



## Comparison of Plain Bupivacaine, Bupivacaine-Butorphanol Combination and Bupivacaine-Fentanyl Combination for Post Operative Epidural Analgesia - A Tertiary Care Teaching Centre Experience

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### Abstract

**Background:** International association for the study of pain (IASP) defines pain as “an unpleasant sensory and emotional experience, associated with actual or potential tissue damage or described in terms of such damage”. Effective pain control is essential for optimal care of surgical patients. Unrelieved pain causes reduction in vital capacity, FRC, tidal volume, all of which lead to hypoxemia, hypercarbia, retention of secretions atelectasis and pneumonia. Postoperative pain can be relieved by using different drugs & different techniques. Epidural analgesia has revolutionized postoperative pain management. aim of the study was to compare the duration of postoperative analgesia for lower abdomen surgeries and other effects produced by epidural injection of 0.25% plain bupivacaine versus 0.25% bupivacaine-butorphanol 2mg, versus 0.25% bupivacaine- fentanyl 50mcg.

**Methods:** The patients were posted to undergo surgery at SAT hospital medical college Trivandrum during 2012-2014. The study was approved by hospital ethics committee. Seventy-five patients undergoing lower abdominal surgeries were randomly selected for this study. Patients were those undergoing elective surgery that could be performed under lumbar epidural anesthesia ASA physical status grade I and II patients of female sex between 35-60 yrs of age and body weight -ranging from 45- 70 Kg.

**Results:** The patients were selected at random to avoid any kind of bias and to allow comparability of results obtained in three groups. The three groups were comparable with regards to mean age and weight and sex distribution. The mean onset of time of pain relief in bupivacaine (group I), bupivacaine butorphanol combination (group II) and bupivacaine fentanyl combination (group III) had been  $16.92 \pm 1.35$ ,  $10.98 \pm 1.38$ ,  $13.24 \pm 1.02$  minutes respectively. There is highly significant difference among the three groups (P value os 0.000). Bupivacaine butorphanol combination has a faster onset time compared other groups.

**Conclusions:** butorphanol given along with 0.25% bupivacaine epidurally for lower abdominal surgeries is a safe and effective analgesic for postoperative pain relief, when compared with 0.25% bupivacaine alone and 25% bupivacaine with fentanyl. The addition of epidural butorphanol to 0.25% bupivacaine cause significantly effective analgesia for a prolonged period

**Keywords:** Bupivacaine, Butorphanol, Epidural Analgesia, Fentanyl, postoperative pain relief.

## Introduction

Millions of patients worldwide undergo surgery each year and benefit from knowledge, skills and sophisticated technology that characterize most aspect of modern surgical treatment. Although effective pain control is essential for optimal care of surgical patients<sup>2A4,5</sup> Postoperative pain is unfortunately under treated due to

- The common idea that pain is merely a symptom and not harmful in itself.
- Concern about the respiratory depression and often opioids related side effects such as nausea and vomiting.
- Lack of understanding of the pharmacokinetics of various agents
- Fear of potential for addiction to opioids
- Use of lower dosage of opioids and delaying opioid administration.

Unrelieved pain can cause several adverse physiological changes, causes reflex skeletal muscle spasm especially in upper abdominal surgery or chest surgery can result in hypoventilation and postoperative chest complications.<sup>8</sup> Pain causes reduction in vital capacity, FRC, tidal volume, all of which lead to hypoxaemia, hypercarbia, retention of secretions atelectasis and pneumonia.

Pain causes reflex vasoconstriction, it can possibly impair wound healing, but particularly in people with compromised blood flow, this can be very damaging. Pain causes stress response, with its adverse effects on the cardiovascular system, like tachycardia, increased oxygen consumption leading to increased risk of myocardial infarction in susceptible patients.

Pain prevents early mobilization results in venous stasis, deep vein thrombosis and pulmonary embolism.<sup>9</sup> Pain also produces physiological effects like anxiety insomnia and apprehension.

Thus effective analgesia improves survival and speeds rehabilitation by promoting activity.<sup>10</sup>

Postoperative pain can be relieved by using different drugs & different techniques. Conventionally parenteral narcotics have been administered to relieve postoperative pain, but

proved unsuccessful due to inadequate doses administered and associated side effects, like respiratory depression.<sup>11,12</sup> Now epidural analgesia has revolutionized postoperative pain management. Initially local anesthetics used but later opioids were added to the local anesthetics to decrease the toxicity of local anesthetics and to improve analgesia.

