A COMPARITIVE STUDY OF BUPIVACAINE AND FENTANYL V/S BUPIVACAINE, FENTANYL AND CLONIDINE IN LABOUR ANALGESIA BY EPIDURAL TECHNIQUE

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ABSTRACT: Pain relief in labour, today, is attracting more clinical and scientific interest. The pain of childbirth is arguably one of the most severe types of pain a woman will experience in her lifetime. Our aim was to compare the duration and quality of analgesia of epidural bupivacaine, fentanyl and combination of epidural bupivacaine, fentanyl, and clonidine by intermittent bolus technique in labour analgesia. Total number of 60 parturients studied was divided into two groups randomly. All of them were between age groups of 18-26 years and their deliveries were expected to be normal vaginal deliveries. Group-I and Group-II are study groups. After delivery an additional dose of the respective drug was given before removal of the epidural catheter for further analgesia. All the newborns in both the groups were assessed for the effect of the drug by determining the APGAR scores immediately after delivery at 1min, 5 mins and 10 mins. Onset of analgesia, Duration of analgesia with the first dose, Total number of doses required, the duration of labor, APGAR score, Motor blockade, type of delivery and Quality of analgesia were the parameters measured. It may be concluded that using a combination of bupivacaine, fentanyl with clonidine during epidural analgesia for labor provides excellent pain relief, prolonged duration of action with simultaneously decreasing the top-ups required, thereby reducing the total local anesthetic requirement compared to bupivacaine with fentanyl.

KEYWORDS: Epidural analgesia, bupivacaine, fentanyl, clonidine, APGAR score, labor analgesia.

INTRODUCTION: “The delivery of the infant into the arms of a conscious and pain free mother is one of the most exciting and rewarding moments in medicine” International association for the study of pain in 1979 defines pain as “An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.”

Pain relief in labour1, today, is attracting more clinical and scientific interest. The pain of childbirth is arguably one of the most severe types of pain a woman will experience in her lifetime. Relief of the pain of childbirth has always been associated with religious & Cultural taboos, myths and controversies. Misinterpretations of biblical scripture “in sorrow thou shalt bring forth children” resulted in centuries of denial of pain relief, as clergy insisted that suffering in labour was consistent with divine intent.

In early 1971, in Sweden, parliament legislated on adequate pain relief in labour. In 1992 the American college of obstetrics and gynecology acknowledged “labour results in severe pain for many women” and ultimately recognized that “maternal request is sufficient justification for pain relief during labour.” Severe labour pains may adversely affect both mother and fetus.
Excessive maternal suffering causes increased mechanical work, marked maternal hyperventilation and increased release of catecholamines which is a physiological response to pain. These natural responses result in maternal hypoxia, hypocapnia leading to decreased uterine blood flow, uterine rhythmicity and contractility. Ultimately these can adversely affect fetus by fetal hypoxia and metabolic acidosis.

The effective pain relief cause reduction in maternal catecholamines, improves utero placental perfusion, uterine contractions become more effective, blunts the hyper – hypo ventilation cycle and adverse haemodynamic response. Thus improve the maternofetal outcome. In the history up to present times there are many approaches to pain relief in labour, such as systemic analgesics, inhalational analgesics and regional anaesthesia.

Out of all regional analgesia techniques, epidural analgesia\(^2\) using local anaesthetics and opioids have gained popularity as effective technique of pain relief. In this technique somatic pain is relieved by local anaesthetics and visceral pain by opioids effectively. Epidural analgesia has advantages in maternal conditions like preeclampsia, respiratory & cardiovascular diseases etc. and the fetal indications are prematurity and IUGR. Due to their excellent analgesia, increase maternal oxygenation and improve fetal outcome.

Many drugs find place in drug armamentarium in regional techniques of obstetric analgesia such as local anaesthetics, opioids, and alpha 2 agonists. Bupivacaine, an amide group of local anaesthetic, is better agent of choice for epidural analgesia for labour. It has long duration of action and produces excellent sensory blockade with less motor block when used in concentrations of 0.0625% to 0.125%. It is having low maternal ratio of 0.3 and minimal effects on neonatal neurobehaviour.

Many opioids like morphine, pethidine, fentanyl, sufentanil and tramadol are used in labour analgesia\(^3\). Fentanyl is a synthetic opioid analgesic, acts upon opioid receptors located in areas of brain and spinal cord. It is widely used for pain relief. Fentanyl has potency of 75 – 125 times that of morphine.

