

## **“Quality of Analgesia with Adjuvants to Epidural Bupivacaine in Active Labor: An Observational Study”**

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### **Abstract**

Labor pain is excruciating and a significant contributor of stress and anxiety. Among various methods of labor analgesia, epidural analgesia has been considered incomparable due to its proven efficacy and flexibility with maternal satisfaction. Total 84 parturients in active labor were included in study. Epidural block was performed using 75 µg clonidine (Group C; n=41) or 50 µg fentanyl (Group F; n=43) combined with 0.125% bupivacaine (10ml). Maternal and fetal vital parameters were measured. Analgesia was evaluated using a visual analogue score (VAS), sedation was scored using a five point scale, neonatal outcome was evaluated by APGAR score.

Results: Demographically, patients were comparable between the groups. Hemodynamic parameters were comparable within and between the groups ( $p > 0.05$ ). The number of epidural top-ups and total bupivacaine requirement were significantly higher in bupivacaine fentanyl group as compared to bupivacaine clonidine group.

Keyword: Epidural labor analgesia, fentanyl, clonidine, bupivacaine.

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### **I. Introduction**

Labor is one of the most painful experiences a woman may face during her lifetime. Providing effective and safe analgesia during labor has remained an ongoing challenge for anaesthesiologists<sup>[1]</sup>.

There are various methods of providing pain relief to laboring mother, but neuraxial analgesia has been considered incomparable due to its proven efficacy and flexibility with maternal satisfaction<sup>[2]</sup>. Low dose bupivacaine 0.125% and 0.0625% has been reported to produce satisfactory analgesia for labor<sup>[3]</sup>. The advantages of using low concentrations are the avoidance of unpleasant awareness of numbness and motor block and lower plasma level of drug in mother and child<sup>[4]</sup>.

## **II. Method**

After approval from the Institutional Scientific and Ethics Committee we studied 84 women of ASA physical status II with singleton vertex pregnancy of at least 37-42 weeks gestation with cervical dilatation of 3-5 cm in spontaneous labor willing for epidural labor analgesia. Study was conducted from February 2018 – April 2019. Parturients with pregnancy induced hypertension(PIH), diabetes mellitus(DM), preterm labor, breech presentation, history of previous caesarean delivery, bad obstetric history, bleeding dyscrasias, spinal deformities, on anticoagulants, hypotension, morbid obese, elderly patients >35 years, having allergy to local anaesthetics, opioids and who refused consent agreement were excluded from the study. Informed and written consent about the anaesthetic procedure was obtained from the patient.

Patient was taken to preoperative preparation room where 18 G cannula was inserted for intravenous access. Monitoring of vital parameters -heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), arterial oxygen saturation (SpO<sub>2</sub>) was done using multipara monitor (BPL-Excello-ECO). Baseline vital parameters and visual analogue score (VAS) were recorded. All patients were hydrated with 10 ml/kg ringer lactate solution preoperatively. Premedication was with injection ranitidine 50 mg and injondansatron 4 mg. Then the parturient was positioned in the sitting position. Under all aseptic precautions, epidural space was identified at L2-L3/L3-L4 interspace and infiltrated with lignocaine 2% with adrenaline. An 18 G Tuohy needle was then inserted in the epidural space which was confirmed by the loss of resistance to air technique. A 20 G multiorifice epidural catheter was inserted into the epidural space and fixed at 4 cm. A test dose of 2% lignocaine with adrenaline 3 ml was injected. Patient was observed for 10 min for any signs of accidental intravascular or intrathecal administration. None of the patient had any such signs. Then the patients were randomly divided by computer generated random number table into 2 groups; drugs were given via epidural catheter according to the groups

Group C – 10 ml of inj. bupivacaine 0.125% with 75 µg clonidine

Group F – 10 ml of inj. bupivacaine 0.125% with 50 µg fentanyl. After each drug administration, vital parameters of the patient (HR, SBP, DBP, MBP, RR, SpO<sub>2</sub>), VAS, maximum sensory & motor blockade level achieved and fetal heart rate were monitored at every 5 min for initial 30 min and then every 15 min after each top-up till delivery.

