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## A CLINICAL COMPARATIVE STUDY ON EFFECTS OF EPIDURAL FENTANYL AND BUTORPHANOL AS ADJUVANTS TO BUPIVACAINE AND BUPIVACAINE PLAIN, ON QUALITY OF SURGICAL ANAESTHESIA AND DURATION OF POSTOPERATIVE ANALGESIA FOR INFRAUMBILICAL SURGERIES

### Anaesthesiology

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### ABSTRACT

**Aim of the Study:** To evaluate the effects of epidural fentanyl and butorphanol mixed with bupivacaine and bupivacaine alone on quality of surgical anaesthesia and duration of post-operative analgesia in patient undergoing infraumbilical surgeries.

**Materials and Methods:** This study was conducted on ninety ASA grade I & II physical status patients of either sex within the age group of 20 to 60 years, undergoing infraumbilical surgeries under epidural anaesthesia. The patients were randomly divided into three groups as per the study drugs.

**Group I:** Bupivacaine & normal saline, **Group II:** Bupivacaine & Fentanyl and **Group III:** Bupivacaine & Butorphanol.

**Results and Observations:** Fentanyl and Butorphanol produces early clinical effects after epidural administration and are attractive choices for intraoperative and postoperative pain relief. Both the drugs can enhance surgical analgesia without any significant effect on cardiovascular and respiratory system. Epidural Fentanyl has rapid onset of action but causes nausea and pruritus. Epidural Butorphanol provides longer analgesia with brief period of sedation.

**Conclusion:** Both epidural Butorphanol and Fentanyl are effective and safe drugs for intraoperative and postoperative analgesia with mild side effects.

### KEYWORDS

Epidural Fentanyl, Epidural Butorphanol, Bupivacaine, Postoperative Analgesia.

### INTRODUCTION

Effective postoperative analgesia is the mainstay of successful culmination of any surgical procedure; it can effectively relieve pain, reduce morbidity, mortality<sup>1</sup> and the postoperative stress responses<sup>2</sup>. Identification of opioid receptors in the spinal cord prompted extensive studies on effect of epidurally administered opioid with local anaesthetic in providing intraoperative anaesthesia and postoperative analgesia.<sup>3</sup> Opioids are the commonest adjuvant used with local anaesthetics in various regional anaesthetic techniques to extend analgesia, Extradural administration seems to be preferable because of lower risk of infection, lack of post spinal headache and a lower incidence of side effects. Opioids exert a synergistic effect by acting directly on opioid receptors in the spinal cord and help to reduce local anaesthetic requirements. The combination of local anaesthetic and opioid appear to enhance the effects and duration of both the agents.<sup>4</sup> Fentanyl, an opioid receptor agonist & has analgesic potency greater than morphine, because of its high lipid solubility, greater affinity for opioid receptor and rapid onset of action making it a suitable choice for epidural administration and it can be safely administered as a mixture with Bupivacaine, Epidurally administered Fentanyl exerts a spinal effect by penetration of the dura, passage through the central nervous system and entering into the dorsal horn of the spinal cord to bind with opioid receptors.<sup>5</sup> Butorphanol, a synthetic morphinan derivative is a mixed agonist and antagonist non-narcotic opioid analgesic. Butorphanol and its metabolites are agonist at kappa receptors and mixed agonists antagonists at  $\mu$  opioid receptors. The analgesic potency of Butorphanol has been found to be greater than morphine and pethidine. Butorphanol unlike morphine exhibit a ceiling effect on respiratory depression<sup>6</sup>. The duration of analgesia of epidural local anaesthetic should cover the post operative period of 24 hours and preferably 48 hours<sup>7</sup>. The combination of epidural bupivacaine and fentanyl can provide better quality of perioperative analgesia for caesarean section also and its safety has been established<sup>8</sup>.

### MATERIALS AND METHODS

This study was conducted on ninety patients of either sex having ASA I & II physical status, aged between 20 to 60 years, undergoing infraumbilical, Inguino-perineal and lower limb orthopaedic surgeries under epidural anaesthesia. The patients were allocated into three groups of 30 patients each, according to study drugs used to compare its effects on quality of surgical anaesthesia and duration of post-operative analgesia.

Group I:-20ml 0.5% Bupivacaine + 1 ml normal saline.