Alpha 2 adrenergic agonist, clonidine, is a selective partial alpha2 agonist with selectivity ratio of about 200:1 in favour of alpha 2 receptors\(^4\). It has different variety of actions including anti-hypertensive effects as well as the ability to potentiate the effects of local anaesthetics and reduces the dose requirement of local anaesthetics. It can provide pain relief by an opioid independent mechanism.

The present study was undertaken to compare Bupivacaine and Fentanyl and combination of Bupivacaine, Fentanyl and Clonidine by intermittent bolus epidural technique in relieving pain during labour\(^5\).

**AIM & OBJECTIVES:** To compare the duration and quality of analgesia of epidural bupivacaine, fentanyl and combination of epidural bupivacaine, fentanyl, clonidine by intermittent bolus technique in labour analgesia.

**MATERIAL & METHODS:** The present clinical study on “Obstetric analgesia by epidural route” has been carried out at Gandhi Hospital, Gandhi Medical College Secunderabad. The study was undertaken to compare the effectiveness of Bupivacaine and Fentanyl v/s Bupivacaine, Fentanyl and Clonidine in relieving pain during labor\(^6\).
A total number of 60 parturients studied were divided into two (2) groups randomly. All of them were between age groups of 18-26 years and their deliveries were expected to be normal vaginal deliveries. Group-I and Group-II are study groups.

Group - I 30 patients Bupivacaine and fentanyl.
Group – II 30 patients Bupivacaine, fentanyl and Clonidine.

Hematological parameters including hemoglobin level, clotting time, bleeding time and Biochemical parameters like blood sugar, blood urea, and serum creatinine were done.

Materials Required: Trolley with towel spread over it, Antiseptic solution for washing hands and cleaning the area of the back, Adhesive tape, Epidural record sheet, Wedge, 18G epidural needle and catheter.

Procedure: All the parturients were explained the procedure of the technique and written consent was obtained. Pulse rate, blood pressure, fetal heart rate were recorded before providing epidural analgesia. An intravenous line was secured with 18G IV cannula and all the parturients were preloaded with 500ml of Ringer lactate. The parturients were placed in left lateral position with hips and knees flexed fully as possible such that the back is perpendicular to the edge of the table. The coronal planes of hips and shoulders should be vertical as nearly as possible so that the median plane is horizontal.

After scrubbing up as for a surgical operation with sterile gown and gloves, the patient’s back was cleaned over an area extending from lower thoracic region to the lower part of the sacrum and including both flanks. The back was draped with a sterile towel with a central hole. Midline approach was used in all cases. Either L₂-₃ or L₃-₄ interspinous space was selected according to the convenience. After local infiltration with 1% lignocaine, 18G epidural needle was placed exactly in midline perpendicular to the skin with the bevel facing upwards. After piercing skin, subcutaneous tissue, supraspinous ligament and interspinous ligament, the stylet was removed and a 5ml syringe was attached with 3 ml of saline. The needle was advanced step by step in millimeters at a time, with simultaneously appreciating pneumatic bounce. Once the epidural space was entered, sudden loss of resistance feel was appreciated at the plunger of the syringe. Epidural space was confirmed with gentle aspiration to ensure that no CSF or blood was aspirated. Care was taken to see that no attempt was made to advance the needle through the ligamentum flavum during active uterine contractions.

Insertion of The Epidural Catheter: With the bevel of the needle directed towards cephalad, the catheter was threaded through the needle while the needle was held steadily. A slight resistance was felt as the catheter enters the epidural space. A further 3-4cm length of catheter was introduced. The needle was withdrawn over the catheter by maintaining pressure on the catheter during withdrawal.

Fixing the Catheter: A gauze piece was placed around the catheter at the site of skin puncture and held in position with waterproof adhesive tape. Catheter was then taped along the midline of the mother’s back towards the right side of the neck. It was attached to the bacterial filter and was covered with a sterile gauze piece.
Test Dose: The position of catheter in epidural space was confirmed once again with aspiration test. 3cc of 1.5% lignocaine with epinephrine (15 mcg) was administered and observed for the development of any subjective symptoms including sensory and motor blockade in the lower limbs, dizziness, light headedness, palpitations and objective signs of rise in pulse rate and blood pressure to rule out either inadvertent intrathecal or intravascular injection of local anesthetic.

The parturients were divided into two groups randomly consisting of 30 parturients in each group.