The extra dural opioids first used in human by Behav et al in 1979 and recent revolution in pain relief by newer opioids has improved control on postoperative pain. Thus addition of opioids to local anesthetic in epidural analgesia was reported to have intensified pain relief and reduced the dose of local anesthetic and opioids required and reduced the side effects by either drugs when used alone. With these ideas, a study was undertaken to compare postoperative pain relief by epidural plain Bupivacaine and combinations of bupivacaine - butorphanol and bupivacaine

## Aim of the Study

The aim of the study was to compare the duration of postoperative analgesia for lower abdomen surgeries and other effects produced by epidural injection of

0.25% plain bupivacaine versus 0.25% bupivacaine-butorphanol 2mg, versus 0.25% bupivacaine- fentanyl 50mcg.

The aim of the comparative study is

To find whether the addition of an analgesic drug to a local anesthetic increases the quality and duration of analgesia.

To compare the incidence of side effects with each group like respiratory depression, pruritis, nausea, vomiting, shivering, urinary retention etc

## Materials and Methods

Seventy-five patients undergoing lower abdominal surgeries were randomly selected for this study Patients were those undergoing elective surgery that could be performed under lumbar epidural anesthesia ASA physical status grade I and II patients of female sex between 35-60 yrs of age and body weight -ranging from 45- 70 Kg.

The patients were posted to undergo surgery at SAT hospital medical college Trivandrum during 2012-2014. The study was approved by hospital ethics committee.

The following were the exclusion criteria for the study

- Patient with a history of bleeding disorders or patients on anticoagulant therapy.
- Patients with mental illness
- Pregnant and lactating mothers
- Patient refusal for regional anesthesia
- Local infections.

These patients were randomly divided into three groups 25each.

Group I → To receive postoperatively, epidural plain bupivacaine 0.25%.

Group II → To receive postoperatively, 0.25% bupivacaine and butorphanol 2mg.

Group III →To receive postoperatively, 0.25% bupivacaine and fentanyl 50mcg.

#### **Pre operative period**

On the eve of surgery, pre anesthetic evaluation was done as regards to history and general physical examination. The consent for epidural anaesthesia was obtained from the patient after briefly explaining the procedure. All the patients had the following routine investigation done.

1. Haemoglobin.
2. Urine albumin, sugar, deposits.
3. Blood sugar.
4. Blood urea, serum creatinine, and serum electrolytes (above 50 years).
5. Electrocardiogram and chest X-ray (above 40 years).

The patients were also introduced to the Visual Analogue Scale (VAS) and were taught how to use it.

Zero end of the scale was taken as no pain and 10cm was taken as the maximum possible pain imaginable. Intensity of pain increases gradually from 0 to 10cms. Patients were instructed to point the intensity of pain on the scale when asked for.

Also, on the eve of surgery, all the patients were given a night sedation with 5-10 mg of diazepam

orally. Metoclopramide 0.2mg/Kg given in the morning on the day of surgery.

#### **Intraoperative period**

Procedure for the epidural block: Once the patient was shifted to the operating room, the patient was monitored with an ECG, non invasive blood pressure and pulse oximeter. Baseline pulse rate and blood pressure were noted.

All patients received a rapid intravenous administration of 500-750ml of Ringer's lactate through an 18G intravenous cannula.

Before the procedure of epidural catheter insertion, all resuscitative equipments like the intubation trolley with airways, laryngoscopes, endotracheal tubes, along with drugs like thiopentone, diazepam, succinylcholine were kept ready. The anaesthesia machine was also checked along with the oxygen delivery system.

The patients were put in left lateral position and under strict aseptic precautions L<sub>2-3</sub> or L<sub>3-4</sub> interspace was punctured (midline approach), with 18G tuohy needle after infiltration of skin and interspinous space with 2% plain lignocaine. The epidural space was identified by loss of resistance technique. An 18G epidural catheter was then threaded through the tuohy needle and 3 cm of the catheter was left in the epidural space in the cephalad direction. The patient was then turned back to the supine position.

A test dose of 3cc of 2% lignocaine with adrenaline 1: 2,00,000 was given after negative aspiration. After confirming that there was no catheter misplacement, the remaining dose of 2% lignocaine with adrenaline was given. The total dose was 18- 20 cc. Top-ups were given at regular intervals with 0.5% bupivacaine.

Intraoperatively, blood pressure, respiratory rate, pulse rate were recorded every minute for the first 20 minutes and every 5 minutes for half an hour and every 15 minutes thereafter till the conclusion of surgery.

At the end of surgery, no epidural top-ups were given and the patients were shifted to postoperative ward.

