

6 COMPARISON OF EPIDURAL BUTORPHANOL VERSUS FENTANYL WITH BUPIVACAINE FOR POST OPERATIVE ANALGESIA IN LOWER ABDOMINAL AND LOWER LIMB SURGERIES

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ABSTRACT:

Background: This prospective randomized controlled clinical comparative study entitled “COMPARISON OF EPIDURAL BUPIVACAINE AND BUTORPHANOL VERSUS EPIDURAL BUPIVACAINE AND FENTANYL FOR POST OPERATIVE ANALGESIA IN LOWER ABDOMINAL AND LOWER LIMB SURGERIES” was conducted in 50 patients of either sex, aged between 18- 60 years of ASA grade I and II admitted for elective surgeries during 2011-2013.

Material & Method: Written informed consent was taken and pre-anesthetic evaluation was done. Epidural catheter was inserted and all patients were given spinal anesthesia using 0.5% hyperbaric Bupivacaine (15mg). In the postoperative period, when patient complained of pain, intensity of pain was assessed using Visual analog scale and when VAS score was 4 or more they received epidural Bupivacaine (0.5%) 2.5 ml and Butorphanol 2mg (group BB) or Bupivacaine (0.5%) 2.5 ml and Fentanyl 50µg (group BF) diluted to 10ml with NS. Parameters were observed were; Onset of analgesia; Duration of analgesia. ; Cardio- respiratory effects and adverse effects.

Demographic profile (age, sex weight hemodynamics and ASA grade) was comparable in both groups.

Onset of analgesia: Mean onset of analgesia was rapid (4.5+1.06S.D) minutes) in group BF when compared to group BB (6+1.32 (S.D) minutes. This was clinically and statistically significant ($p < 0.001$).

Duration of analgesia: Duration of analgesia was longer in group BB which ranged from 300-550 minutes with a mean of 410+50.29 minutes compared to group BF which ranged from 250-450 minutes with a mean of 330+39.32 minutes. This was clinically and statistically significant ($p < 0.001$).

Cardio- respiratory effects: There was no significant difference in heart rate, blood pressure and respiratory rate monitored at regular intervals for 12 hours postoperatively between the two study groups.

Adverse effects: Sedation was the main side effect in group BB. Frequency of pruritis and nausea-vomiting was more in group BF. Hypotension and respiratory depression were not found statistically significant in either group.

All patients were monitored for 12 hours postoperatively for any untoward effects.

Introduction:

The International Association for the study of pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”.

Pain after surgery is inevitable. Postoperative pain causes stress and upsets most of the major organ functions. Hence, relieving pain is one of the fundamental responsibilities of anesthesiologists.

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. Epidural administrations of opioids and local anesthetics have evolved in parallel with intrathecal techniques.

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 as an adjuvant to Bupivacaine for postoperative epidural analgesia.

Aims and objectives

A comparison of epidural Bupivacaine and Butorphanol versus epidural Bupivacaine and Fentanyl for post operative analgesia focusing on Onset and duration of analgesia, Cardio respiratory effects, Sedation, Adverse effects.

MATERIAL AND METHOD

Fifty adult patients of ASA grade I and II, of either sex, belonging to 18-60 years of age, posted for elective lower abdominal and lower limb surgeries in general surgery, orthopedics, gynecology, urology and plastic surgery were selected for the study. Patients were randomly divided into two groups of 25 each.

GROUP BB- Bupivacaine (0.125%) with Butorphanol (2mg)

GROUP BF- Bupivacaine (0.125%) with Fentanyl (50µg).

EXCLUSION CRITERIA:

1. *Patients with cardio-respiratory disorders.*
2. *Patients with renal and / or hepatic disorders.*

3. *Contraindications for epidural anesthesia.*
4. *Patients physically dependent on narcotics.*
5. *Patients with history of drug allergy.*
6. *Head injury cases.*

PRE- ANESTHETIC EVALUATION:

Patients were visited on the previous day of the surgery, a detailed clinical history was taken, and general and systemic examinations were done. Basic laboratory investigations ECG and chest x-ray were carried out routinely on all patients. The patients were explained about the spinal-epidural technique and VAS scale. A written informed consent was taken from each patient.

