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# A comparison of epidural butorphanol 2mg and fentanyl 75 mcg for postoperative analgesia using combined spinal epidural anaesthesia technique: A randomized double blind clinical study

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**Abstract**

**Objectives:** The aim of this study was to assess the effect of Butorphanol & Fentanyl used as epidural analgesic agent in patients undergoing elective Abdomino-Pelvic and lower limb surgeries. Primary Objective is to compare duration of analgesia (hours) and quality of analgesia. Secondary objective is to compare hemodynamic changes and any adverse reaction.

**Materials and Methods:** Forty patients of either sex, scheduled for elective Abdomino-Pelvic surgeries and Lower Limb surgeries under CSEA technique were included in the study. In postoperative period, patients received either epidural butorphanol 2mg in 10ml NS or fentanyl 75mcg in 10ml NS. Duration of analgesia, which is the time interval between start of analgesia till patient complaints of pain (VAS >4) was noted in both groups. Quality of analgesia was assessed using pain score in both the groups. Heart rate, blood pressure and respiratory rate were monitored at regular intervals and were compared between the 2 groups. Side effects like sedation, pruritus, nausea, vomiting, hypotension and respiratory depression were noted.

**Results:** Demographic profile was comparable in both groups. Duration of analgesia was longer in butorphanol group (357.30 ± 53.52 minutes) in comparison to fentanyl group (207.50 ± 30.24 minutes), which was clinically and statistically significant. Quality of analgesia was better in butorphanol group. Sedation was the main side effect in butorphanol group. Incidence of pruritus, vomiting, hypotension and respiratory depression was more in fentanyl group.

**Conclusion:** Epidural butorphanol provides longer duration of analgesia, better quality of analgesia with less number of epidural doses and fewer side effects like sedation, which are statistically significant when compared to epidural fentanyl.

**Keywords:** butorphanol, fentanyl, postoperative analgesia, epidural analgesia, lower abdominal surgeries

## Introduction

Pain after surgery is inevitable. Hence, relieving pain is one of the fundamental responsibilities of anaesthesiologists and is frequently a primary goal for which patients are seeking care.

Acute postoperative pain is a complex physiologic reaction to tissue injury, visceral distension or disease. Its manifestation of autonomic, psychological and behavioural responses results in unpleasant, unwanted sensory and emotional experience. Despite advances in knowledge of patho-physiology of pain, pharmacology of analgesics and development of effective techniques for post- operative pain control, many patients continue to experience considerable discomfort [1, 2].

The epidural route is more popular for postoperative pain management as the technique can be used alone or in combination with general anaesthesia. Epidural technique has been found to provide better pain relief than systemic opioids and also decreased incidence of postoperative complications. Lumbar epidural catheters can be kept in place for prolonged periods. Epidural catheter placed in a location congruent to the incisional dermatome has been shown to provide superior analgesia.

Among opioids, morphine, pethidine, fentanyl, sufentanyl, buprenorphine and butorphanol are most commonly used drugs epidurally. In the present study, fentanyl and butorphanol have been selected for postoperative epidural analgesia.

Fentanyl, a mu opiate receptor agonist has analgesic potency greater than morphine. Respiratory depressant effect of Fentanyl is less pronounced and of shorter duration of action as compared to morphine and pethidine.

Butorphanol tartarate is a synthetically derived agonist-antagonist opioid analgesic. It is an agonist on kappa receptor and either antagonist or partially agonist on mu receptor. Epidural butorphanol has been employed successfully for the relief of postoperative pain. It is considered safer than pure agonist opioids because of its ceiling effect on respiratory depression, lower addiction potential, lesser nausea, vomiting, pruritus and urinary retention. It produces sedation comparable to or more than that of morphine, which is desired in postoperative period.

## Materials and Methods

The study was conducted at a tertiary medical college hospital in Karad, Maharashtra during 2015-2017. The Institute Ethical Committee approved the study.