### Postoperative Period

For better supervision and care all patients were nursed in the postoperative ward. Once the patient in the postoperative ward complained of pain (visual analogue scale of 6 or more) the study was begun and the patients were randomly divided into 3 groups to receive epidurally any of the following drugs.

Group I -0.25% plain bupivacaine

Group II-0.25% bupivacaine and butorphanol 2mg

Group III-0.25% bupivacaine and fentanyl 50mcg

After the drug was given the following parameters were noted.

1. Onset of analgesia - is the time interval between administration of the drug and decrease in pain.
2. The pain score, by using the visual analogue scale.
3. Duration of analgesia - is taken as the time interval from the onset of pain relief till the time at which the patient complains of intolerable pain and requests for further analgesia or when the VAS pain score becomes 6cm, whichever is earlier.
4. Vital parameters blood pressure, pulse rate, respiratory rate.
5. Side effects -Nausea, vomiting, respiratory depression, numbness, shivering, pruritis, hypotension, motor weakness and seizures.

To note: Most of the patients were catheterized.

The degree of pain relief was assessed by the patient and by the observer.

Since the perception of pain is highly subjective, this variable was standardized by using data from 'visual linear analogue scale.'

Visual linear analogue scale involves the use of a 10cm line on a piece of white paper, one end of the line represents no pain at all (0cm) and the other end of the line represents the worst possible pain he or she can imagine (10cm). Patients were directed to rate the degree of pain by marking it on the scale, whenever asked. Values were obtained from measuring the distance from zero to the mark which the patient had pointed.

After the drug was given epidurally the time of onset of pain relief was noted, blood pressure, pulse rate and respiratory rate which were measured every 5 minutes for half an hour and every hour after then.

The intensity of pain was charted on visual analogue scale every hour, and the quality of analgesia was assessed at the end of first and third our post injection, from the alteration in score.

Break through pain, if any, was treated with injection Pethidine 1mg/Kg intramuscularly, and these patients were to be withdrawn from the study. When the patient requested for more analgesia, a second dose of the drug (belonging to the concerned group) was given epidurally as a top up and further analgesia was maintained through regular top ups. Patients were monitored for all vital parameters and managed appropriately till they left the postoperative room. Patients were observed for side effects like nausea, vomiting, respiratory depression, numbness, shivering, pruritis, hypotension, motor weakness and seizures during the study period and treated accordingly.

### Observations and Analysis

Observation and analysis presents the findings of the study the seventy-five patients included in the study were randomly divided into three groups. Group I (Plain Bupivacaine), group II (Bupivacaine Butorphanol combination), group III (Bupivacaine Fentanyl combination). For statistical analysis ANOVA test and students t test applied wherever necessary.

### Distribution

**Table I** Distribution according to age

Age (in yrs)	Group I	Group II	Group III
Mean $\pm$ SD	48.16 $\pm$ 5.5	48.08 $\pm$ 5.06	48.2 $\pm$ 4.7

The age distribution of patients ranging from 35yrs to 60yrs is given in table I. No significant differences were observed between the three

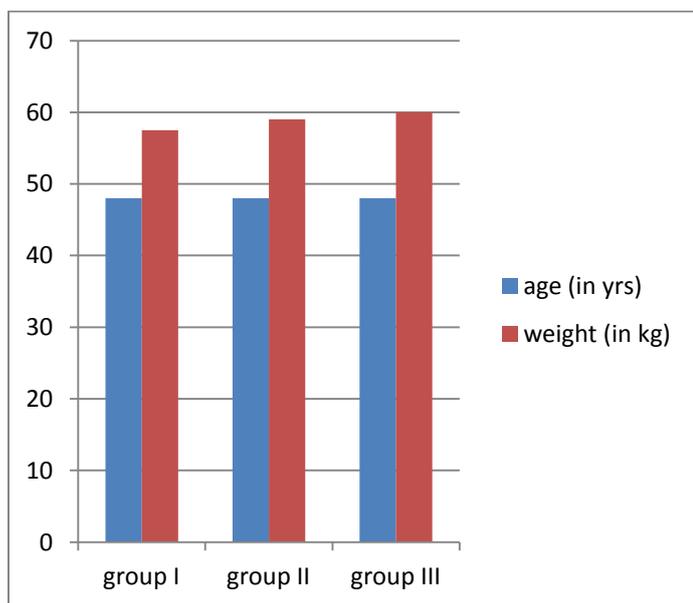
groups, with respect to age of the patient. P<sup>1</sup> value is 0.9964.

**Weight Distribution**

Mean weight of group I, group II, and group III patients were compared. No significant difference were observed. P value is 0.139.