After the initial dose, top up doses (10 ml bupivacaine 0.125% with similar concentrations of clonidine or fentanyl) were injected when pain recurred or when VAS >3 and further top-ups were done with 10 ml of plain 0.0625% bupivacaine without any adjuvants.

Sensory block was assessed by pin prick with 23 G needle in mid-clavicular line, every 5 min till maximum level was achieved. Motor block was assessed using modified Bromage scale. (bromage 0= Free movement of legs, feet with ability to raise extended legs, bromage 1= Inability to raise extended legs, but able to move knees and feet, bromage 2= Inability to raise extended legs or move knees, but able to move feet, bromage 4= Inability to raise extended legs, flex knees, ankle or move toes). Baseline pain intensity was defined as the intensity of pain assessed just prior to the block, measured with 10 cm visual analogue pain scale (VAS) where 0 – no pain and 10 – worst pain.

Duration of analgesia was defined as the time taken from the onset of analgesia to first feel of uncomfortable contractions by the patient. Onset of analgesia was defined as the time to reach T10 dermatome level. Maternal satisfaction level was assessed by parturient's acceptance regarding quality of analgesia throughout labor by following scoring system (Excellent- when mother was completely pain free from the 1<sup>st</sup> or the 2<sup>nd</sup> injection until the end of delivery, Good- when the mother was satisfied but some pain was experienced for a short period during labor or delivery, Incomplete- when the mother had significant pain relief, but experienced some pain during most of the time of labor and delivery, Failure- when, after the start of epidural analgesia, pain was experienced during most time of labor and delivery)

Fetal outcome was evaluated by APGAR score at 1<sup>st</sup> and 5<sup>th</sup> minute. Side effects like hypotension, nausea, vomiting, maternal sedation (0 = awake, 1 = drowsy, 2 = dozing, 3 = asleep), pruritus (0 = no pruritus, 1 = pruritus present, 2 = pruritus present necessitating treatment) shivering, respiratory depression, maternal bradycardia, dry mouth and degree of motor block (modified bromage scale) were recorded.

Statistical analysis was performed using graph pad in stat software. Results were analysed by various statistical percentage, mean and standard deviation. The unpaired student t test was applied to compare the mean of two independent samples. p Value < 0.05 and < 0.001 was considered as significant and highly significant respectively.

## **III. Results**

There were 41 parturients in bupivacaine-clonidine group (group C) and 43 parturients in bupivacaine-fentanyl group (group F). There was no difference between groups in age, weight, height, parity, gestational age and cervical dilatation before insertion of epidural catheter.

There was no difference between groups in initial VAS, onset of sensory block, maximal height of block. Mean time for onset of analgesia in group F was  $13.84 \pm 3.36$  min and  $11.75 \pm 3.37$  min in group C and there was no statistically significant difference between the groups ( $p=0.067$ ). Duration of analgesia after the first injection was longer in the bupivacaine-clonidine group when compared with bupivacaine-fentanyl group,  $136.7 \pm 22.7$  min and  $127.2 \pm 25.6$  min respectively. Base line & mean VAS after each and every top-up till delivery was comparable between the groups during the entire duration of labor ( $p>0.05$ ). Maternal satisfaction score, neonatal outcome at 1 and 5 min were comparable between the groups.

Average duration of 1<sup>st</sup> stage of labor was  $430.4 \pm 35.29$  min in group F and in group C it was  $435 \pm 27.19$  min while duration of 2<sup>nd</sup> stage of labor in group F was  $42.20 \pm 12.25$  min and in group C it was  $44.60 \pm 11.72$  min, the difference in time was statistically not significant ( $p>0.49, 0.47$  respectively). The average number of epidural top-ups used in our study was  $2.92 \pm 1.17$  &  $2.36 \pm 1.1$  in Group F and Group C respectively, this difference was statistically significant ( $p=0.03$ ). Total amount of bupivacaine used was  $30.03 \pm 8.68$  mg &  $25.33 \pm 9.6$  mg in group F and group C respectively, this difference was statistically significant ( $p=0.02$ ).