Forty participants of either sex, scheduled for elective

Abdomino-Pelvic surgeries (Gynaecologic & Surgery procedures) and Lower Limb surgeries under CSEA technique, belonging to physical status of American Society of Anaesthesiologists class I and II were included in the study.
After getting informed consent from the patients they were randomly divided into two groups, each group containing 20 patients. Computer generated codes and closed envelope technique was used for randomization and double blinding.
**Group B:** Patients received 2mg Butorphanol in 10 ml Normal Saline.
**Group F:** Patients received 75 mcg Fentanyl in 10ml Normal Saline.

A routine pre-anaesthetic examination was conducted on the evening before surgery. Procedure was explained to each patient. They were kept Nil by mouth as per ASA guidelines, without (prior) administering any sedative premedication.
Under proper monitoring like ECG, NIBP, Pulse Oximetry baseline parameter were noted, all patients were preloaded with 10 ml/kg infusion of ringer lactate solution. Combined spinal epidural analgesia initiated under aseptic precautions, a skin wheal was raised at L2- L3 or L3- L4 interspace with 2 ml of 2% lignocaine. The epidural space was identified using 18G disposable Tuohy needle with loss of resistance technique then 18G epidural catheter was passed through the epidural needle till about 2-3 cm of the catheter was in the space. The needle was withdrawn and the catheter was fixed to the back using adhesive tape.
3ml of 2% lignocaine with adrenaline 1:2,00,000 was injected through the catheter as a test dose and observed for any intravascular or intrathecal injection. After confirming correct placement of the catheter, subarachnoid block given in one segment lower using 4 ml of 0.5% heavy inj. bupivacaine hydrochloride. Level of sensory and motor block was noted and hemodynamic parameters monitored intraoperative. No narcotics were administrated throughout intraoperative period.
In postoperative period, immediately after surgery, group B Patients received Inj. Butorphanol tartrate 2mg in 10ml NS and group F patients received Inj. Fentanyl Citrate 75 mcg in 10ml NS through epidural catheter.
Patients assessed at half-hourly intervals for first two hours then at 4, 8, 12, 24 hours after giving first dose of epidural opioid for the following variables.
Sedation score was invoked as in table 1. HR, BP, RR and SpO2 were monitored. Patients were observed for side effects such as nausea, vomiting, urinary retention, pruritus and respiratory depression. After the surgery, patient was shifted to recovery room and monitoring was continued. When patient recovered from motor blockade, they were shifted to postoperative ward.
To assess pain, VAS was utilized. Patients were called upon to mark a point in the 10-point VAS scale according to the intensity of pain in fig. 1 at 5,10,15,30,60 minutes and thereafter hourly for 8 hours and then at 4 hours interval for 24 hours postoperatively. As and when the patient complains of further pain during the period of observation, intensity of pain was assessed again using VAS to know the effect of the study drug given earlier.
Half top up doses i.e. 1mg of Butorphanol tartrate and 50 mcg of Fentanyl Citrate in 10ml NS were given in respective group B and F when VAS ≥ 4.
If analgesia was inadequate even after two consecutive incremental epidural doses given 20-30 minutes apart, patients were given rescue medication in form of injection Diclofenac Sodium 75 mg intramuscular and excluded from the study.

**Table 1:** Sedation Score

| Grade | Conscious Level |
|---|---|
| 0 | Fully awake |
| 1 | Slightly drowsy |
| 2 | Asleep but easily arousable |
| 3 | Fully asleep but arousable |
| 4 | Fully asleep and not arousable |

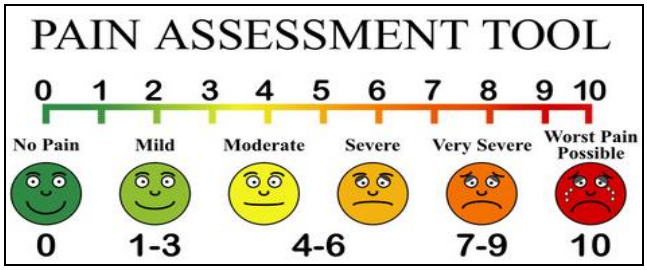


**Fig 1:** Linear Visual Analoge Scale

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Student t test (two tailed, independent) has been used to find the significance of duration of analgesia, quality of analgesia and vas scores between two groups, Chi-square and Fisher Exact test has been used to find the significance incidence of side effects between two groups, General linear model for repeated measures was used for haemodynamic parameters.

