Combined spinal epidural for labor analgesia comparison of two different doses of intrathecal bupivacaine 1.25 mg and fentanyl 25 µg with bupivacaine 2.5 mg and fentanyl 25 µg

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ABSTRACT

Background and Objective: The responsibility of the anesthetist in obstetrics is very high. This study compares two different low doses of intrathecal bupivacaine 1.25 mg and 2.5 mg along with 25 µg fentanyl as the spinal component of combined spinal epidural (CSE) analgesia in the early part of labor, followed by epidural top-up.

Methodology: Approval was obtained from the institutional review board and written informed consent was obtained from 60 healthy term primigravida or the second gravid parturients, with cephalic singleton pregnancy between 36 and 42 weeks, ASA Grade I/II patients. The study was conducted using low-dose intrathecal bupivacaine 1.25 mg and fentanyl 25 µg (Group I) with bupivacaine 2.5 mg and fentanyl 25 µg (Group II) as the spinal component of CSE analgesia in the early part of labor. We compared the two with respect to their onset, duration of sensory and motor block, quality of analgesia during early part of labor and the side effects of the drugs.

Results: The onset of analgesia was equally rapid with both groups within 5 min, lower incidence of motor block with Group I compared to Group II. Duration of analgesia was longer in Group II, associated with higher dermatome levels of sensory block with longer time for regression of the block.

Conclusion: We found that bupivacaine 1.25 mg was as effective as bupivacaine 2.5 mg when added to fentanyl 25 µg for CSE.

Key words: Bupivacaine, fentanyl, Labour analgesia

INTRODUCTION

Unrelieved stress in labor produces increased plasma cortisol and catecholamines concentrations which reduce uteroplacental blood flow⁴ by 35–70% compounding the effects of hyperventilation on the oxygen supply to the fetus.

Metabolic acidosis as a result of increased metabolic rate, especially in the second stage of labor is transferred to the fetus. There is delayed gastric emptying and urinary emptying.⁵

Effective pain relief reduces plasma noradrenaline,⁴ prevents the rise during the first and second stage of labor of 11-hydroxycorticosteroid,⁶ and prevents metabolic acidosis by reducing the rate of rise of lactate and pyruvate.⁵ It decreases maternal oxygen consumption by up to 14%.⁴

The pain-induced hyperventilation and hypocapnia⁷ reduces uteroplacental blood flow by up to 25%. The respiratory alkalosis further impairs fetomaternal gas exchange by shifting the oxyhemoglobin dissociation curve to the left and fetal PaO₂ may fall up to 23%.⁶

Various techniques available for pain relief during labor include non-pharmacological methods, pharmacological methods, inhalational analgesics, systemic analgesics, and regional techniques.

Low-dose combined spinal epidural (CSE) analgesia has gained widespread acceptance as an approach to labor analgesia. The rapid onset of analgesia is one of the major advantages of CSE analgesia and with its increased association with maternal satisfaction.⁷

CSE analgesia is an effective method of analgesia in labor. Intrathecal administration of combination of local anesthetic and lipophilic opioid provides rapid analgesia.

The present study compares the efficacy of low dose of bupivacaine 1.25 mg and 2.5 mg with fentanyl 25 µg intrathecally (single dose) in terms of onset, duration of block, and quality of analgesia during labor, followed by epidural analgesia.

Objectives of the study

1. To study the onset and duration of sensory and motor block in early part of labor with two different low doses of intrathecal bupivacaine (1.25 mg and 2.5 mg) along with 25 µg fentanyl.
2. To study the quality of analgesia during early part of labor.
3. To study the side effects of the drugs.

**METHODOLOGY**

**Patients Selection**
- Healthy primigravida and gravida 2 patients at term.
- ASA I and ASA II.
- Maternal request for epidural analgesia.
- Age group of 18–35 years.
- Women in active labor with cervical dilatation in primi about 4–5 cm and gravid a 2 with cervical dilatation of 3–4 cm.

