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Research Article

Comparison between Continuous Epidural Infusion and Intermittent Epidural Bolus of Bupivacaine Fentanyl Combination for Labour Analgesia

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Abstract: Labour analgesia has become almost synonymous with central neuraxial analgesia. Various techniques are in use from single epidural injection, continuous epidural infusion, combined spinal epidural, patient controlled epidural analgesia to programmed intermittent epidural bolus. Each method has its own advantages and disadvantages though the purpose remains the same:a painless labour and a healthy neonate. We have compared two methods (continuous infusion and intermittent bolus) of epidural analgesics in our study. Sixty women were divided into two groups (Group A = 30 and Group B = 30) to receive either intermittent boluses or continuous infusion of a combination of bupivacaine and fentanyl (0.125% bupivacaine and 2microgram/ml fentanyl) in the first stage of labour. Pain relief was better in the intermittent bolus group (lower VAS score) with less requirement of rescue analgesics (four in Group A and twelve in Group B). Incidence of side effects was similar in both the groups. Timed intermittent boluses of epidural analgesics provided better analgesia than a continuous infusion of the same mixture. This method can be advocated where infusion pumps and automated delivery devices are not readily available in the labour suites.
Keywords: labour analgesia, bupivacaine and fentanyl, intermittent bolus, continuous infusion

INTRODUCTION

Labour pain is one of the most intense pains a woman can experience. Epidural analgesia is the most popular techniques of labour pain management and has evolved from intermittent bolus injections to continuous infusions with or without patient controlled epidural analgesia (PCEA). Intermittent bolus administration of epidural local anaesthetics has been recognised for many years to be more efficacious than continuous infusions.

This study was carried out to find which of the techniques, intermittent bolus or continuous infusion of a combination of bupivacaine and fentanyl was superior in terms of drug requirement (primary outcome), better maternal analgesia and lesser incidence of maternal and foetal adverse effects.

PATIENTS AND METHODS

This prospective randomized single blind study was carried out in our institution over a period of one year. Approval from Hospital Ethics Committee was obtained. Mothers attending antenatal clinic were assessed for eligibility.

Inclusion criteria:

- ASA Grade I &II
- Nulliparous
- Uncomplicated pregnancy
- Cephalic presentation
- Full term (> 37wks)
- Cervical dilatation 2 - 5 cm
- At least one uterine contraction every 2 – 3 min

Exclusion criteria:

- Body weight > 110 kg
- Height < 140 cm
- Cervical dilatation > 5cm
- Parenteral opioids within 2 hrs
- Hypersensitivity to drugs
- Neurological/psychiatric disease
- Any irregularity in foetal heart rate

Sample size was calculated using the difference of mean visual analogue pain scores as the main criterion for calculation. According to a previous study by Sia A, Chua S [1] the mean (SD) visual analogue pain scores at four hours was 36(20) mm in the continuous group and 12(7) mm in the intermittent group. Assuming the alpha risk at 5% and power of the study at 0.8 the sample size in each group was calculated as 11. Allowing for loss of cases due to inadequate analgesia, misplaced catheters and early delivery, the sample size of 62 was chosen. One hundred and nineteen parturients were assessed for eligibility, 57 met the exclusion criteria and 2 opted out of the study. Sixty mothers were taken up and

randomized into two groups according to the drug delivery technique (intermittent bolus group and continuous infusion group).

Parturients attending antenatal clinic who met the inclusion criteria were explained the benefits and risks of labour analgesia. Those who consented for the procedure underwent a thorough preanaesthetic check up. The randomization was done by lottery of sealed envelope marked A and B.

In the operation theatre, the necessary monitors were attached to the mother. After intravenous cannulation with 18G cannula, the parturient was preloaded with 15ml/kg Ringer Lactate (RL) solution over 20 – 25 min. The procedure was started with the mother in left lateral position. A 18G Tuohy needle was inserted at the L_4 /L_5 interspace with full aseptic precautions. A 20G multiorifice epidural catheter was advanced through the needle up to 3 – 5 cm in the epidural space. A 5ml test dose of 0.125% bupivacaine was injected between the uterine contractions. After waiting for 5min another 10ml of 0.125% bupivacaine was injected slowly. Time zero started on achievement of bilateral T10 sensory block. The parturients were then transferred to the labour room.

