To Compare and Assess Quality of Analgesia and Side Effects following the use of Fentanyl, Buprenorphine Hydrochloride, Bupivacaine Hydrochloride, through the Thoracic Epidural Catheter

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ABSTRACT

Introduction: Epidural anaesthesia and analgesia has justified use in the perioperative care of high-risk surgical patients, as they give better analgesia, and also improved outcome. Thoracic Epidural analgesia is an excellent method of postoperative and post injury pain control in procedures involving significant thoracic and abdominal injury weather traumatically or surgically induced. Though Bupivacaine is considered to be the drug of choice, many other agents are being used for epidural anesthesia.

Material and Methods: This study was carried out on 105 ASA grade I and II nulliparous patients, between 20 to 70 years of age undergoing laparotomy, voluntary donor nephrectomy and renal surgeries. They were randomly divided in the Buprenorphine, Bupivacaine and Fentanyl Groups. Quality of analgesia and post-operative complications were monitored.

Results: Analgesic failure was observed in all the three Groups. But complete pain relief was better in the Buprenorphine Group. Also, complications (hypotension, bradycardia, sedation) were less in the Buprenorphine Group than in the Bupivacaine and Fentanyl Groups.

Conclusion: Buprenorphine is safer and provides better quality analgesia than Bupivacaine and Fentanyl.

Keywords: Epidural Analgesia, Postoperative Pain Relief, Buprenorphine, Bupivacaine, Fentanyl.

INTRODUCTION

The international association for the study of pain has defined as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage described in the terms of such damage."[1]

Surgery produces local tissue damage with consequent release of algesic substances and generation of noxious stimuli that are transduced by nociceptors and transmitted by A-delta and C fibers to the neurons.[2]

Perioperative pain is a potent trigger for the stress response, activates the autonomic system, and is a cause of adverse effects on various organ systems.[2]

A "stress free" perioperative period may attenuate detrimental physiological responses and decrease resultant morbidity.[3]

Pain relief causes:

1. Minimizes the cardiovascular side effects.
2. Early mobilization.
3. Early return to enteral nutrition.
4. Prevention of postoperative fatigue and impairment in pulmonary function.
5. Early discharge.[1]

Epidural anaesthesia and analgesia has justified use in the perioperative care of high-risk surgical patients, as they give better analgesia, and also improved outcome.[4] Thoracic Epidural analgesia is an excellent method of postoperative and post injury pain control in procedures involving significant thoracic and abdominal injury weather traumatically or surgically induced.[5]

In this study, the quality of analgesia and side effects were compared following the use of 3 different drugs bupivacaine, fentanyl, and buprenorphine via thoracic epidural route.

MATERIAL AND METHODS

This was a randomized, prospective, single – blind (patients), non-crossover type study conducted in Kamineni Hospital, after obtaining clearance from the Institutional Ethics Committee.

It was carried out on the American Society of Anaesthesiologists (ASA) Grade I and II patients between the ages of 20 to 70 years, undergoing laparotomy, voluntary donor nephrectomy and renal surgeries. The patients having preoperative coagulation abnormality, severe systemic and local infection, history of allergy to Fentanyl, Bupivacaine, Buprenorphine, history of myocardial infarction, dysrrythmias, compromised respiratory function, hepatic dysfunction and cerebrovascular diseases, were excluded from the study.

A written informed consent was obtained. A total of 105 patients of either sex were included in the study. These were than divided randomly in three groups (Groups I, II and III) of thirty-five patients each.

Preanaesthetic evaluation was done and premedications (Inj Tramadol 1mg/kg and Inj Promethazine hydrochloride 0.5 mg/kg) were given. Preloading was done with dextrose normal saline. ECG, NIBP and oxygen saturation SpO2 were monitored continuously. Epidural catheter was placed before