PREMEDICATION:

To allay the anxiety and apprehension all patients were given Tablet Alprazolam (0.25mg) at 10pm in the night before the surgery. Patients were kept nil orally for 8 hrs before surgery.

ANESTHESIA:

Epidural catheter was inserted for postoperative analgesia and all patients were operated under spinal anesthesia using hyperbaric Bupivacaine (0.5%) 3ml (15 mg).

ANESTHETIC TECHNIQUE:

- *An intravenous line was secured with 18G cannula and Ringer lactate (R.L.) 1 litre infusion was started.*
- *Routine monitors like ECG, NIBP, Pulseoximetry were connected for every case and basal vital signs were recorded before starting the procedure*
- *Drugs and equipments necessary for resuscitation and general anesthesia administration were kept ready. An autoclaved spinal-epidural tray was used.*
- *Sterile disposable epidural set was used and checked for any manufacturing problems..*
- *Under all aseptic and antiseptic precautions The epidural space was identified using 18G disposable Tuohy needle with hanging drop technique at L2- L3 interspace. Then 20G PORTEX epidural catheter was passed through the epidural needle in upward direction till about 4cms of the catheter was in the space. The needle was withdrawn and the catheter was fixed to the back using adhesive tape. Then spinal anesthesia was given in the one interspace below the catheter with 23 G Quinke needle using hyperbaric Bupivacaine (0.5 %) 3ml.(15 mg)*
- *Intraoperatively level of sensory and motor blockade, blood loss, urine output and other routine monitors as described above were observed.*
- *No narcotics were administered during the intraoperative period.*
- *Fluid management: To begin with, R.L was infused and maintained with R.L, N.S or D.N.S. Blood was transfused only when indicated.*

POST OPERATIVE PERIOD:

After completion of the surgery, patient was shifted to recovery room and monitoring was continued. When patient recovered from motor blockade, they were shifted to postoperative ward.

In the postoperative period, when the patient first complained of pain, intensity of pain was assessed using VAS scale. When the VAS score was 4 or more, **study drug** was given through epidural catheter after confirming its proper position as:

GROUP BB- received Bupivacaine (0.5%) 2.5 ml and Butorphanol 2mg diluted to 10ml in NS.

GROUP BF- received Bupivacaine (0.5%) 2.5 ml and Fentanyl 50µg diluted to 10 ml in NS.

The intensity of pain and pain relief was assessed using VAS at 5, 10,15,30,60 minutes 2hours, and thereafter 2 hourly for12 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. If it was 4 or more, rescue analgesia was given in form of Injection Diclofenac 75 mg intravenously slowly as per the ward protocol and the study would end at this stage.

VISUAL ANALOG SCALE SCORE

Visual analog scale (VAS) consisted of a 10 cm line, marked at 1cm each on which the patient makes a mark on the line that represents the intensity of pain he/she was experiencing. Mark '0' represents no pain and mark '10' represents worst possible pain. The numbers marked by the patient was taken as units of pain intensity.

OBSERVATIONS:

1. *Onset of analgesia.*
2. *Duration of analgesia.*
3. *Cardio- respiratory effects: Heart rate, blood pressure and respiratory rate.*
4. *Adverse effects like sedation, pruritis, nausea, vomiting, respiratory depression and hypotension. Urinary retention could not be studied, as most patients in the study had indwelling urinary catheter inserted as part of the surgical management.*

Onset of analgesia: is the time interval from administration of the study drug (VAS score of 4 or more) to first reduction in pain intensity by at least 10 mm in VAS.

Duration of analgesia: is the time interval between onset of analgesia, till patient complaints of pain (VAS score 4 or more) when rescue medication was given.