There were no differences between groups in heart rate, systolic, diastolic or mean blood pressure during entire duration of labor. Bradycardia was observed in 1 patient in group C while none in group F ( $p=0.53$ ). 5 patients in group F and 7 patients in group C ( $p=0.71$ ) experienced nausea but none of the patient experienced vomiting during the entire duration of labor. Maternal sedation was seen in 2 patients in group F 5 patients in group C ( $p=0.48$ ), both the patients in group F and 3 patients in group C were drowsy (score 1) at 30-60 min after establishment of epidural analgesia. Two patients in group C were asleep (score 3) at 60-90 min after initiation of epidural analgesia but none of the patient was unarousable at any point of time.

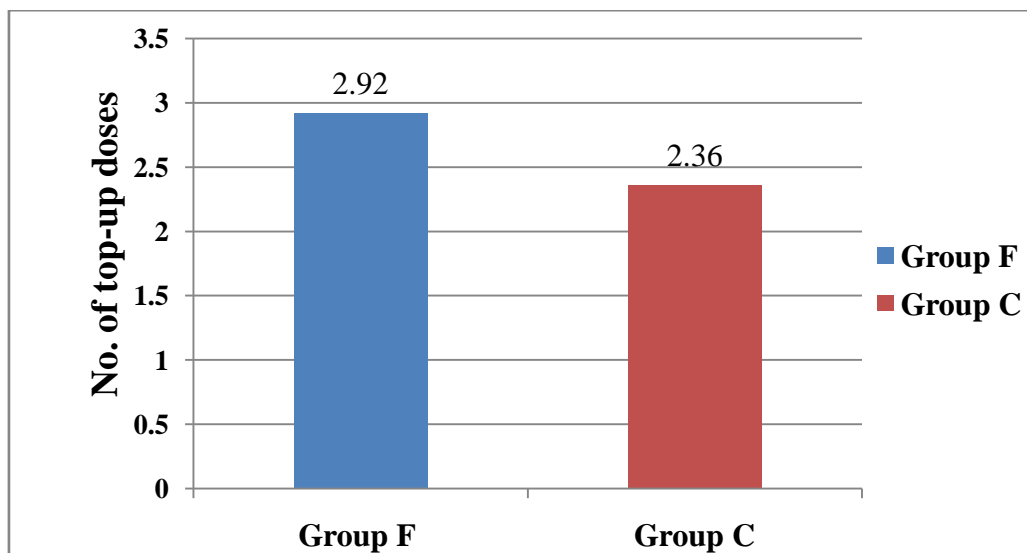
**Table 1: Demographic data, onset & duration of analgesia, mode of delivery, APGAR Score.**

	Group F	Group C	p Value
Age (years)	23±3.6	24±3.3	0.710
Weight (kg)	41.9±3.1	44±4.8	0.365
Height (cm)	155±6.4	154±7.0	0.52
Parity	1.36±0.48	1.32±0.31	0.344
Onset of analgesia (min)	13.84 ± 3.36	11.75 ± 3.37	0.067
Duration of analgesia (min)	127.2 ± 25.6	136.7 ± 22.7	0.084
<b>Mode of delivery</b>			
Spontaneous	27 (62.7%)	23 (56%)	0.67
Instrumental	12 (27%)	13 (31%)	0.89
Caesarean	4 (9%)	5 (12%)	0.82
<b>APGAR Score</b>			
1 min	8.07 ± 0.7	7.52 ± 0.55	0.56
5 min	9.07 ± 0.7	9.02 ± 1.4	0.41

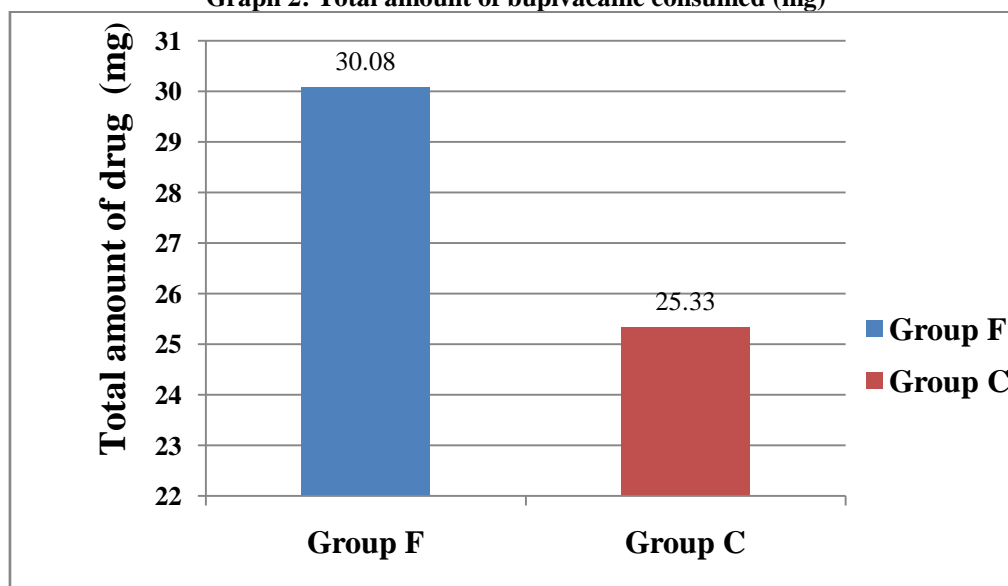
**Table 2 :Incidence of adverse events**