**Exclusion Criteria**
The following criteria were excluded from the study:
- Patients unwilling for procedure.
- Parturient with gravid 3 or more.

**Inclusion Criteria**
The following criteria were included in the study:
- Parturients with multiple pregnancies.
- Pregnancy-induced hypertension.
- Severe anemia.
- Cephalopelvic disproportion.
- Previous lower segment cesarean section.
- History of antepartum hemorrhage.
- History of allergy to local anesthetic.
- History of cyclic vomiting syndrome/RS disease.
- History of bleeding disorders.
- Diabetes mellitus.
- History of psychiatric/neurologic disease.

**Methodology**
About 60 parturients with ASA I and ASA II in established labor with cervical dilatation <5 cm were randomly selected informed written consent was taken from patients.

Group I received intrathecal injection bupivacaine 1.25 mg and injection fentanyl 25 µg.

Group II received intrathecal injection bupivacaine 2.5 mg and injection fentanyl 25 µg for CSE.

**Procedure**
After infiltration of local anesthetic using needle through needle technique 18 Gauge Tuohy needle, epidural space was identified with loss of resistance to air technique. Then, a 15 mm (25 G) long “Whitacre” spinal needle was introduced through the epidural needle, and the correct position of the tip in the intrathecal space was confirmed by observation of free flow of cerebrospinal fluid.

Patients were allocated randomly to receive intrathecal injection of bupivacaine 1.25 mg (0.5% bupivacaine 0.25 ml) with fentanyl 25 µg (Group I n = 30) or bupivacaine 2.5 mg/0.5% bupivacaine 0.5 ml with fentanyl 25 µg (Group II, n = 30) both made up to total volume of 2 ml with saline.

Patients visual analog scale (VAS) pain score was recorded every 5, 10, 15, 30, 45, 60, 75, 90, 105, and 120 min, i.e., (every 5 min for 15 min and then every 15 min for 2 h) until the next request for analgesia.

After positioning the patient in supine position, onset of analgesia and dermatomal level were checked by loss of sensation to pinprick, time of onset, and degree of motor blockade was checked by Bromage classification.

VAS pain score for all patients at the next request for analgesia was recorded and the study was terminated. Continuation of epidural analgesia was done with 0.125% bupivacaine + 2 µg fentanyl in 10 ml.

Monitoring - mother’s vital parameters, progress of labor, efficacy of analgesia, and fetal welfare were watched in coordination with attending obstetrician and all standard monitoring required.

**Parameters Studied**
The following parameters are studied:
1. Assessment of sensory blockade: sensory blockade assessed by pinprick and time noted for block to reach different dermatomal level.
   - Onset of sensory block
   - Maximum height reached and time required,
   - Duration of analgesia,
   - Quality of analgesia.
2. Assessment of motor block:
   - Motor blockade was assessed by Bromage scale.
   - Time required for complete recovery.
3. Untoward effects:
   - The patients were carefully monitored for any untoward effects such as inadequate block, hypotension, bradycardia, respiratory distress, nausea, vomiting, restlessness, pruritus, shivering, anaphylactic reaction, and fetal bradycardia.

**Terms and Definitions**
Time of onset of analgesia, this was taken as time from deposition of drug to the feeling of tingling sensation in the legs.

Time of onset of paralysis (motor blockade), this was taken as time from onset of paresis to loss of power; i.e., patient was not able to lift the legs (modified Bromage Scale, onset of motor block).

**Duration to Reach Maximum Dermatomal Level**
This was taken as the time interval between the deposition of drug and loss of sensation at highest dermatomal level.

**Statistical Analysis**
In the present study, results are given as mean ± standard deviation and range values for continuous data. Student’s t-test was used to compare the two groups, categorical data are expressed as number and percentages, and the difference between the groups was compared by Chi-square test. P value of 0.05 or less was set for statistical significance.