Sedation - Quality of sedation after giving the study drug was based on ramsay sedation assessment scale.

Hypotension - A fall of 30 % in BP from baseline value.

Respiratory depression – A respiratory rate of less than 10 breaths/ min

Bradycardia - A fall of 20% in pulse rate from base line value.

MANAGEMENT OF ADVERSE EFFECTS

Hypotension: IV fluids and Injection Ephedrine 6 mg SOS.

Bradycardia: Injection Glycopyrolate 0.2 mg IV.

Respiratory depression and deep sedation: Supportive measures like Stimulation, Oxygen with nasal prongs and IV Naloxone 0.4 to 2 mg SOS.

Nausea-vomiting: Injection Ondansetron 4 mg IV.

STATISTICAL METHODS⁵... Student t test (two tailed, independent) has been used to find the significance of duration of analgesia, onset 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. Microsoft word and Excel have been used to generate graphs, tables etc.

OBSERVATION AND RESULTS

Fifty adult patients belonging to ASA grade I and II, of either sex, in age group between 18- 60 years, posted for elective lower abdominal and lower limb surgeries under spinal anaesthesia were selected for the study. They were randomly allocated to two groups with 25 patients in each group. In **Group BB**- Bupivacaine (0.125%) + Butorphanol (2 mg) were used as the study drug and in **Group BF**- Bupivacaine (0.125%) + Fentanyl (50µg) were used as the study drug for the relief of postoperative pain. This comparative clinical study was undertaken to study the efficacy based on onset of analgesia, duration of analgesia and adverse effects.

DEMOGRAPHIC DATA:

VARIABLES	GROUP BB	GROUP BF
AGE (MEAN+SD)	39+11.58	40+11.63
SEX RATIO (M:F)	12:13	12:13
WEIGHTMEAN+SD)	67+6.04	68+5.58
PULSE(MEAN+SD)	77+8.13	77+8.11
SBP(MEAN+SD)	123+9.42	122+10.01
DBP(MEAN+SD)	75+7.47	75+6.48
RR(MEAN+SD)	14+1.41	14+1.45

ASA GRADE(I:II)	19:6	19:6
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Both group were also comparable with respect of sex distribution, weight, haemodynamics and ASA GRADE ($p>0.05$).

ONSET OF ANALGESIA:

ONSET OF ANALGESIA(MIN)	GROUP BB	GROUP BF
2-4	3	13
4-6	15	10
6-8	6	2
>8	1	0
MEAN \pmSD	6 \pm 1.32	4.5 \pm 1.06

60% of the patients in group BB had onset of analgesia between 4-6 minutes and 24% between 6-8 minutes. In group BF, 52% of patients had onset of analgesia between 2-4 minutes and 40% of patients had onset between 4-6 minutes.

Statistical analysis showed that onset of analgesia in group BB was delayed and statistically strongly significant with $t=4.43$ and $p<0.001$.

DURATION OF ANALGESIA:

DURATION OF ANALGESIA(MIN)	GROUP BB	GROUP BF
250-300	0	5
300-350	4	14
350-400	5	4
400-450	12	2
450-500	3	0
500-550	1	0

MEAN+ SD	410±50.29	330±39.32
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Statistic al analysis showed that duration of analgesia was less in group BF and statistically strongly significant with $t=6.26(p<0.001)$.

CARDIOVASCULAR AND RESPIRATORY EFFECTS:

There was no differences with regard to pulse rate and blood pressure (both systolic and diastolic) between the two groups observed ($p >0.05$). It can also be noted that the difference in respiratory rate was not statistically significant ($p>0.05$) in both the groups.

ADVERSE EFFECTS:

ADVERSE EFFECTS	GROUP BB		GROUP BF	
	no	%	no	%
SEDATION	9	36	3	12
PRURITIS	0	0	4	16
NAUSEA-VOMITING	2	8	7	28
RESPIRATORY DEPRESSION	0	0	2	8
HYPOTENSION	0	0	1	4

From the above chart it can be observed:

Sedation was observed in 9 patients (45%) of group BB and 3(12%) patients of group BF. This was statistically strongly significant ($p<0.001$).