**Table II** Distribution according to weight

Weight (in Kg) Mean ±SD	Group I	Group II	Group III
	57.28±5.44	58.32±5.6	60.20±4.3

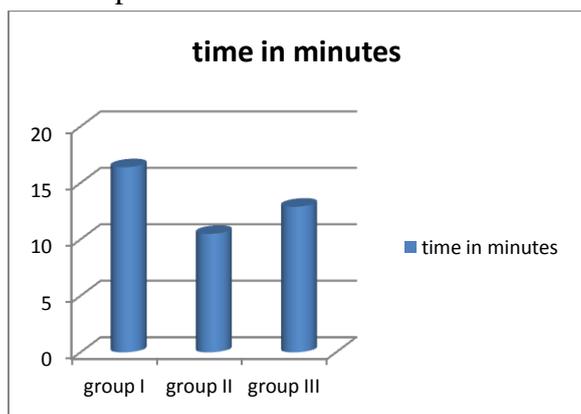


**Mean Onset of Pain Relief**

**Table II**

Time in minutes Mean ±SD	Group I	Group II	Group III
	16.92±1.35	10.98±1.38	13.24±1.02

The three groups were compared according to the onset of pain relief



Mean onset of 16.92 minutes and group II 10.98 minutes, group III 13.24 minutes

The onset of analgesia is significantly earlier in group II (Bupivacaine butorphanol combination) compared to other groups, which is highly significant, P value is 0.000.

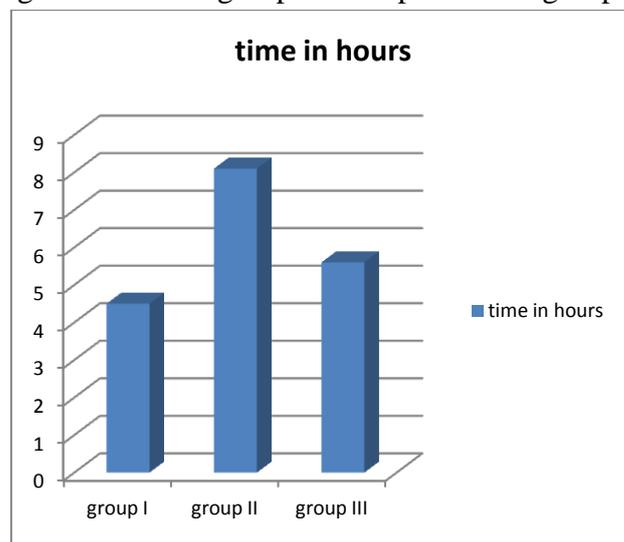
**Mean Duration of Analgesia**

**Table IV** Mean duration of analgesia

Time in hours mean ±SD	Group I	Group II	Group III
	4.8+0.70	8.5+0.50	5.9+1.06

Plain bupivacaine 0.25% has a mean duration of 4.8 hours (SD + 7 hours) Bupivacaine fentanyl combination has 5.9 hours. But butorphanol bupivacaine combination has a significantly long duration of analgesia i.e 8.5 hours. The difference in duration of analgesia was significantly very high in group II patient compared with group I and group III patients. P value is 0.0000.

The difference in duration of analgesia is significant when group III compared with group I.



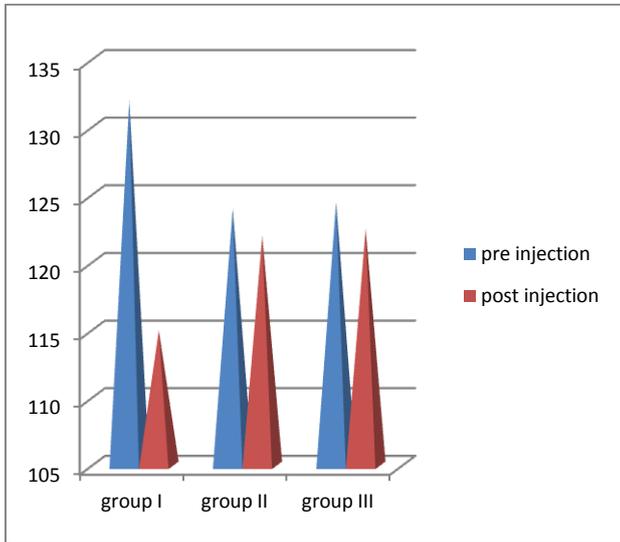
**Change In Systolic Blood Pressure**

**Table V** Mean change in systolic blood pressure

Pre injection Mean (mm Hg)	Group I	Group II	Group III
	129.76±13.2	124.72±8.7	125.28±8.9
Post injection*	115.60±14.16	122.24±8.9	123.52±10.55