All parturients were given a mixture of 0.125% bupivacaine and 2microgram/ml fentanyl. Group A mothers received intermittent boluses and Group B mothers received a continuous infusion. The study solution was prepared in 50ml syringes. 25ml of 0.25% bupivacaine and 100 microgram fentanyl were diluted in normal saline to make a total volume of 50ml. The resultant solution consisted of 50ml 0.125% bupivacaine and 2microgram/ml fentanyl. Two such 50 ml syringes containing the study solution was prepared for each parturient. The first syringe was fitted on the infusion pump and connected to the epidural catheter. The second syringe was kept ready to administer rescue bolus.

In Group A the infusion pump was not started, but a bolus of 10ml was administered at 60min interval. In Group B the infusion pump was started to deliver at the rate of 10ml/hr. The pumps were covered so that the person making the observations did not know the mode of drug delivery.

Baseline cervical dilatation, foetal heart rate, blood pressure, pulse and oxygen saturation were recorded and monitored throughout the period of study. Pain was measured using a 0 -100 mm visual analogue scale (VAS 0mm = no pain, VAS 100mm = worst pain imaginable). VAS was assessed every 5min for the first 15min and subsequently every 30min for the next 5hr. VAS < 30mm even at the height of uterine contraction was considered as effective pain control. Breakthrough pain meant VAS > 30mm requiring a top up of 10ml study solution (0.125% bupivacaine and 2microgram/ml fentanyl).

Adverse effects such as hypotension, bradycardia, pruritis, urinary retention, nausea and vomiting were noted. Progress of labour was managed by the obstetrician.

The mothers were allowed sips of water and fruit juices. They were nursed in left lateral position with intermittent posture changing. Ambulation was not encouraged but allowed only in the presence of attendants.

Statistical analysis:

Observations were tabulated and analyzed statistically. It was performed by SPSS for Windows (version 7.0). Comparisons of continuous data with a normal distribution were performed using the independent t-test and were presented as mean ± standard deviation (SD). Continuous, but not normally distributed data, were analyzed using the Mann – Whitney U – test. Categorical variables were analyzed with Contingency tables using Chi-Square test and Fisher exact test when the number of values was less than 5. Statistical test was considered significant when p value was < 0.05.

RESULTS:

The demographic profile, baseline vital signs, gestational age, cervical dilatation and Visual Analogue Scale scores were comparable in Group A and Group B. (Table 1 and Table 2).

The VAS score in Group A (intermittent bolus) was similar to that of Group B (continuous infusion) in the first 2hr of study period ($p > 0.05$). From 2.5hr to 5hr the VAS score in Group A was significantly lower than VAS score in Group B. The maximum difference was observed at 3.5hr ($p < 0.01$). (Table 3 and Figure 1)

Table 1: Demographic Profile

	Group A (n = 30)	Group B (n = 30)
Age (years) Mean +/- SD	23.33 +/- 2.56	23.57 +/- 2.54
Body weight (kg) Mean +/- SD	62 +/- 1.74	62.30 +/- 1.75
Height (cm) Mean +/- SD	156.63 +/- 4.46	156.17 +/- 4.67
Gestational age (weeks) Mean +/-SD	39.58 +/- 3.67	39.12 +/- 2.56

Table 2: Pre procedure vital signs and VAS score

	Group A (n = 30)	Group B (n = 30)
Heart rate (beats/min) Mean +/- SD	89.23 +/- 5.35	88.37 +/- 5.05
Oxygen saturation (%) Mean +/- SD	97.57 +/- 1.25	97.13 +/- 1.76
Systolic Blood Pressure (mm Hg) Mean +/- SD	125.13 +/- 5.49	124.60 +/- 3.95
Diastolic Blood Pressure (mm Hg) Mean +/- SD	78.23 +/- 3.67	78 +/- 3.29
Mean Arterial Pressure (mm Hg) Mean +/- SD	94.19 +/- 3.39	93.49 +/- 2.94
Cervical dilatation (cm) Mean +/- SD	3.57 +/- 0.97	3.37 +/- 0.92
Foetal heart rate (beats/min) Mean +/- SD	128 +/- 7.04	129 +/- 7.37
VAS score (mm) Mean +/- SD	56.47 +/- 11.70	56.53 +/- 12.50