Adverse Events	Group F	Group C	p Value
Hypotension	06	10	0.52
Maternal sedation	02	05	0.48
Nausea	05	07	0.71
Vomiting	0	0	–
Bradycardia	0	01	0.53
Pruritus	02	0	0.39
Respiratory depression	0	0	–
Dry mouth	0	0	–
Shivering	0	0	–

**Graph 1 : Number of top-up doses**



Graph 2: Total amount of bupivacaine consumed (mg)



#### IV. Discussion

We collected data of 41 and 43 patients who had delivered under epidural analgesia using clonidine with bupivacaine (Group C) and fentanyl as an adjuvant with bupivacaine (Group F). After giving the test dose, motor block was seen in 1 parturient in group F who was excluded from the study and those who delivered by caesarean section were also excluded from the study. So the final number of parturients who remained in the study were 36 in group C and 38 in group F. In this study we observed that the addition of clonidine to bupivacaine provided longer duration of analgesia after the first epidural injection. This was not statistically significant but the epidural top-ups requirement thereafter and total bupivacaine requirement was significantly less in the bupivacaine-clonidine group. The aim of our study was to minimize the concentration and volume of local anaesthetic along with fentanyl and clonidine, so as to provide maximum labor analgesia with higher maternal satisfaction without affecting fetal well being.

The primary outcome of our study was duration of analgesia and secondary outcomes were onset of analgesia, number of epidural top-ups requirement, total bupivacaine requirement, maternal satisfaction and fetal outcome. Fentanyl acts by combining with the opioid receptors in the dorsal horn of spinal cord and may also have its action via supraspinal spread when given via epidural route and has been used as an adjuvant to local anaesthetics and reduces both visceral and somatic pain. Clonidine an  $\alpha_1$  agonist is known to increase the effectiveness of local anaesthetics in epidural labor analgesia, producing analgesia by spinal mechanism<sup>[5]</sup>. Clonidine may potentiate the effect of bupivacaine by reducing the blood flow to the spinal cord and prolonging the effective availability of bupivacaine<sup>[6]</sup>.

In our study, the mean time for onset of analgesia in group F was  $13.84 \pm 3.36$  min and  $11.75 \pm 3.37$  min in group C ( $p=0.067$ ). The similar results were observed in the studies of Soliman R et al (2016)<sup>[7]</sup>, Ahirwar A et al (2014)<sup>[8]</sup>. Onset time for bupivacaine-fentanyl group was similar which might be due the use of similar concentration of fentanyl (50 $\mu$ g) in all the studies. Chassard D et al (1996)<sup>[9]</sup> reported that the mean onset of analgesia was 6 & 7 min in bupivacaine clonidine 100  $\mu$ g & 150  $\mu$ g group respectively. Reason for shorter onset could be use of higher concentration of clonidine i.e. 100  $\mu$ g & 150  $\mu$ g as compared to only 75  $\mu$ g in our study. Though the onset was shorter with these dosages of clonidine but the unwanted side effects like sedation, hypotension were avoided.