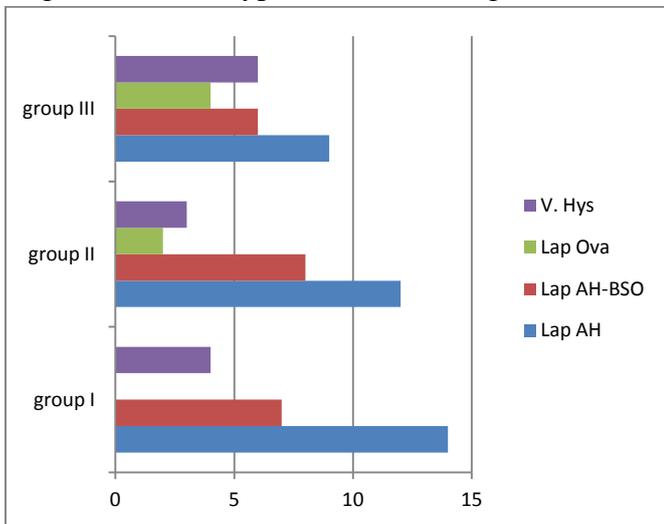
15 minutes post injection

When the systolic blood pressure of group I, II, III compared before giving the drug and after giving the drug, it is found that the difference is significant in group I comparing the other groups.



**Type of Surgery**

There were three types of surgeries included in this study which include lower Abdominal surgeries of three types. Which is insignificant.



**Distribution According to ASA Grape**

**Table VII**

ASA Grade	Group I	Group II	Group HI
ASA 1	20	20	18
ASA 2	5	5	7
Total number	25	25	25

It is attempted to see whether three groups identical with respect to ASA grades. In group I and group II ASA grade were identical and with a mild difference among group HI. ASA grade found statistically insignificant

**Side Effects**

Side effects	Group I	Group II	Group IH
Nausea, Vomiting	1		2
Numbness	4		
Hypotension	3		
Shivering	4		2
Pruritus			1
Motor weakness	2		
Sedation		1	2

While considering the side effects of three groups. Nausea and vomiting was seen in group I and group EH. Side effects are more in group I patients, which include nausea, vomiting, numbness, weakness, hypotension, shivering. Group III patients had nausea, shivering, pruritus, sedation. None of the patients had delayed respiratory depression or urinary retention

**Discussion**

The aim of the postoperative pain relief is to reduce the morbidity and mortality and to provide increased patient satisfaction. The evaluation of pain and its relief is one of the most difficult judgments to be made in therapy. Numerous factors influence the occurrence and intensity of pain following surgery. These include the site and extent of the operative wound, the amount of surgical manipulation of organs rich in sensory fibres, and the patient’s attitudes towards his or her condition.<sup>51</sup> The age and the sex of the patient also play a role.

In our study we decided to compare effects of single dose of 0.25% of plain bupivacaine, 0.25% bupivacaine with 50mcg fentanyl and 0.25% bupivacaine with 2mg butorphanol combination for postoperative epidural pain relief. The duration of analgesia of these drugs compared. The incidence of side effects such as pruritis, nausea, vomiting, hypotension, delayed respiratory depression, urinary retention were also compared. Though the practice of using mixtures of drugs as continuous infusion has become wide spread, we chose to study the effects of single bolus dose of drug or drugs for reasons of experimental economy and feasibility.

Most commonly used method of postoperative pain relief is the administration of intramuscular 'on demand' bolus of narcotic. However this method frequently lead to inadequate pain relief due to profound pharmaco variability and considerable break through pain<sup>52</sup>. Administration of small incremental doses of intravenous opioids has a rapid onset of action, but this carries the risk of rapid induction of ventilatory depression and inadequate analgesia in between. There are many other methods of postoperative pain relief like local nerve blocks, central neuraxial block, patient controlled analgesia and physical means of pain relief (Transcutaneous electrical nerve stimulation and cryoanalgesia). But each technique has its own advantages and disadvantages. If a method of analgesia is to be successful and available to large number of patient, it must be suitable for use in a general surgical ward and require only simple routine nurse monitoring. So postoperative pain management requires continued input to refine, explore and open new avenues to further improve current techniques<sup>53</sup>.