**RESULTS**
Regarding age, height, and weight, P value is not significant [Tables 1-10 and Figure 1].

**DISCUSSION**
Obstetricians and anesthetists have always feared the incidence of instrumental deliveries in women receiving labor analgesia could be higher than in those who do not receive it.\[^{6}\]
Table 1: Time of onset of sensory analgesia after spinal component of CSE

| Parameter                        | Mean±SD | Mean difference | P* value | Sig. |
|----------------------------------|---------|-----------------|----------|------|
|                                  | Group I | Group II        |          |      |
| Sensory onset of action in seconds | 204.3±31.06 | 87±30.61        | 117      | <0.001 | HS   |

P<0.001 was highly statistically significant. SD: Standard deviation, CSE: Combined spinal epidural

Table 2: Maximal dermatomal level of sensory blockade after spinal component of CSE

| Dermatomal level | Group I (%) | Group II (%) |
|------------------|-------------|--------------|
| T6               | 0           | 2 (7)        |
| T7               | 0           | 11 (37)      |
| T8               | 5 (17)      | 11 (37)      |
| T9               | 13 (43)     | 4 (14)       |
| T10              | 10 (33)     | 2 (7)        |
| T11              | 2 (7)       | 0            |

χ²=27.3 P<0.001 was highly statistically significant. CSE: Combined spinal epidural

Table 3: Grade of motor blockade after spinal component of CSE

| Motor onset of action | Group I (%) | Group II (%) |
|-----------------------|-------------|--------------|
| 0                     | 26 (87)     | 18 (60)      |
| I                     | 4 (13)      | 9 (30)       |
| II                    | 0           | 3 (10)       |

χ²=6.3 P=0.04 was statistically significant

Table 4: Changes in heart rate

| Heart rate | Mean±SD | Mean difference | P* value | Sig. |
|------------|---------|-----------------|----------|------|
|            | Group I | Group II        |          |      |
| 0          | 97±11   | 95±18           | 2.0      | 0.43 | NS   |
| 1          | 89±18   | 81±15           | 0.8      | 0.80 | NS   |
| 5          | 89±19   | 81±16           | 0.2      | 0.29 | NS   |
| 15         | 79±16   | 80±17           | 0.3      | 0.87 | NS   |
| 25         | 79±17   | 80±18           | 0.4      | 0.83 | NS   |
| 30         | 79±17   | 77±18           | 1.8      | 0.37 | NS   |
| 45         | 78±17   | 75±19           | 3.3      | 0.26 | NS   |
| 60         | 83±16   | 76±16           | 6.6      | <0.001 | HS   |
| 90         | 83±16   | 75±17           | 5.5      | 0.001 | HS   |

*Student’s unpaired t-test. P<0.001 which was highly statistically significant. NS: Not significant, HS: Highly significant

Table 5: Changes in systolic BP

| Systolic BP | Mean±SD | Mean difference | P* value | Sig. |
|-------------|---------|-----------------|----------|------|
|             | Group I | Group II        |          |      |
| 0           | 110±7   | 111±8           | -0.4     | 0.84 | NS   |
| 1           | 111±10  | 112±9           | -1.5     | 0.52 | NS   |
| 5           | 110±10  | 112±10          | -1.8     | 0.48 | NS   |
| 15          | 107±22  | 106±13          | 0.5      | 0.92 | NS   |
| 30          | 113±19  | 106±13          | 0.7      | 0.02 | S    |
| 45          | 117±13  | 110±13          | 6.3      | 0.07 | NS   |
| 60          | 115±9   | 115±8           | 0.4      | 0.86 | NS   |
| 90          | 127±8   | 115±7           | 2.1      | 0.29 | NS   |
| 180         | 129±15  | 110±13          | 8.3      | 0.002 | S    |

*Student’s unpaired t-test. S: Significant, NS: Not significant, BP: Blood pressure