Group II:-20ml 0.5% Bupivacaine + 1 ml (50ug) Fentanyl.

Group III:-20ml 0.5% Bupivacaine + 1 ml (2mg) Butorphanol.

**Exclusion criteria:** Patients with marked dehydration, severe hypotension or hypotension, gross anaemia, active bleeding, vertebral column deformity, area of sepsis in proposed site of epidural needle insertion, diabetes mellitus, patients on anticoagulant therapy or with coagulopathy, patients with psychological disorder, patients unwilling to have epidural block and those with history of allergy to any local anaesthetic agent were excluded from the study.

Informed consent was taken and the procedure was explained to all patients in a simple language during the pre anaesthetic visit. All patients were preloaded with 500ml of Ringer's lactate solution before administration of epidural block.

L2-3/L3-4 intervertebral spaces were selected for epidural catheter insertion. The epidural catheter was inserted 3-5cm in the epidural space and fixed with adhesive. 20ml solution of 0.5% Bupivacaine, with either of the study drug as per group was injected through the catheter after the patient was made supine. No analgesics or sedatives were used during the pre or intra-operative period.

The pulse rate, blood pressure, SpO<sub>2</sub> and respiratory rate was recorded before and after establishment of the block at specified intervals. All patients were administered oxygen through face mask; hypotension and other complications in the intraoperative period were treated accordingly.

Onset of analgesia was calculated from the interval between injection of study drugs to complete sensory loss and duration of analgesia was calculated from loss of sensation to pinprick to the state of VAS > 4.

Quality of surgical anaesthesia was assessed as Excellent: No complaints, Good: Minimal discomfort relieved by assurance. Fair: Minimal pain relieved by opioid, Poor: If larger dose of opioids or General Anaesthesia required.

Grading of analgesia was done according to VAS score at two hourly interval in the postoperative period till the state of VAS 4, thereafter the patients were given top up dose of local anaesthetic with opioid and excluded from the study, considering VAS: 0-2 Excellent, 2-4: Good, 4-6: Fair and > 6: Poor, as criteria of assessment.

Grades of sedation during surgery were assessed by 0-Alert & conversant, 1-Mildly sedated, 2-Moderately sedated and drowsy, 3-Asleep but arousable, 4-Asleep and not arousable.

Side effects like sedation, hypotension, nausea, vomiting, urinary retention, pruritus and respiratory depressions were recorded and treated accordingly.

All the parameters were recorded at regular intervals during intraoperative and post-operative periods for data analysis. Chi-square analysis, one way ANOVA test, two samples T-test and Levene's test were used to compare different variable among the three study groups.

**RESULTS AND OBSERVATION**

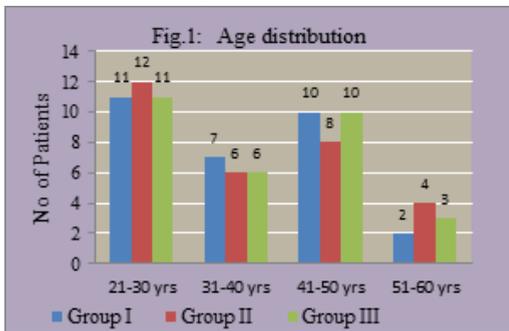
Pulse rate, mean arterial pressure (MAP), respiratory rate and SpO<sub>2</sub> were recorded till the postoperative period of observation. Times of onset, quality of surgical anaesthesia, grades of sedation were recorded intraoperatively. VAS score was used to measure the intensity of pain subjectively and side effects of the study drugs were closely monitored throughout the period of observations.

Group wise distribution of patients was homogeneous. ASA status variation in three groups were 26 (86.67%) in group I and 27 (90%) in group II and III. Rest of the patients were of ASA grade II, suggesting comparable ASA status across all groups.

Sex distribution of patients in Group I: Male 63.23% Female 36.77%, Group II: Male 63.42% Female 36.58%, Group III: Male 60% Female 40%. The Chi-square test did not suggest any dependency between the groups and the sex distribution at 5% level of significance, suggesting similar sex distribution (p>0.05).