Pruritis was seen 4 patients (16%) of group BF and in none of the patients of group BB which was statistically significant ($p<0.05$).

Nausea and Vomiting were observed in 2 patients (8%) in group BB and in 7 patients (28%) in group BF which was statistically significant ($p<0.05$).

Respiratory depression was seen in only 2 patients (8%) and **Hypotension** in only 1 patient (4%) of group BF and in none of the patients of group BB. These were statistically insignificant ($p>0.05$).

SEDATION SCORE:

Sedation was observed in 9 patients (36%) in group BB whereas 3 patients (12%) in group BF had sedation which was statistically significant ($p < 0.001$). The quality of sedation was acceptable in the interest of patients well being.

Discussion:

The present study is a prospective randomized controlled clinical comparative study done to assess the efficacy and safety of epidural Bupivacaine and Butorphanol versus epidural Bupivacaine and Fentanyl for the management of postoperative pain in lower abdominal and lower limb surgeries. A total of 50 patients belonging to age groups 18-60 years of ASA grade I-II have been taken. Male and female patient ratio was equal. Patients undergoing elective lower abdominal and lower limb surgeries in general surgery, orthopedics, gynecology, urology and plastic surgery were selected. During the preoperative assessment patients were explained about the epidural procedure and VAS score. Pre-medication Tablet Alprazolam 0.25mg orally was given the night before the surgery.

Patients were randomly divided into two groups of 25 each, Group BB – Bupivacaine and Butorphanol and Group BF – Bupivacaine and Fentanyl. Epidural catheter was inserted and all patients were given spinal anaesthesia. In the postoperative period, when patient complained of pain, intensity of pain was assessed using VAS and when VAS score was 4 or more, patients in group BB received epidural Bupivacaine 0.5% 2.5 ml and Butorphanol 2mg diluted to 10ml NS and patients in group BF received epidural Bupivacaine 0.5% 2.5 ml and Fentanyl 50µg diluted to 10ml in NS. Observations recorded are Onset of analgesia, Duration of analgesia, Cardio-respiratory effects and adverse effects.

ONSET OF ANALGESIA:

In our study, the mean time for onset of analgesia in group BB was 6 ± 1.32 (SD) minutes and in group BF was 4.5 ± 1.06 (SD) minutes. Majority of patients in group A had onset of analgesia between 4-6 minutes whereas in group BF between 2-4 minutes. Statistical analysis showed that onset of analgesia was delayed in group BB compared to group B ($t=4.43$; $p < 0.001$).

We can correlate our study with the studies conducted by:

Mok et al,¹⁵ in 1986 did a study to evaluate the analgesic efficacy and safety of epidural Butorphanol 4mg in comparison to that of epidural morphine 5mg in patients with postoperative pain. Onset of pain relief with epidural Butorphanol appeared at 15 minutes.

Rutter DV et al¹², in 1981 reported that 100µg of epidural Fentanyl for postoperative pain relief had a rapid onset of action i.e. almost 50% reduction in mean pain within 5 minutes.

Aswini A. et al³, in 2009 conducted a comparative study of epidural Butorphanol 4mg and epidural Fentanyl 100 µg for the relief of postoperative pain in lower abdominal and lower limb surgeries. The onset of analgesia was clinically and statistically significantly late (6minutes) in Butorphanol group when compared to Fentanyl group (3minutes).

DURATION OF ANALGESIA:

In the present study, duration of analgesia in group A ranged from 300-550 minutes(5 - 9 hrs) with a mean \pm S.D of 410 ± 50.29 min and in group B ranged from 250-450 minutes(4 - 7.5 hours) with a mean \pm S.D of 330 ± 39.32 min. The statistical analysis showed that duration of analgesia in group A was significantly longer when compared to group B ($t=6.26$; $p<0.001$).