Table 6: Changes in diastolic blood pressure

| Diastolic BP | Mean±SD | Mean difference | P* value | Sig. |
|--------------|---------|-----------------|----------|------|
|              | Group I | Group II        |          |      |
| 0            | 78±7    | 81±5            | -2.6     | 0.10 | NS   |
| 1            | 75±10   | 78±8            | -2.9     | 0.21 | NS   |
| 5            | 74±10   | 74±9            | -0.1     | 0.98 | NS   |
| 15           | 75±11   | 72±11           | 2.6      | 0.36 | NS   |
| 30           | 77±19   | 74±11           | 3.0      | 0.25 | NS   |
| 45           | 75±10   | 75±10           | -0.6     | 0.81 | NS   |
| 60           | 78±10   | 77±8            | 1.4      | 0.56 | NS   |
| 90           | 74±10   | 74±10           | 0.0      | -   | -    |
| 180          | 76±9    | 76±9            | 0.0      | -   | -    |

*Student’s unpaired t-test. SD: Standard deviation

Table 7: Duration of two segment regression

| Parameter                        | Mean±SD | Mean difference | P* value | Sig. |
|----------------------------------|---------|-----------------|----------|------|
|                                  | Group I | Group II        |          |      |
| Time of two segment regression in min | 82±7±16±17 | 104±33±19±37 | -21.6   | <0.001 | HS   |

P<0.001 which was highly statistically significant. SD: Standard deviation

Table 8: Epidural top-up needed or not after spinal

| Epidural needed | Group I (%) | Group II (%) |
|-----------------|-------------|--------------|
| Yes             | 29 (97)     | 23 (77)      |
| No              | 1 (3)       | 7 (23)       |

χ²=5.8, P=0.01

Table 9: VAS score

| VAS after spinal | Group I (%) | Group II (%) |
|------------------|-------------|--------------|
| 1–2              | 20 (67)     | 28 (93)      |
| 3–4              | 10 (33)     | 2 (7)        |

χ²=6.7, P=0.01. Significant. VAS: Visual analog scale

Table 10: Complications

| Parameter      | Present cases | P* value | Sig. |
|----------------|---------------|----------|------|
| Sedation       | Group I (%)   | Group II (%) |          |      |
|                | 10 (33)       | 11 (37)   | 0.78     | NS   |
| Fetal bradycardia | 3 (10)       | 7 (23)    | 0.16     | NS   |
| Nausea         | 8 (27)        | 8 (27)    | -        | -    |
| Vomiting       | 5 (17)        | 5 (17)    | -        | -    |
| Pruritis       | 10 (33)       | 11 (37)   | 0.78     | NS   |
| Hypotension    | 3 (10)        | 13 (43)   | 0.004    | S    |

*Chi-square test

Ideally, pain relief with regional techniques should be produced with the minimum disturbance to the progress of labor or to sympathetic functions, sensory functions (proprioception), and motor functions of central nervous system. Thus, it is intriguing
Michaal J. Paecch et al. did a randomized, double blinded controlled clinical trial aimed to determine whether the addition of subarachnoid clonidine 15-45 µg to fentanyl 20 µg and bupivacaine 2.5 mg increased the duration of labour analgesia. They concluded that onset of analgesia and duration was almost similar addition of clonidine had increased incidence of hypotension. In the group with fentanyl and bupivacaine thoracic sensory dermatomal level was T5. Onset was within 5 min and duration was more than 90 min with small incidence of motor blockade.[12]

A study by Wong et al. revealed that neuraxial analgesia in early labor did not increase the rate of cesarean delivery and it provided better analgesia and resulted in shorter duration of labor than systemic analgesia.[13]

The comparative obstetric mobile epidural trial study confirmed that low-dose techniques influence the mode of delivery in both CSE and low-dose infusion groups there was an increased percentage of spontaneous vaginal deliveries compared to traditional technique.[14]

In our study, spontaneous vaginal delivery occurred in 84% of cases in Group I and 63% of cases in Group II. Instrumental delivery with forceps was conducted in 13% of cases in Group I and 20% of cases in Group II. Cesarean section was done in 3% of cases in Group I and 17% of cases in Group II.[15]

They concluded that the concentration of bupivacaine and fentanyl achieved during the use of routine CSE for labor was not detrimental to the fetus.[15]

In our study, there was not much difference in fetal heart rate changes.