Group I: This group of parturients received Bupivacaine with fentanyl during the procedure until the delivery of fetus. The loading dose consisted of 10ml of Bupivacaine 0.1% and Fentanyl 2mcg/ml (20mcg). The top up doses were 10-15ml of 0.1% Bupivacaine and Fentanyl 2mcg/ml, administered whenever the parturients complained of pain. When parturients enters into second stage a further 12-15ml was injected with parturients in sitting position or semi-sitting position.

Group II: This group of parturients received Bupivacaine, Fentanyl with clonidine. The loading dose consisted of 10ml of Bupivacaine 0.1%, Fentanyl 2mcg/ml with Clonidine 1.5 mcg/ml. The top up doses were 10-15ml of same solution whenever the parturients complained of pain.

When parturients enter into second stage, then an additional dose of 12-15ml was injected with parturients in sitting position or semi-sitting position.

The stages and progress of labor was monitored with the help of an obstetrician.

TIMING OF INDUCTION OF EPIDURAL ANALGESIA: Epidural analgesia for childbirth is administered in two stages and depending upon the demand of the parturient. Identification of the stage of labor was done with the help of the obstetrician.

(A) Assessment of Stage-I:

1. Presenting part: Engaged
2. Cervical effacement: 100%
3. Cervical dilatation: 2-3cm for primigravida
4. Uterine contractions: Duration>30 seconds

Interval: 3 uterine contractions/ 10 min.

Segmental sensory block T₁₀ - L₁ is required in relation to stretching of uterine tissues and simultaneously dilatation of cervix and stretching of lower segment.

(B) Assessment of Stage-II:

1. Cervical effacement: 100%
2. Cervical dilatation: Complete
3. Uterine contractions: Duration > 30 seconds

Interval: every 3 minutes or less.

4. Clinical findings: Perineal bulging, moderate to severe bearing down pains, completed fetal flexion and internal rotation.
Segmental sensory T₁₀ - S₄ is required in relation to stretching of pelvic structures and perineum added to pain of uterine contractions.

**MONITORING:** Maternal blood pressure, pulse rate, SPO₂, fetal heart rate were monitored every 1-2 minutes for first 10 minutes and then every 5-10 minutes for subsequent 30 minutes and later every half an hour. Progress of labor and side effects if any were noted in the epidural record sheet. During the procedure the supine position was avoided as far as possible, care was taken to ensure that urinary bladder does not become over distended. Intravenous fluid administration through the intravenous cannula was continued throughout the procedure with either Ringer lactate or normal saline depending on the blood pressure of the mother.

After delivery an additional dose of the respective drug was given before removal of the epidural catheter for further analgesia. Catheter was checked for any damage and ensured that no portion of the epidural catheter was retained. The puncture site at the skin was cleaned with antiseptic and covered with adhesive tape over a sterile gauze pieces. All the newborns in both the groups were assessed for the effect of the drug by determining the APGAR scores immediately after delivery at 1min, 5 mins and 10 mins.

**The parameters measured were:**
1. Onset of analgesia: The onset of analgesia was taken as the time from injection of the drug and the time at which parturient appreciated pain relief (in minutes).
2. Duration of analgesia with the first dose: The duration of analgesia with the first (loading dose) was taken as a time from complete pain relief to the time when the parturients first complained of pain (in minutes/seconds).
3. Total number of doses required.
4. The duration of labor was calculated from the initiation of epidural analgesia to the time of delivery of fetus (in minutes).
5. APGAR score - The neonatal outcome was assessed by APGAR scoring system at 1min., 5min., and 10min intervals.
6. Quality of analgesia - Visual Analogue Pain Scale (VAPS) assessed pain at different time intervals.
7. Mode of delivery - was recorded as normal spontaneous vaginal deliveries, vaginal deliveries with instrumental intervention and cesarean section.
8. Motor blockade – assessed by Bromage scale.

**BROMAGE SCALE:**

| Description                                              | Score |
|----------------------------------------------------------|-------|
| No motor block, full flexion of knee and foot            | 0     |
| Inability to raise extended leg, just able to move knee  | 1     |
| Inability to flex knee but able to move foot only        | 2     |
| Inability to flex ankle joint, unable to move foot or knee | 3     |
**Exclusion Criteria:** Parturients were thoroughly assessed such that the parturients having associated diseases like PIH, heart disease and diabetes mellitus were excluded from the study.

