018, "Equipotent dose of levobupivacaine reduce the incidence of instrumental vaginal delivery when compared to ropivacaine during epidural labour analgesia", Sri Lankan Journal of Anaesthesiology,;vol.26, no.2, pp. 105–110.
11. Van de Velde, M. 2009, "Modern neuraxial labor analgesia: options for initiation, maintenance and drug selection", Periodicum Biologorum,;vol. 111, no. 2, pp.171-185.
12. Yvonne Lim Y et al ,2004– Comparison ofIntrathecal levobupivacaine with andwithout fentanyl in combined spinalepidural for labor analgesia