**CONCLUSION**

The onset of analgesia was equally rapid with both doses of bupivacaine, and the two groups achieved of excellent in major proportion within 5 min. Duration of analgesia was longer in patients who received the larger dose of bupivacaine. This was associated with higher dermatome levels of sensory block which was reflected in corresponding longer time for regression of the block.

We found lower incidence of motor block with bupivacaine 1.25 mg compared with bupivacaine 2.5 mg. Our results also showed a significantly smaller decrease in arterial pressure with bupivacaine 1.25 mg. This is important clinically as maternal hypotension affects uteroplacental perfusion.

**REFERENCES**

1. Maltau JM, Eielsen OV, Stokke KT. Effect of stress during labour on the concentration of cortisol and estriol in maternal plasma. Am J Obstet Gynecol 1979;134:681-4.
2. Holdcroft A. Regional Anaesthetic Techniques. In: Principles and Practice of Obstetric Anaesthesia and Analgesia. Ch. 15. Philadelphia, PA: Black Well Science Publishers; 2000. p. 243-59.
3. Falconer AD, Powles AB. Plasma noradrenaline levels during labour-influence of elective lumbar epidural blockade. Anaesthesiology 1982:37:16-8.
4. Sanguol F, Fox GS, Houle GL. Effects of regional analgesia on maternal oxygen consumption during the first stage of labour. Am J Obstet Gynecol 1975;121:1086-9.
5. Marx GF, Greene NM. Maternal lactate, pyruvate and excess pyruvate production during labour and delivery. Am J Obstet Gynecol 1964;90:786-9.
6. Livinson G, Shnider SM, De Loremen AA, Steffenson JL. Effects of maternal hyperventilation on uterine blood flow and foetal oxygenation and acid base status. Anaesthesiology 1974;40:340-7.
7. Lee BB, Kee WD, Hung VY, Wong EL. Combined spinal epidural analgesia in labour: Comparison of two doses of intrathecal bupivacaine and fentanyl. Br J Anaesthesia 1999;83:868-74.
8. Cohen SE, Tan S, Albright GA, Halpern J. Epidural fentanyl/bupivacaine mixture for obstetric analgesia. Anaesthesia 1987;67:403-7.
9. Stoddant AP, Nicholson KE, Pophain PA. Low dose bupivacaine fentanyl epidural infusion in labour and mode of delivery. Anaesthesia 1994;39:1087-90.
10. Collis RE, Davies DW, Aveling W. Randomised comparative of combined spinal epidural and standard epidural analgesia in labour. Lancet 1996;343:1413-6.
11. Perch MJ, Samantha LF. Banks FRCA. Lyle Gurrih Ph.D. A randomized, double blinded trial of subarchnoid Bupivacaine and fentanyl, with or without clonidine, for combined spinal epidural analgesia during labour. Anaesth Analg 2002;95:1396-401.
12. Wong CA, Scavone BM, Peaceman AM, Mccarthy RJ, Sullivan JJ, Diaz NT, et al. The risk of cesarean delivery with neuraxial analgesia given early versus late in labour N Engl J Med 2005;352:655-65.
13. Lewis M, Calthorpe N. Combined spinal epidural analgesia in labour. Fetal Mater Med Rev 2005;16:29-50.
14. Fernandes R, Bonello E, Gill P, Urquhart J, Reynolds F, Marga B. Neonatal welfare and placental transfer of fentanyl and bupivacaine during ambulatory combined spinal epidural analgesia for labour. Anaesthesia 1997;52:517-24.