Table 3: VAS score during the study period

Time	Group A VAS score (mean +/- s d)	Group B VAS score (mean +/- s d)
0 hr	27.40 +/- 8.93	26 +/- 8.76
30 min	3.77 +/- 7.83	2.20 +/- 6.04
1 hr	1.63 +/- 5.00	1.60 +/- 4.91
1hr 30 min	2.27 +/- 6.12	2.17 +/- 5.89
2 hr	3.93 +/- 8.25	3.93 +/- 8.34
2hr 30 min	5.73 +/- 13.84	12.17 +/- 15.83
3 hr	5.17 +/- 12.85	15.97 +/- 20.19
3 hr 30 min	2.45 +/- 7.52	15.40 +/- 17.94
4 hr	1.79 +/- 4.61	14.80 +/- 15.69
4 hr 30 min	4.59 +/- 14.03	11.83 +/- 13.07
5hr	3.07 +/- 6.35	9.00 +/- 9.14

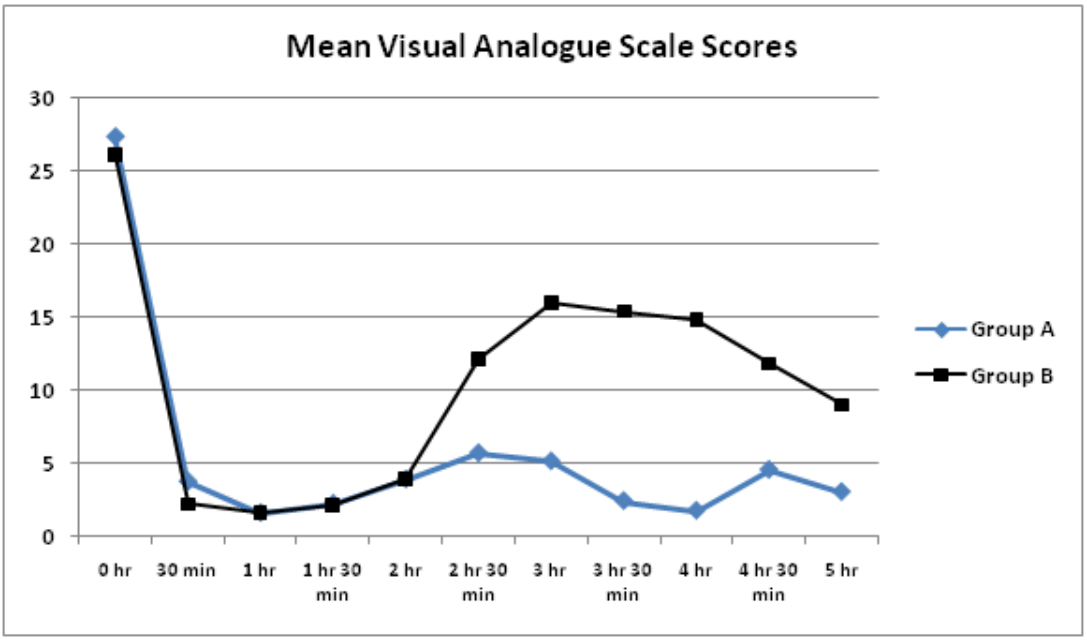

Figure 1: VAS score during the study period

Rescue analgesia was not required for the mothers in either group in the first and second hour of study. After that the requirement of rescue bolus was significantly higher in Group B than in Group A.(Figure 2) Three mothers in Group A and seven mothers in Group B required a single rescue bolus ($p < 0.05$). Two rescue boluses had to be administered to 1 mother in Group A as compared to 5 mothers in Group B ($p < 0.05$).