The identification of opiate receptors in the mesencephalic central grey matter of the brain and substantia gelatinosa of the posterior horn cells of the spinal cord has led to the important research in the area of the epidural analgesia and narcotics ( John Ebut 1980). Small doses of the intrathecally and epidurally administered opioids produce suppression of pain even when adequate doses of systemic narcotics have failed to produce analgesia. In the study conducted by Farrante FM, Vade TR et al noted that extra dural analgesia with opioids and local anesthetics commonly used for postoperative pain relief.<sup>54</sup>

Epidural bupivacaine produces neural blockade of longer duration, differential blockade of sensory rather than motor fibres and it possesses relative resistance to tachyphylaxis in contradistinction to the short acting amides like lignocaine and prilocaine. Butorphanol is highly lipophilic, has high opiate receptor occupancy and dissociates slowly from its receptor site.

The patients were selected at random to avoid any kind of bias and to allow comparability of results obtained in three groups. The three groups were comparable with regards to mean age and weight and sex distribution

The mean onset of time of pain relief in bupivacaine (group I), bupivacaine butorphanol combination (group II) and bupivacaine fentanyl combination (group III) had been  $16.92 \pm 1.35$ ,  $10.98 \pm 1.38$ ,  $13.24 \pm 1.02$  minutes respectively. There is highly significant difference among the three groups (P value os 0.000). Bupivacaine butorphanol combination has a faster onset time compared other groups.

In a double blind randomized study by Lippman et al 1977 noted that the onset of analgesia occurred very rapidly (within 1 minute) following butorphanol injection. Similarly a comparative study by Young et al 1977,1978 obtained similar results. Study by Steg et al 1978 using butorphanol for acute postoperative pain showed that the onset of pain relief was rapid, after intramuscular injection. In another doubleblind, randomized dose response study of combination of 0.25% bupivacaine combined with 0,1,2, or 3mg butrphanol was studied in 40 laboring parturients. The optimal dose of butorphanol with 8.5 to 10ml 0.25% bupivacaine was 2mg. With 2mg the duration of analgesia was significantly greater and the time to onset of analgesia signifcantly shorter. There were no adverse fetal or neonatal effects. It is concluded that epidural butorphanol can be useful and safe adjunct to bupivacaine used for epidural analgesia during labor. In our study the bupivacaine butorphanol combination resulted in a faster onset of analgesia compared to other groups. The efficacy of pain relief at the end of every hour after injection of the drug epidurally were noted.

#### **Selection of the dose**

Selection of analgesic drugs to be used as part of an anesthetic technique depends on a number of variables: onset and duration of action, metabolism and excretion and the effects that

different analgesics may have on vital functions. Also frequently involved, but often not recognized is familiarity of the anesthetist with the analgesic being used.

It is said that the dose of drug to produce analgesia, through epidural route should be such that it will be insufficient when given by parental route (Murphy DF et al 1984). The recommended ratio between clinically common intravenous single injection dose and epidural injection dose are 2-3:1 for morphine and 1:1 for buprenorphine, fentanyl and lofentanil. The usual dose of epidural fentanyl is 1-2 micro gram/Kg and butorphanol is 0.03-0.06mg/Kg. Here the lowest recommended doses are used to prevent associated side effects.

#### **Time of administration of epidural analgesic drug**

In this epidural analgesic was given along with epidural local anesthetic through epidural catheter which was maintained postoperatively.

#### **Duration of analgesia**

Postoperative pain was rated by the Visual Analogue Score, noted at the end of every hour after the injection of the drugs epidurally and analyzed the efficacy of the pain relief at the end of 1 hour & 3 hour.

In this study it shows that the addition of butorphanol markedly increases the duration of analgesia compared to epidural fentanyl which has a duration, slightly more than that of 0.25% bupivacaine alone. The duration of analgesia for group I is  $4.8 \pm 0.7$ , group II  $8.5 \pm 0.5$ , group III  $5.9 \pm 0.6$ . Bupivacaine butorphanol group (II) is found to be superior for postoperative pain relief compared to other groups.

Hunt et al 1989, Rodriguez et al 1990 and Lawhorn et al 1997 in their studies noted that the duration of pain relief was significantly increased after addition of butorphanol to epidural bupivacaine the only adverse effect noted was dose related somnolence.

The difference in duration between bupivacaine alone and bupivacaine fentanyl combination is significant and many of these patients were found to be calm and sedated in the postoperative period.

The addition of fentanyl to 0.25% bupivacaine improve the quality of analgesia compared with that produced by bupivacaine 0.25% alone without any increases in the incidence of side effects.

Most studies showed improved pain relief, decreased postoperative morbidity, and a shortened hospital stay after the postoperative administration of epidural opioids.<sup>56</sup> Regarding butorphanol, studies report that the addition of epidural butorphanol to bupivacaine can significantly increase the duration of analgesia and reduced opioid induced nausea and pruritis.