In our study, mean duration of analgesia in group F was  $127.2 \pm 25.6$  min and  $136.7 \pm 22.7$  min in group C ( $p=0.084$ ). Chassard D et al (1996)<sup>[9]</sup> reported that the mean duration of analgesia in bupivacaine clonidine 100  $\mu$ g group was 130 min & bupivacaine clonidine 150  $\mu$ g group was 144 min. Various studies show that low dose clonidine 30  $\mu$ g or less failed to increase the duration of analgesia, clonidine 120  $\mu$ g increased the mean duration of analgesia & clonidine 75  $\mu$ g was the optimal dose for providing labor analgesia<sup>[6, 11, 12]</sup>. On the contrary, Buggy DJ et al (1996)<sup>[13]</sup> reported that the mean duration of analgesia in clonidine fentanyl group was 80 min. Shorter duration in their study might be because of dilution of clonidine and fentanyl with normal saline and lack of use of local anaesthetics.

Total amount of bupivacaine used in our study was  $30.03 \pm 8.68$  mg &  $25.33 \pm 9.6$  mg in group F and group C respectively ( $p=0.02$ ). Similar results were found by Polain BLE et al (1993)<sup>[12]</sup>. The consumption of bupivacaine was lesser in the groups using clonidine because on activation of postsynaptic  $\alpha_2$  receptors in the substantia gelatinosa of the spinal cord, clonidine produces analgesia<sup>effects[14]</sup>. When given with local anaesthetics it also potentiates their analgesic effect thereby reducing the requirement of bupivacaine. VAS score was comparable between the groups during the entire duration of labor. Maternal satisfaction score in our study was excellent in 23 (60%) parturients of group F and 21 (58%) in group C, good in 11 (28%) parturients of group F and 12 (33%) in group C, incomplete in 4 (10%) and 3 (8%) parturients of group F and group C respectively and no failure was observed in any of the patient. This difference was statistically not significant ( $p>0.05$ ). Similar results were found by Tomar GS et al (2011)<sup>[4]</sup>, James KS et al (1998)<sup>[15]</sup>, using 0.125% and 0.0625% of bupivacaine. Use of higher concentration of local anaesthetics (0.25%, 0.5%) causes higher degree of pelvic and lower limb muscle relaxation, lengthening of 2<sup>nd</sup> stage and decreases the bearing down effort of mother and ultimately reduces the maternal satisfaction level.

We observed that in group F 27 (62.7%) parturients delivered via spontaneous, 12 (27%) via instrumental and 4 (9%) via caesarean section and in group C 23 (56%) parturients delivered via spontaneous, 13 (31%) via instrumental and 5 (12%) via caesarean section ( $p<0.05$ ). Bazin M et al (2011)<sup>[16]</sup> reported a higher rate of instrumental delivery in the levobupivacaine (0.0625%) clonidine (150  $\mu$ g) group (35.2% vs 17.6% for placebo). This may be due to direct or indirect effect of clonidine causing improved analgesia, encouraging the obstetricians to use instrumental delivery, while studies of Hart EM et al (2003)<sup>[17]</sup>, James KS et al (1998)<sup>[15]</sup> studies explain the decreased incidence of instrumental delivery as low dose bupivacaine (0.1%) is known to protect the sensation of pelvic floor and motor function allowing co-ordinated pushing during the second stage of labor, which improves rotation and descent of the fetal head, hence reduced incidence of instrumental deliveries. Hypotension responded to fast infusion of IV fluids, none of the patient required injection of mephentermine. Bradycardia was seen in only 1 patient in bupivacaine-clonidine group and only oxygen supplementation was given to the patient, injection atropine was not required. Nausea, vomiting did not require any treatment. Pruritus was seen in 2 patients in bupivacaine-fentanyl group which was self limiting. Other side effects like respiratory depression, shivering or dry mouth were not seen in any of the patient. APGAR at 1 and 5 min was  $>7$  and  $>9$  respectively.

## V. Conclusion

Duration and onset of analgesia provided by addition of 50  $\mu$ g fentanyl and 75  $\mu$ g clonidine to 0.125% bupivacaine were comparable. Both the adjuvants prolonged the duration of labor analgesia and provide very good maternal satisfaction. There were no significant differences in terms of mode of delivery, neonatal outcome and side effects between the groups but the number of top-up doses required and the total amount of bupivacaine used was significantly higher in bupivacaine-fentanyl group as compared to bupivacaine-clonidine group.

**Conflicts of interest-** There are no conflicts of interest.

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