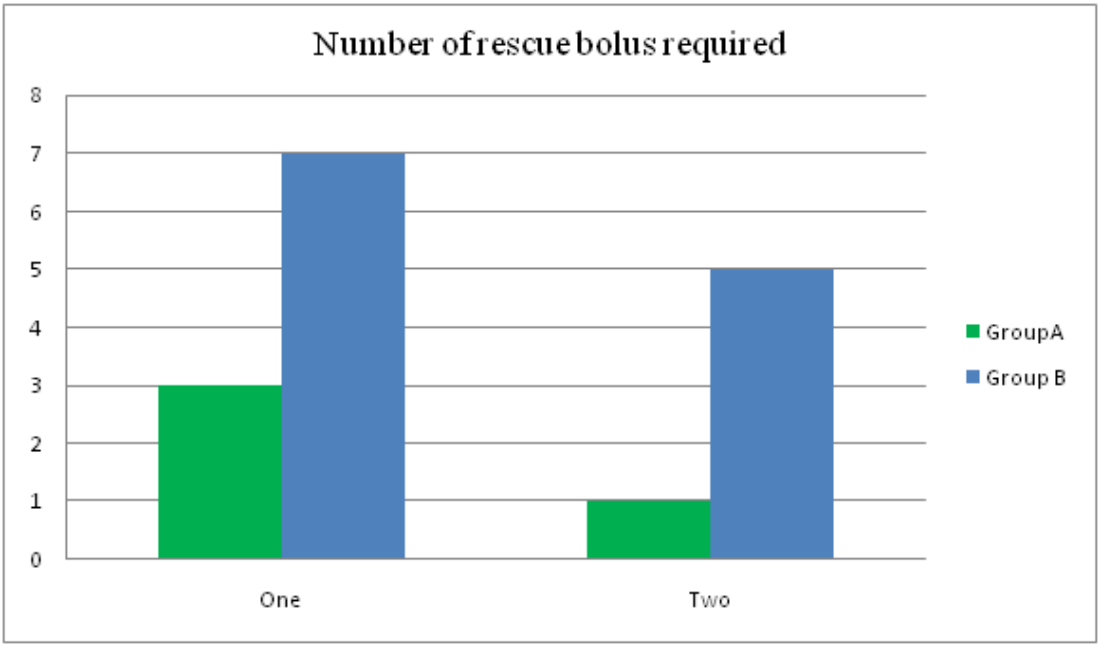

Figure 2: Requirement of rescue bolus

As the number of rescue boluses were less in Group A than in Group B, the total amount of drug consumed (bupivacaine and fentanyl) in Group A was significantly less than that in Group B ($p = 0.022$).Table 4.

Table 4: Drug consumed

	Group A (n = 30)	Group B (n = 30)
Bupivacaine (mg) Mean +/- SD	83.40 +/- 5.85	88.33 +/- 9.67
Fentanyl (microgram) Mean +/- SD	103.45 +/- 9.36	111.33 +/- 15.48

Table 5: Adverse Effects

	Group A (n = 30)	Group B (n = 30)
Hypotension	3	4
Bradycardia	1	2
Desaturation	4	4
Pruritus	1	2
Nausea/Vomiting	2	4
Urinary retention	1	3

The incidence of adverse effects was similar in the two groups.(Table 5)

DISCUSSION

Labour analgesia is a challenging journey with gratifying end points. Any drug or intervention of the parturient is automatically experienced by the foetus. Labour analgesia has grown from chloroform to the Queen in the 19th century [2] to automated central neuroaxial delivery devices of the 21st century [3]. The search for an ideal technique or drug continues as it has to produce effective pain control to the mother without any adverse physiological effect to the foetus.

Nulliparous women have longer duration of labour and more intense pain than multiparous women. Also the rate of cervical dilatation, neonatal weight, time of epidural catheter placement are predictors of breakthrough pain in labour analgesia.[4] To avoid these confounding factors we chose only nulliparous women in the first stage of labour and placed the epidural catheter when cervical dilatation was between 2 to 3 cm. The study duration was limited to 5hrs, so that none of the parturients delivered during that time.