**Inclusion Criteria:** All ASA Grade I who were between age groups of 18-26 years and their deliveries were expected to be normal vaginal deliveries with no other co-morbid conditions like PIH, diabetes, heart and renal diseases were included in the study.

**RESULTS:** In our study data was expressed as mean + standard deviation where appropriate, statistical analysis for parametric data which included age, height, weight, cervical dilatation, onset of analgesia, duration of analgesia, number of top up doses, drug delivery interval time. Probability values < 0.001 were considered as statistically significant.

| Group-I | Group-II |
|---------|----------|
| Mean    | 22.20    | 22.46    |
| Standard Deviation | +1.72 | +1.65 |

**Table I: Age Distribution**

The P value is 1.0, Table 1 shows age distribution which is comparable in both the groups, P is >0.001 so it is not statistically significant with regarding to parturient's age among both groups.

| Group-I | Group-II |
|---------|----------|
| Mean    | 155.5    | 155.0    |
| Standard Deviation | +3.65 | +2.81 |

**Table II: Height Of the patients**

The P value is 0.619.

Table II shows height of the patients, the P value is > 0.001 which is not statistically significant. Indicating the mean height is comparable in both the groups.

| Group-I | Group-II |
|---------|----------|
| Mean    | 60.86    | 60.40    |
| Standard Deviation | +3.61 | +3.66 |

**Table III: Weight of the patients**

The P value is 0.633. Table III shows mean weight of the patients which is comparable in both the groups, The P value is > 0.001 which is not statistically significant.

| Group-I | Group-II |
|---------|----------|
| Mean    | 3.06     | 3.16     |
| Standard Deviation | +0.44 | +0.59 |

**Table IV: Initiation of epidural analgesia**
Table IV shows that P value is > 0.001 which is not statistically significant. So in most of the parturients the epidural analgesia was initiated when the cervical dilatation was 3cms in both the groups.

|                | Group-I | Group-II |
|----------------|---------|----------|
| Mean           | 7.56    | 7.13     |
| Standard Deviation | +1.19   | +1.38    |

Table V: Onset of Analgesia

The ‘P’ value is 0.157, Table V shows mean onset of analgesia which is comparable in both the groups. P >0.001, which is statistically insignificant.

|                | Group-I | Group-II |
|----------------|---------|----------|
| Mean           | 76.2    | 97.3     |
| Standard deviation | +5.98   | +5.98    |

Table VI: Duration of Analgesia with First Dose

Table VI shows that mean duration of analgesia which is more in group-II parturients compared to group-I parturients. The ‘P’ value is < 0.001. So, it is statistically significant.

|                | Group-I | Group-II |
|----------------|---------|----------|
| Mean           | 4.53    | 3.4      |
| Standard deviation | +0.77   | +0.67    |

Table VII: Total Number of Doses Required

Table VII shows that the group-I parturients required more number of doses than group-II parturients. The ‘P’ value < 0.001, which is statistically significant.

|                | Group-I | Group-II |
|----------------|---------|----------|
| Mean           | 301.3   | 309.2    |
| Standard deviation | +42.22  | +41.32   |

Table VIII: Duration of Labor (Drug-Delivery Time)

Table VIII shows that mean duration of labor which is comparable between group-I and group-II parturients. The ‘P’ value > 0.001. It is statistically not significant.

|                | 1Min | 5Min | 10Min |
|----------------|------|------|-------|
| Mean Gr-I      | 7.23 | 8.83 | 10    |
| Mean Gr-II     | 7.33 | 8.76 | 10    |

Table IX: ‘APGAR’ scores
Table IX shows the APGAR scores which are comparable in both groups at all times. The P values for 1 min, 5 min, 10 min, is > 0.001, which is statistically insignificant.

|                | No pain 0(cm) | 1-3(cm) | 4-6(cm) | 7-9(cm) | Worst pain 10(cm) |
|----------------|---------------|---------|---------|---------|------------------|
| Group – I      | 15(50%)       | 9(30%)  | 6(20%)  | -       | -                |
| Group – II     | 25(83%)       | 4(13%)  | 1(3.3%) | -       | -                |

Table X: Quality of Analgesia (visual analogue pain scale)

Table X shows that parturients of Group-II had better quality of analgesia than Group-I Parturients.

|                | Spontaneous   | Instrumental deliveries | Cesarean section |
|----------------|---------------|-------------------------|------------------|
| Group-I        | 24(80%)       | 5(16.6%)                | 1(3.3%)          |
| Group-II       | 24(80%)       | 4(13.3%)                | 2(6.6%)          |

Table XI: Mode of Delivery

Table XI shows that instrumental deliveries are slightly less in group-II parturients compared to group-I parturients.

| Bromage score | Group – I | Group – II |
|---------------|-----------|------------|
| 0             | 30 (100%) | 30 (100%)  |
| 1             | -         | -          |
| 2             | -         | -          |
| 3             | -         | -          |

Table XII: Motor Blockade (Bromage Scoring Method)

Table XII shows the bromage scoring which is comparable in both the groups at all the times.