#### **Side effects**

Butorphanol was associated with lower frequency of side effects (Abboud et al 1991). Similar results also reported (Abboud et al 1994, Joyce et al 1993) in post episiotomy pain management. The adverse effects following extradural administration of opioid is due to rostral spread of the drug especially if it is less lipophilic.

Many studies have demonstrated that a single epidural morphine produces prolonged postoperative analgesia without interfering with neuro muscular function or depression of the sympathetic nervous system<sup>57</sup>. However its use has been associated with occurrence of undesirable side effects as pruritis, nausea, vomiting, urinary retention and respiratory depression. A recent report on the use of epidurally administered butorphanol in post-cesarean section indicated the reliable production of analgesia with a lack of undesirable side effects.<sup>58</sup>

In our study bupivacaine group (I) had a fall in systolic blood pressure noted, whereas bupivacaine-butorphanol group (II) and in group (III) the systolic blood pressure fall is not significant. The systolic blood pressure fall in bupivacaine group is found to be statistically significant compared to other groups. In our study, 3 patients in bupivacaine group (I) had hypotension who needed therapeutic intervention. While observing for side effects, 14 patients in bupivacaine group (I) had various complaints. 4

patients had numbness, 4 patients had shivering, 3 had hypotension, 2 complained of muscle weakness, one had nausea and vomiting (some patients had more than one complaint). Hypotension was regarded as a fall in systolic blood pressure of more than 30% of pre injection value or below 90mmHg. These patients were treated with injections mephentermine 6mg IV followed by infusion of 250- 500 ml crystalloid to avoid further fall and its complications. Numbness and shivering are well-known complications of epidural local anesthetics like bupivacaine. 2 patients in bupivacaine group were unable to lift the lower limbs. This may be due to the mild motor block produced by 0.25% bupivacaine. Other two groups did not complain of muscle weakness.

Pruritis, a known complications of opioid occurred in one patient in bupivacaine-fentanyl group (III). The incidence of pruritis varies from 0 to 100% in various studies and this complication has been reported with intra spinal morphine and fentanyl. The incidence is higher after intrathecal than after epidural morphine.

We had come across only one case of pruritis as a side effect in group III, in contrast to other studies which highlighted pruritus as an important side effect of epidural opioids. Non of the patients in group II(bupivacaine butorphanol) combination had pruritus. In a study by Lawhorn et al, the addition of butorphanol 3mg to epidural morphine 4mg significantly decreased the incidence of pruritus and nausea without affecting quality of analgesia. In a double blind study by Commann et al 1992 showed that butorphanol 2mg by either intravenous or epidural route decreased nausea and pruritus. The only advantage of epidural route over intravenous was that epidural route produced less sedation.

The exact cause of itching is not well established. Currently it is speculated that pruritus is due to supraspinal effect secondary to rostral spread of opioid injected epidurally. A central enkephalinergic component has also been proposed by scott. et al 1982 as a probable mechanism of

pruritus. The itching produced can be managed with antihistamines or by naloxone.

Nausea vomiting occurred in one patient group I, and two patients in group III. In group I (Bupivacaine group) which may be associated with hypotension. In group (Bupivacaine fentanyl combination), nausea and vomiting thought to be an opioid related side effect. Opioids are known to cause nausea, vomiting and pruritus. All patients with nausea and vomiting were treated with 10mg of metoclopramide intravenous injection.

When complications were compared it is worth noting that non of the patients studied in all groups had respiratory depression. Respiratory depression by opioids is the main obstacle for any physician while prescribing it. The under administration of drugs for fear of respiratory depression is one of the reasons for inadequate pain relief using parenteral narcotics. Immediate respiratory depression is seen in some opioids which are highly lipophilic. Late respiratory depression is mainly due to the rostral spread of opioids like morphine. Jaffe and Martin have postulated that mu receptors are responsible for respiratory depression and kappa refers for miosis. There was no cardiovascular collapse or bradycardia in any of the patients in our study. No statistically significant haemodynamic changes occurred in studies by Foldes 1976, Foldes et al 1975. and Pacter and Evans 1985. Nagashima et al 1976, in his study among 10 healthy volunteers receiving butorphanol 0.03 and 0.06mg/ Kg intravenously also found no haemodynamic changes following butorphanol injection. In another study, Gensini 1976 Popio et al 1978, some parameters measured suggested that butorphanol treated patients may have had a slight improvement in pump performance of the heart and in left ventricular function.

Addition of butorphanol to bupivacaine via caudal epidural space is a safe and effective means of prolonging analgesia after genitourinary procedures in children (Lawhorn et al 1997). Administration of analgesics after discharge was

less in butorphanol group. There were no untoward side effects reported in this study

While analyzing the side effects in our study it is observed that there is a tendency to increased incidence of side effects of bupivacaine when it is used alone.