In the 1960s administration of epidural analgesics either via the lumbar or the caudal route was considered to be the ultimate in providing pain relief for the parturient.[5] This was a breakthrough as the maternal and foetal adverse effects of systemic analgesics could now be avoided. Epidural injection of 4 to 6 ml lignocaine at hourly interval in the first stage

of labour did not markedly prolong the duration of labour, excellent analgesia was achieved and the Apgar score of the baby remained above 7.[6]

Epidural opioids have gained popularity over the last three decades. This route was welcome as there was less total dose requirement, decreased systemic adverse effects and did not cause foetal depression.[7] There have been controversies about prolongation of labour, uterine dystocia and increased requirement of instrumentation with the use of central neuraxial opioids for labour analgesia. However, exact cause effect relationships could not be established. [8]

After placement of the epidural catheter labour analgesia can be maintained by intermittent boluses, continuous low-dose infusions, patient controlled epidural analgesia (with or without background infusion) and combined spinal-epidural analgesia.[9]

With increased availability of infusion pumps, the use of continuous infusion of analgesics became more widespread. There have been reports that continuous epidural infusion of local anaesthetics produce better uninterrupted analgesia when compared with intermittent bolus injections.[10, 11] Duncan et al reported better quality of analgesia by intermittent bolus compared to continuous infusion of extradural bupivacaine after lower abdominal surgery.[12] There was significantly less consumption of bupivacaine over 24hrs in the intermittent bolus group than in the continuous infusion group. In our study too there was significantly less consumption of bupivacaine in the intermittent bolus group than in the continuous infusion group ($p = 0.022$). In our study the VAS score remained below 6mm in the intermittent bolus group whereas it rose above 15mm in the continuous infusion group.

Several mechanisms have been proposed to explain the better quality on analgesia obtained by intermittent bolus injections through the epidural catheter. Kaynar and Shankar used methylene blue and white semiabsorbent paper to demonstrate that intermittent boluses through the epidural catheter have a wider spread than continuous infusion. This probably contributes to the better quality of block in the clinical setting. [13] Shankar et al administered bupivacaine 0.125% and fentanyl 2 microgram/ml to forty parturients either in continuous infusion or intermittent boluses and concluded that the higher driving pressure in the intermittent boluses probably result in better spread of local anaesthetic in the epidural space, thus reducing need for additional top-ups.[14] In cadaveric study, cryomicrotome section examination showed that the distribution of solution in the epidural space is nonuniform. When high pressure is used to inject the solution, it spreads as rivulets through numerous small channels rather than a unified front. The solution preferentially travels along the nerve root sheath through the intervertebral foramina. This probably explains why block is better when local anaesthetic is injected with higher pressures as in intermittent bolus.[15] Ginosar et al suggested that the lipophilic opioids like fentanyl bind more in the spinal cord receptors when delivered in bolus into the epidural space. Whereas continuous infusion of epidural fentanyl produces nonsegmental analgesia due to binding in the brain.[16]

Capogna et al found that in nulliparous women with spontaneous onset of labour, the maintenance of epidural analgesia with programmed intermittent epidural anaesthetic bolus compared to continuous epidural infusion resulted in less motor block during labour and was associated with lower incidence of instrumental vaginal delivery.[17] In a meta-analysis van der Vyver et al concluded that patient controlled epidural analgesia reduced the number of unscheduled rescue top-ups, less amount of total drug administered and less motor block of lower extremities when compared with continuous epidural infusion. Both methods were safe for the mother and newborn.[18] In a systemic review and meta-analysis George et al concluded that intermittent epidural bolus slightly reduce local anaesthetic usage and improve maternal satisfaction when used for labour analgesia.[19]

In conclusion we can say that timed intermittent epidural bolus of local anaesthetic and lipophilic opioid is a good choice for providing labour analgesia. This method has the advantage that it can be used by manual injections even where automated programmable drug delivery devices are not readily available in the labour suites.

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