## Results

In present study, in Group B mean age of patient was 39. 9 ± 11.6 years and in Group F it was 41.40 ± 11.4 years. Highest age was 60 years and lowest age was 18 years. In Group B 11 patients were male and 9 were female, while in Group F 8 were male and 12 were female. There was no significant difference of patient's age ($p>0.781$) and sex ($p>0.366$) between both the groups as shown in table. The demographic data such as age and sex being comparable has no influence on outcome of the study.

**Table 2:** Demographic Data

| | Group B (n=20) Mean ± SD | Group F (n=20) Mean ± SD |
|---|---|---|
| Age | 39. 9 ± 11.6 | 41.40 ± 11.4 |
| Sex (M:F) | 11:9 | 8:12 |

The total duration of postoperative analgesia is calculated from the time of epidural drug injection to the time at which patient demands analgesic i.e. VAS of 4 and above. Duration of analgesia in group B (butorphanol group) ranged from 200-500 minutes (3.5 – 8.5 hrs.) with a Mean ± S.D of 357.00 ± 53.52 min and in group F (fentanyl group) ranged from 150-

250 minutes (2.5- 4 hours) with a mean ± S.D of 207.5 ± 30.24 min.

**Table 3:** Duration of analgesia

| Duration of analgesia (min) | Group B (n=20) | Group F (n=20) |
|---|---|---|
| 100 – 200 | 0 | 12(60%) |
| 201-300 | 4(20.0%) | 8(40%) |
| 301-400 | 13(65%) | 0 |
| 401-500 | 3(15%) | 0 |
| Mean ± SD | 357.30 ± 53.52 | 207.50 ± 30.24 |

Significance Duration of analgesia in minutes is significantly less in Group F with t=13.740; P<0.001

Quality of analgesia was assessed using pain score. 80% of patients in butorphanol group had good pain relief and 10% had excellent pain relief. In fentanyl group, 75% of patients had good pain relief and 15% had fair pain relief. Accordingly, butorphanol provided fairly better quality of analgesia than fentanyl. However comparison between the two was statistically insignificant.

The NIBP variation between the two groups was compared by General Linear Model for Repeated Measures. The test showed no significant difference (p = 0.275). The Respiratory rate variation between the two groups was also compared by General Linear Model for Repeated Measures. The test showed no significant difference (p = 0.120).

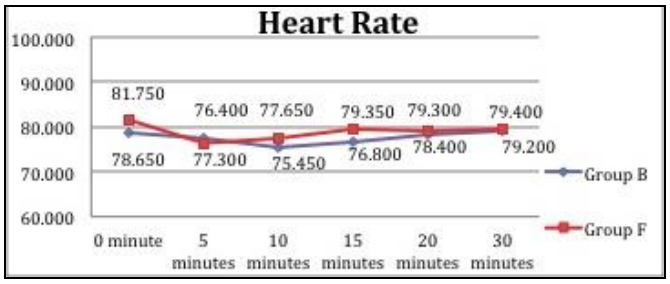


**Fig 2:** Heart Rate

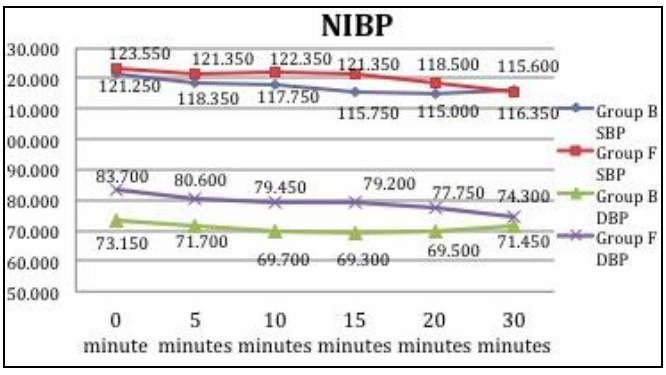


**Fig 3:** Blood Pressure

Sedation was the main side effect in butorphanol group, which constituted 50%, and none of the patients in fentanyl group had sedation. 20% of patients in butorphanol group had nausea whereas in fentanyl group only 5% of patients had nausea, which was not significant statistically (p>0.05).