Our study is in agreement with the studies conducted by:

Mok et al, in 1986¹⁵ concluded that duration of analgesia with Butorphanol 4mg averaged 5.4 hrs.

Shivakumar T. C. et al¹³, in 2006 evaluated analgesic efficacy and side effects of 2 doses of epidural Butorphanol in lower abdominal surgeries. Patients were randomly assigned to three groups to receive epidural Bupivacaine 0.5% 16 ml (n=25 control group I), Bupivacaine 0.5% 15 ml + 1 ml 2 mg Butorphanol (n=25, group II) and Bupivacaine 0.5% 14 ml + 2 ml of 4 mg Butorphanol (n=25, group III). Maximum patients demanded rescue analgesics in Group I (36%) and Group II (32%) at 7th hour and in group III (40%) at 9th hour.

Neerja Bharti et al⁸, in 2009 The duration of analgesia was prolonged in patients receiving Butorphanol (2 mg, 4 mg) with Bupivacaine (0.125%) combination (8.68 ± 0.82 hrs, 9.82 ± 0.54 hrs) as compared with Butorphanol alone (4.35 ± 0.66 hrs; $P < 0.05$).

Aswini A. et al³, in 2009 Duration of analgesia was clinically and statistically longer in Butorphanol group (350 minutes) in comparison to Fentanyl group (230 minutes).

CARDIOVASCULAR AND RESPIRATORY EFFECTS:

In the present study heart rate, blood pressure and respiratory rate remained stable throughout the observatory period. 1 patients in group BF had hypotension (fall in systolic BP $<20\%$ of basal reading) and 2 patients in group BF had respiratory depression ($RR<10/min$) which was not statistically significant ($p> 0.05$). Our study can be compared to the following studies:

Premila Malik, Chhavi Manchanda, Naveen Malhotra⁹in Their study showed that there were no significant changes in pulse rate, systolic and diastolic BP, RR and SpO₂ in the 2 groups at different time intervals throughout the 24 hours study period ($p> 0.05$).

Aswini A. et al³, in 2009 There were no significant changes in pulse rate, BP and RR in either group throughout post operative period.

ADVERSE EFFECTS: In our study;

Sedation: It was the main side effect in Bupivacaine and Butorphanol group which constituted 45% compared to Bupivacaine and Fentanyl group (12%). Majority of the patients had mild sedation, patient sedated but arousable. This was statistically significant.

Catherine O Hunt⁷ in his study has reported a higher incidence of sedation with epidural Butorphanol and is a dose dependent side effect.

Pruritis: In our study none of the patients in group BB had pruritis and 4 patients (16%) in group BF had pruritis which was statistically significant ($p < 0.05$).

Premila Malik, Chhavi Manchanda, Naveen Malhotra⁹ 2006 shows that pruritis was higher in epidural fentanyl group ($p < 0.05$).

Nausea and vomiting: In our study 2 patient in group BB had nausea-vomiting whereas in group BF 7 patients had nausea-vomiting which was significant statistically ($p < 0.05$).

No patients on epidural Butorphanol had nausea or vomiting in study conducted By **Catheline O Hunt et al**⁷.

Premila Malik, Chhavi Manchanda, Naveen Malhotra⁹ in 2006 shows that the incidence of nausea and vomiting was higher in Fentanyl group.

Respiratory depression and Hypotension: In our current study, in group BF 2 patients had respiratory depression and 1 patient had hypotension and in none of the patients in group BB had hypotension or respiratory depression which were not significant ($p > 0.05$).

No patients had respiratory depression or hypotension with Butorphanol in studies conducted by **Catherine O Hunt et al in 1989**⁷.

Conclusion:

It can be concluded from the above study that Butorphanol 2 mg administered epidurally in comparison to Fentanyl 50 μ g (along with 0.125% Bupivacaine) is safe and effective in providing good pain relief of moderate duration in the postoperative period and is associated with only minimal adverse effects.

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