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CONSORT
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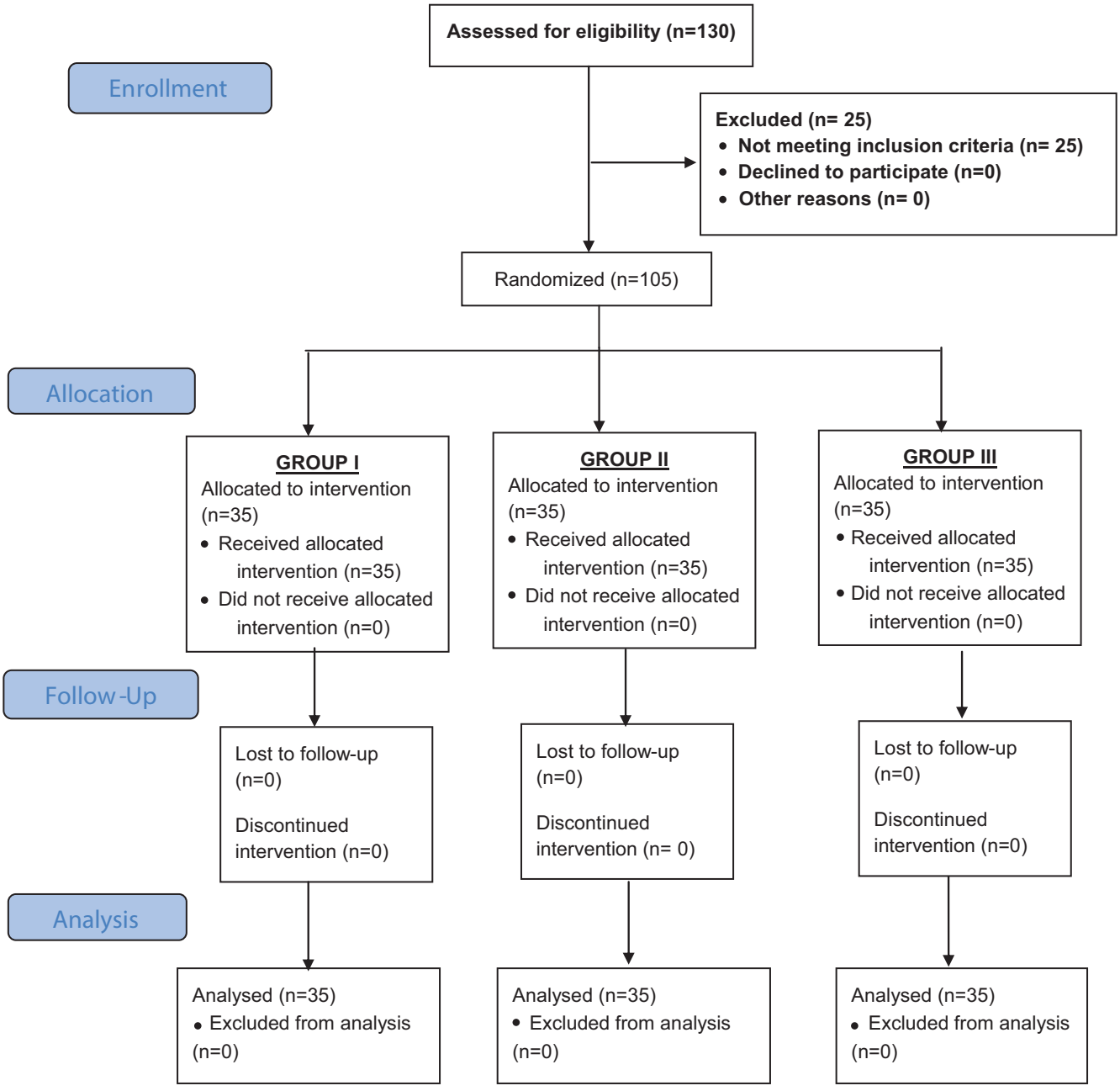
CONSORT 2010 Flow Diagram



induction of anaesthesia in the lateral position with midline approach, at the thoracic T6-7, T7-8 level with 18 G Touhy's needle. Epidural space identification was done by hanging drop technique. The proposed surgical procedure was continued after the administration of the general anaesthesia. After the arrival of the patients in the post anaesthesia care unit, the following drugs were administered:

Group I: Buprenorphine-3 µg/kg

Group II: Bupivacaine-0.25% -3 ml

Group III: Fentanyl- 2 µg/kg

All the patients were transferred from the post anaesthetic care unit to the surgical ward, unless the patient requires intensive care observation. The patient's pain status was assessed and recorded. Pain relief was scored with the visual analogue score (1 to 100) by observer after questioning the patient and asking them to breath deeply and cough and

move about. Any problems, complications or side effects were recorded and managed appropriately.

The definitions used include:

- Pruritus defined as itch of sufficient severity requiring specific management is
- Recorded and treated on patient's request.
- Observer on a five-point scale judged sedation
  - 0-alert
  - 1-mildly drowsy
  - 2-moderately drowsy, easily arousable
  - 3-very drowsy, but arousable
  - 4-difficuilt to arouse
  - 5-unarousable
- Presence of nausea was defined as patient's request for antiemetic treatment.
- Presence of respiratory depression was defined as respiratory rate equal to or less than 8 breathes per minute independent of patient's conscious state. Naloxone was given for respiratory depression associated with excessive sedation, as judged by the anaesthesiologist.
- Hypotension was defined as systolic blood pressure less than 90 mm Hg and was treated accordingly.

Patient's consumption of Bupivacaine, Buprenorphine, and Fentanyl was recorded. Use of adjuvant analgesic was recorded. Epidural analgesia was terminated after 48 hours.

STATISTICAL ANALYSIS

Analysis was done using t-test and Chi-square test. Continuous variables were expressed in forms of mean ± 1 standard deviation. For comparison of continuous variables or mean t-test was done. To analyze discrete variables chi-square test was used. *P value <0.01* was considered statistically significant.