We did not observed any side effects like pruritis, respiratory depression in our study.

**DISCUSSION:** Labor pain is a subjective experience with sensory and emotional components. The intensity of pain during labor is related in large measure to emotional tension. Epidural analgesia using low concentration of local anesthetic and opioid, gained wide popularity, addition of Clonidine has improves safety and effective pain relief during labor.

The present clinical study is undertaken to compare Bupivacaine and Fentanyl V/s Bupivacaine, Fentanyl and Clonidine in relieving the pain and its effect on neonatal outcome.

A total number of 60 parturients, all primigravidae belonging to ASA-I & II were selected and randomly divided into two groups of 30 each. The parameters observed were onset of analgesia, duration of analgesia with loading dose, total number of doses required during the labor, APGAR scores at 1min, 5min, 10min and expression of parturients regarding pain relief. Fetal heart rate, level of sensory block and level of motor block are noted and statistically
analyzed. In a study conducted by D. Celleno et al, 1995 concluded that, there was no difference between bupivacaine, fentanyl group and bupivacaine, fentanyl, Clonidine group in onset of analgesia. In our study the onset of sensory blockade is comparable in both Group-I and Group-II, it is statistically insignificant.¹

Tremlett et al, 1999, conducted a study with two different doses of clonidine with control group of bupivacaine alone, they observed that duration of analgesia with 1st dose is increased, number of top ups required was less in Clonidine group than in control group.²

In our study the mean duration of analgesia with 1st dose in group-II is more than that seen in the group – I. And the requirement of top up doses is also significantly less in the Group-II when compared to that in the Group – I.

Study done by Brigitte et al. (1998) concluded that Clonidine improves duration of analgesia and quality of analgesia in Clonidine added to bupivacaine – epinephrine – sufentanil group compared with control group.³

In a study by Michael J. Paech et al. (2000), concluded that addition of Clonidine to epidural bupivacaine and fentanyl in labor has improved analgesia, reduced supplementation rate.⁴ In our study quality of analgesia is better in Group – II compared to Group – I as assessed by visual analogue scale, which could be due to addition of Clonidine to local anesthetic and opioid.

Robert K. Parker et al. (2007) observed APGAR scores were nearly identical in both groups.⁵ In a study by Tremlett et al. also found that there were no adverse effects on the new born infants. M.E. O’Meara and T. Gin noted that no differences in the fetal heart rate, mode of delivery, APGAR scores of neonates in both groups.

In our study APGAR scores of the newborn in 2 groups is comparable and correlates with these studies. In our study the mode of delivery in both the groups was comparable, the requirement of instrumental intervention and caesarian section were almost similar in both the groups. These are correlates with study by D. Chassard et al. (1996).⁶ In our study motor blockade is comparable in both groups, and statistically insignificant. This is correlates with no motor blockade by D. Celleno et al. (1995).

CONCLUSION: Sixty parturients in the age group of 18-26 years belonging to ASA grade I & II, all being primigravidae were randomly selected and divided into 2 groups of 30 each. Thorough haemodynamic monitoring of the mother and fetus were done during the procedure. The duration of analgesia with the 1st dose was significantly longer in duration in the Group-II. The requirement of top up doses was also less in Group-II. The quality of analgesia is better in bupivacaine, fentanyl and clonidine than in bupivacaine and fentanyl group. There was no significant increase in the requirement of instrumentation, surgical intervention in both the groups. Neonatal outcome was good and almost equal in both the groups without any respiratory depression even with addition of low dose of clonidine by epidural route. From this study it may be concluded that using a combination of bupivacaine, fentanyl with clonidine during epidural analgesia for labor provides excellent pain relief, prolonged duration of action with simultaneously decreasing the top-ups required, thereby reducing the total local anesthetic requirement compared to bupivacaine with fentanyl.
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