Summary of the descriptive statistics of weight distribution suggest homogeneity in Group I: 58.4±3.85, Group II: 58.3±3.51, Group III :58.3±3.80. The observed difference of mean and variance were tested for statistical significance by using two sample T-Test and Levene's test respectively suggesting observed differences are not statistically significant both at 5 and 10 percent level of significance. Groups are found to be similar with respect to weight distribution of the patients (p>0.05).

The descriptive statistics of age distribution reveal homogeneity with respect to the age variation of the patients across the groups (Fig.1). Observed differences in mean and standard deviations across the groups with respect to age variables when tested statistically by two Sample T-Tests, groups wise observed differences of means among the groups were found to be insignificant.



It could be observed from the descriptive statistics of height distributions of the patients across the three groups as homogeneous Group I: 161.57±4.82 centimetres, Group II: 161.90±4.92 centimetres and in Group III: 161.86±4.81 centimetres. Further two sample T test and Levene's Test were conducted. The result of these tests indicated the differences as insignificant (p>0.05).

Analysis of different surgeries performed in each group was of fairly similar nature. Orthopaedic surgeries in Group I: 19 (63.34%), Group II: 18 (60%) and Group III: 17 (56.67%). Gynaecological surgeries in Group I: 5 (16.67%), Group II: 8 (26.67%) and in Group III: 9 (30%). General surgeries in Group I: 6 (20%), Group II: 4 (13.34%) and in Group III: 4 (13.33%).

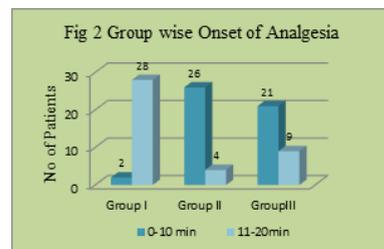
SPO<sub>2</sub> variation across the group exhibited fair amount of homogeneity. In Group I: SPO<sub>2</sub> variation was in the range of 99.43 ±0.57 to 99.60±0.54, In Group II: 99.60±0.57 to 99.23 ±0.63 and in Group III: 99.03 ±0.67 to 98.67 ±0.99.

There was no significant variation in pulse rate across the study group. In Group I: pre operative pulse rate was 82.83±4.64 and variation at 10 min post epidural administration of study drugs up to 240 min was in the range of 77.66±5.15 to 79.13±5.12 beats/minute. In Group II pre operative pulse rate was 82.20±5.83 and post epidural variation at 10 min to 240 min was in the range of 75.23±7.41 to 78.67±7.13 beats/minute. Similarly in Group III, pre operative recording was 82.77±7.68 and post epidural variation at 10 min to 240 min was 75.90±8.68 to 79.93±7.13 beats/minute.

Post epidural mean arterial pressure variation in Group I: pre operative 91.27±7.04 mm of Hg and at 10 min post epidural administration of study drugs up to 240 min was in the range of 79.20±6.56 to 87.83±5.18 mm of Hg. In Group II pre operative 91.43±8.68 mm of Hg and 10 min to 240 min post epidural administration of study drug was in the range of 80.03±10.13 to 87.06±4.79 mm of Hg, In Group III pre operative 91.86±6.53mm of Hg and 10 min to 240 min post epidural administration of study drug was in the range of 80.13±8.12 to 83.67±7.95 mm of Hg, changes were comparable in each group without any significant differences.

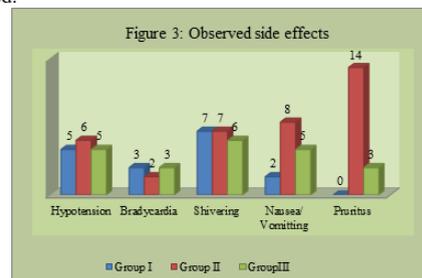
Variation in respiratory rate during preoperative and post administration of epidural drugs were recorded for analysis, however no significant variation was observed. In Group I pre operative 17.77±0.86 breaths/min and post epidural administration of study drug (10 to 240 min) was in the range of 17.80±0.85 to 17.93±0.73 breaths/min, in Group II 18.60±1.19 breaths/min and 18.50±1.04 to 18.6±0.48 breaths/min and in Group III 18.60±1.19 breaths/min and 17.56±0.69 to 18.20±1.42 breaths/min respectively.

The time required for onset of analgesia was comparatively fastest in group II: 9.47±11.01 minutes as compared to 10.30±10.92 minutes in group III and 14.33±12.6 minutes in group I. (Fig.2).