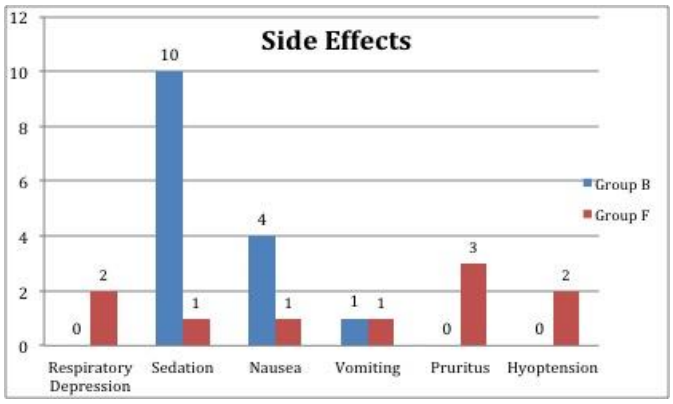


**Fig 4:** Side Effects

## Discussion

Severe pain can result in splinting, with resultant atelectasis and hypoxia. In addition, poor control of pain may result in increased catecholamine secretion in response to pain, which may in turn increase myocardial oxygen demand. A number of studies in the past have proved that improved postoperative analgesia may reduce the incidence of cardiac and pulmonary morbidity and mortality in patients undergoing major abdominal surgery.

Since the discovery of opioid receptors in the spinal cord, the action of narcotics through opioid receptors has become more clearly understood. One of the opioid receptors, kappa are mainly involved with the mediation of visceral pain. After this, achieving satisfactory postoperative analgesia with epidural and intrathecal administration of narcotics has been the subject of much research. The use of epidural opioids had become an increasingly popular technique for management of acute postoperative pain in recent times. Recent studies would indicate that it is possible to achieve better analgesia with lower doses of opioid medication when these drugs are administered in extradural space as compared to intramuscular or intravenous routes of administration. However, there are disadvantages associated with narcotics as they are not always simple to use and may be associated with some unpleasant adverse effects, like nausea and vomiting (PONV), pruritus, respiratory depression and urinary retention.

Stimulation of spinal opiate receptors (kappa, κ) can also produce spinal analgesia but with fewer side effects. Therefore, a drug such as butorphanol, a mixed narcotic agonist/antagonist, first introduced in 1978 acts as a mu (μ) agonist/antagonist and kappa agonist, also produces analgesia, associated with fewer side effects and also low abuse potential. It's high lipid solubility and high affinity for opioid receptors are additional factors that contribute to paucity of side effects with its use.

Fentanyl was chosen for the study for advantages like no neurolytic preservatives, highly lipophilic, so better retained within the epidural space, short half-life, so less circulating blood levels resulting from absorption and finally because it is stable in salt solutions for more than 72 hours.

The present study was done to assess the efficacy and safety of epidural butorphanol and epidural fentanyl for the management of postoperative pain. A total of 40 patients belonging to age groups 18-60 years have been taken, out of which majority of patients belonged to 31-50 years of age. Male and female patient ratio was equal. Patients undergoing elective lower abdominal and lower limb surgeries in general surgery, orthopaedics, gynaecology and plastic surgery were selected. All surgeries were done under combined spinal epidural anaesthesia. In the postoperative period, immediately after surgery was over, patients in group B received epidural butorphanol 2 mg diluted to 10ml in NS and patients in group F received epidural fentanyl 75 mcg diluted to 10ml in NS.

It was found that all patients experienced some pain relief. However duration and quality of analgesia was found to be variable because of differences in the type of drug used, severity of pain, pain threshold, type of surgery etc.