One patient in group II and two patients in group III in our study had sedation and none of the patients in any group had urinary retention.

Incidence of shivering is more in group I (bupivacaine group). But in the study group (bupivacaine butorphanol group) no one had shivering.

The effectiveness of opioid analgesics varies in different pain syndromes. Butorphanol was first introduced in 1978. Butorphanol produces analgesic effect, and has been employed successfully for the relief of postoperative pain. Butorphanol can be used as a single shot technique or with a catheter that allowed intermittent boluses and or continuous infusion. Butorphanol is a strong synthetic opioid agonist antagonist analgesic with a well established pharmacological and therapeutic profile. Published studies of butorphanol have shown that butorphanol is a potent, highly effective and well tolerated drug for postoperative pain relief and in the treatment of moderate to severe pain.

Butorphanol is a definite advancement over the conventional opioids with regard to the efficacy in the pain management and as well as safety and tolerability. It is evidenced by clinical trials that butorphanol is less apt to produce physical dependence and unlike the currently used opioids, do not cause pruritis or urinary retention.

Mixed agonist antagonist opioid analgesic, like butorphanol is considered safer than pure opioids, because of their ceiling effect for respiratory depression and their lower addiction potential. Its high lipid solubility increases diffusion in the spinal cord and limits the amount of drugs remaining in the CSF capable of reaching the brain stem, where the side effects are detected.<sup>59</sup>

So butorphanol, a mu agonist antagonist, k

agonist, produces analgesia and associated with fewer side effects.

### Conclusion

The results of this study demonstrate that butorphanol given along with 0.25% bupivacaine epidurally for lower abdominal surgeries is a safe and effective analgesic for postoperative pain relief, when compared with 0.25% bupivacaine alone and 0.25% bupivacaine with fentanyl. The addition of epidural butorphanol to 0.25% bupivacaine cause significantly effective analgesia for a prolonged period. The advantages noted in this study are

- Faster onset of analgesia and longer duration of analgesia.
- Superior quality of analgesia when comparing with 0.25% bupivacaine.
- Less side effects like nausea, vomiting, pruritus, respiratory depression and sedation when compared with other opioids.

The study was conducted in 75 patients in the age group between 35 and 60 years in ASA I & II, who were to undergo elective lower abdominal surgeries. The patients were randomly divided into three groups of 25 cases each. Group I received 0.25% bupivacaine, group II received 0.25% bupivacaine with butorphanol 2mg, III group received 0.25% bupivacaine with fentanyl 50mcg.

All patients were given tab diazepam 5-10mg on the eve of surgery. Metaclopramide 0.2mg/Kg given on the day of surgery.

Under strict aseptic precautions lumbar epidural block was given. Surgery started after confirming the adequacy of block. Vital signs were monitored at regular intervals. After surgery patients were shifted to postoperative ward. Once the patient in the postoperative ward complained of pain, the drugs were given through epidural catheter. Vital parameters, side effects etc. were noted. In the postoperative ward patients were monitored at 0 hour, 1 hour, 3 hours, 6 hours and 12 hours. The duration of effective analgesia in each group were

noted and also the side effects. The mean duration of analgesia was longest in the second group i.e. 0.25% bupivacaine with butorphanol (8.5 hours). Other groups required systemic analgesics after a mean period of 5.5 hours.

The side effects like nausea, vomiting, respiratory depression, shivering, sedation, urinary retention were absent in the second group. The intensity of analgesia was greatest with butorphanol group. The patients had profound analgesia and required systemic analgesics only after a period of 8.5 hours which is highly significant when comparing the other groups.

This short study, thus concludes that analgesics (Opioids) combined with local anesthetic given postoperatively to the epidural space is a good technique for postoperative analgesia. It was also observed that 0.25% bupivacaine with butorphanol 2mg provided a greater duration of analgesia. In this study no clinically significant differences in vital signs were found.

Thus the study highlights butorphanol, a synthetic mixed agonist-antagonist

- More potent than other opioids
- Rapid onset of action
- Low respiratory depression
- Less nausea and vomiting
- Less constipation and urinary retention
- No local issue complications
- No euphoria
- As non narcotic analgesic
- Conscious sedation
- Low potential for abuse

Since pain is a subjective phenomenon associated with wide variability of responses among individual to individual it is difficult to standardize. What may be tolerable to one person may be intolerable to another person. Under these circumstances it is difficult to assess and grade the pain on a standard manner leading to a lot of

unwanted bias on the study, which is a limitation of this study.

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