On analysis of quality of surgical Anaesthesia it was found to be Excellent: Group I: - 19 (63.33%) patients and in Group II & III 30(100%). and Good: Group I: - 11 (36.67%) none in Group II&III. Maximum duration of analgesia observed in this study was found to be highest with Butorphanol (Group III) 6.42±1.69 hrs followed by Fentanyl (Group II) 5.08±0.97 hrs and in control group (Group I) 3.78±0.6 hrs. These observed differences in duration of analgesia among the groups when tested by ANOVA yielded highly statistical significances (p<0.001).

Side effects like sedation, hypotension, nausea, vomiting, and pruritus was recorded during the period of observation and treated accordingly (Fig.3) no incidence of respiratory depression or urinary retention was reported.



In Group I all the patients were alert and conversant. In Group II 28 (93.33%) patients were mildly sedated and 2 (6.67%) were moderately sedated & drowsy. Significantly in Group III 15 (50%) were mildly sedated, 8 (26.67%) were moderately sedated & drowsy and 7 (23.33%) patients were asleep but arousable, suggesting higher overall

sedation with Butorphanol than Fentanyl (Table 1).

Sedation score	Group I		Group II		Group III	
	No of Patient	%	No of Patient	%	No of Patients	%
0-Alert& conversant	30	100				
1-Mildly sedated			28	93.33	15	50
2-Moderately sedated &drowsy			2	6.67	8	26.67
3- Asleep but arousable					7	23.33
4- Asleep but not arousable						

## DISCUSSION

Results and observations of the present study were analysed with observations of previous investigators. No significant changes in pulse rate, mean arterial pressure, peripheral arterial oxygen saturation and respiratory rate were observed between any groups. There were highly significant differences regarding the onset of analgesia among the groups. The time required for onset of analgesia was comparatively fastest in Group II (Fentanyl) as compared to Group III (Butorphanol) and Group I (Control group).

There were no significant differences as regard to the duration of surgery. Surgical anaesthesia was excellent in treated groups as none of the patients in the study groups (I & II) complained of discomfort & required assurance as compared to control group where 36.67% patients required assurance. In the control Group 63.33% had excellent and 36.67% patients had good surgical anaesthesia. It was found that total duration of analgesia was highest in the Group III (Butorphanol) followed by Group II (Fentanyl). Maximum 10 hours of analgesia in Group III, 6.5hrs in Group II and 3.87 hrs in Group I was recorded in the present study. These differences in duration of analgesia across the groups when tested by ANOVA yielded highly statistical significances ( $p < 0.001$ ).

Incidences of side effects like sedation, nausea & vomiting, pruritus, respiratory depression when occurred, either intra or post operatively were recorded for data analysis. No patient in any group developed major-side effects like respiratory depression or excessive sedation.

All the patients in control group were alert & conversant. None of the patient developed urinary retention, backache or neurological complications. Incidence of hypotension, bradycardia was similar in all groups. No significant differences were found in their incidences compared to control Group I. In the present study, the most common side effect encountered was pruritus. Incidence of pruritus recorded in Group II was 46.67% and 10% in Group III. In all cases the intensity was mild and self limiting; it was confined to the facial region only and responded to assurances. The incidence of nausea and vomiting was comparatively highest in Group II (Fentanyl) than Group III (Butorphanol) and Group I (Control group). When tested for statistical significance it was found to be significant ( $P < 0.05$ ), the groups were otherwise more or less similar in terms of side effects except pruritus, nausea and vomiting.

Demographic characteristics were homogenous across all the groups. The striking differences observed between the control and the study groups, were onset & duration of analgesia. Since the groups were otherwise homogenous, the differences observed were considered to be due to the influences of study drugs on the population under study. From the present study, epidural Butorphanol appeared to be better postoperative analgesic than epidural Fentanyl with minimal side effects.

## CONCLUSION

Fentanyl and Butorphanol both produces rapid clinical effects after epidural administration with Bupivacaine and can be attractive choice for intraoperative and postoperative pain relief with mild side effects. Both the drugs can enhance surgical analgesia without any significant cardiovascular and respiratory effects. Epidural Butorphanol can provide longer postoperative analgesia than epidural Fentanyl.

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