Duration of analgesia in group B (butorphanol group) was 357.00 ± 53.52 min and in group F (fentanyl group) was 207.5 ± 30.24 min which correlate with most of the other studies. Quisqueya T *et al*., in 1991 compared epidural butorphanol (1,2 and 4mg) and morphine 5mg for post caesarean section analgesia and concluded that epidural butorphanol 4mg produced duration of analgesia for 8hrs[3]. Rutter DV *et al*., in 1981 reported that 100µg of epidural fentanyl for postoperative pain relief has a relatively shorter duration of action i.e. by 3rd hour almost 50% of patients complained of increase in pain [4]. Premila malik, Chhavi manchanda, Naveen malhotra in 2006 conducted a study to assess and compare the safety and efficacy of postoperative analgesia with epidural butorphanol 2mg and fentanyl 50µg. They concluded that duration of analgesia with butorphanol 2mg was longer when compared to fentanyl 50µg [5].

The quality of analgesia as assessed by VAS was excellent in 10% and good in 10% of patients who received butorphanol whereas 75% of patients who received fentanyl had good pain relief. This correlates with other studies on epidural butorphanol and fentanyl [6, 7, 8, 9].

Hwang KB, Chung CJ, Lee *et al*., in 2004 compared analgesic efficacy of epidural butorphanol and epidural fentanyl and concluded that there was no significant difference in the quality of analgesia between the two groups [10].

In Group B majority of the patients (65%) required 4 doses of epidural, whereas in group F almost half of the patients (45%) required 5 doses of epidural in 24 hours for pain relief.

Blood pressure and respiratory rate remained stable throughout the observatory period. 2 patients in fentanyl group had hypotension (fall in systolic and or diastolic BP <20% of basal reading) and respiratory depression (RR<10/min), which was not statistically significant (p> 0.05). Our study can be compared to the following studies: Gough *et al*., in 1988 used epidural fentanyl 1.5µg/ kg body weight in 10ml of sterile solution and concluded that the range of mean (S.D) of cardio- respiratory variables like heart rate 84(2)- 95(18) beats/ min, systolic BP of 121(19)- 133(14) mm of Hg, diastolic BP of 70(10)- 76(10) mm of Hg and RR- 21(3)- 23(4) / min varied negligibly from basal recordings [11].

The principal advantage of butorphanol is its fewer side effects. Previous studies have shown significantly lower frequencies of pruritus, nausea, and vomiting in patients receiving epidural butorphanol as compared with epidural morphine and fentanyl [3, 6, 7, 8, 9, 12]. The two major complications noted with epidural butorphanol in our study are sedation and vomiting. In our study, about 50% had sedation of which Majority were mildly sedated, patient awake but drowsy. Previous studies have also reported drowsiness in 50% to 72% of patients receiving epidural butorphanol [12, 13]. Mild sedation may be beneficial to patients in the immediate postoperative period [8]. Vomiting was reported in 5% of cases in both butorphanol group and fentanyl group. This figure is similar to most of the other studies done on epidural butorphanol [3, 6, 12].

10% of patients in fentanyl group had respiratory depression and in none of the patients in butorphanol group, which was not significant (p>0.05). No patients had respiratory depression with butorphanol in studies conducted by Maurice Lippmann *et al*. in 1988[14], Catherine O Hunt *et al* in 1989[13] and JS Naulty *et al*. in 1989[15]. Rutter DV *et al*., in 1981 reported decrease in respiratory rate in patients who received 100µg of fentanyl [4]. Negre I *et al*., in 1987 observed the effect of 200µg of fentanyl on ventilatory response to carbon dioxide and concluded that fentanyl induces a non-systemic ventilatory response that may be due to rostral spread of the drug [16].

Ackerman showed that 60% of patients receiving epidural morphine and 46.7% of patient receiving epidural fentanyl developed pruritus as compared with only 6.7% of patients in the epidural butorphanol group. None of the patients developed pruritus in the present study. No patient had urinary retention in either of the groups, consistent with the study by Ackerman *et al.* [17]

## Conclusion

It can be concluded from the above study that epidural butorphanol provides longer duration of analgesia, better quality of analgesia with less number of epidural doses and fewer side effects like sedation, which are statistically significant when compared to epidural fentanyl. In view of safety profile, epidural butorphanol can be routinely employed in the management of postoperative pain relief for various surgical procedures. It is safe and effective in providing postoperative analgesia.

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