RESULTS

All the Groups were identical in terms of demographic variables, viz, age, sex and weight.

Some patients had analgesic failure requiring supplementation with inj. Diclofenac sodium 75 mg IM for pain relief. For complete relief of pain, there was significant difference between Group-I and Group-II (*P<0.0001*) and also in Group-I and Group-III (*P<0.0001*) (Table 1).

VAS scale	Group – I	Group – II	Group – III	Significance
No pain VAS (0-15)	22.62 ± 3.11	7.37 ± 1.30	1.37 ± 1.60	Significant intergroup differences between Groups I and II (*P<0.0001*) and Groups I and III (*P<0.0001*)
Mild pain VAS (15-30)	7.00 ± 2.44	18.37 ± 1.83	12.75 ± 2.18	
Analgesic failure VAS (>30)	5.37 ± 1.30	8.62 ± 1.38	20.37 ± 2.06	

Table-1: Comparison of quality of pain relief between Groups I, II and III.

Groups	No of Patients	*P*-value	Significance
-Group – I	0		
Group – II	28	P<0.0001	Significant
Group – III	0		

Table-2: Comparison of incidence of Hypotension in Groups I, II and III.

Groups	No of Patients	*P*-value	Significance
Group – I	0		
Group – II	12	P=0.003	Significant
Group – III	9	P=0.01	Significant

Table-3: Comparison of incidence of bradycardia in Groups I, II and III.

Groups	No of Patients	Significance
Group – I	0	Significant difference between Groups I and III (P<0.0007)
Group – II	2	
Group – III	16	

Table-4: Comparison of incidence of pruritus in Groups I, II and III.

Sedation Scale	Group – I	Group – II	Group – III	Significance
0	0	0	0	Significant difference between Groups I and III (*P<0.002*)
1	0	4	8	
2	0	0	6	
3	0	0	0	
4	0	0	0	
5	0	0	0	

Table-5: Comparison of sedation scale between Groups I, II and III.

Hypotension was observed in Group II (*P<0.0001*), which was statistically significant (Table 2).

Bradycardia was observed in Group II (*P=0.003*) and Group-III (*P=0.01*), which was statistically significant (Table 3).

Incidence of severe nausea and vomiting was observed in Groups II and III, which was not statistically significant (*P<0.03*).

Pruritus was seen in Groups II and III. There was statistically significant difference between Group-I and Group-III (*P<0.0007*) (Table 4).

Sedation was observed in Groups II and III and there was statistically significant difference between Group-I and Group-III (*P<0.002*) (Table 5).

DISCUSSION

Postoperative pain relief is one of the goals of perioperative patient care and specialty of anaesthesiology. The provision of good quality of analgesia in postoperative period is important, not only to ease patient suffering and improve well-being, but because poor pain control can lead to cardiovascular and respiratory complications. Analgesia for high-risk patients through epidural route may result in shorter intensive care unit stay.[6]

A stress-free perioperative period attenuates detrimental physiological responses and decreases morbidity.[3] Administration of local anaesthetics, opioids or a combination neuraxially (subarachnoid or epidural) is excellent technique for managing postoperative pain following abdominal, pelvic, thoracic or orthopedic procedures on the lower extremities.

Local anaesthetic solution can alone provide excellent analgesia but produce sympathetic and motor blockade. The former can cause hypotension while later limits patient's ambulation.

Bupivacaine is considered as drug of choice for epidural analgesia as it has wide margin of safety and gives least motor blockade for any given degree of sensory blockade. But it is also associated with side effects, which include motor block and sympathetic block with consequent hypotension and haemodynamic instability.[7]

One research has reported less hypotension if continuous infused dosage of Bupivacaine is used while others have reported significant decrease in blood pressure as well as motor block, numbness, nausea and urinary retention with this technique. Maintenance of degree of pain relief is often difficult due to regression of analgesia and tachyphylaxis.[7]

Epidural opioids have found to overcome these problems. Epidural opioid administration provides good postoperative analgesia and has been used to treat pain and improve pulmonary mechanics after chest trauma.[8]

Morphine is prototype drug used in epidural analgesia. It provides improved analgesia and postoperative pulmonary functions when compared with IV morphine.

The side effects include respiratory depression, Pruritus and urinary retention, as well as nausea and vomiting. This has led to use of lipid soluble opioid such as fentanyl.[9]

Numerous clinical studies has established lumbar epidural fentanyl provide inadequate spinal selectivity, leading plasma fentanyl level equivalent to those provided by IV fentanyl analgesia.[10]

To overcome this disadvantage, Chamberlin et al have suggested that delivery of fentanyl into thoracic epidural space close to its site of action in spinal cord diminish the amount of fentanyl required for the analgesia and reduces the systemic exposure seen with lumbar delivery.[11]

Buprenorphine is relatively new synthetic opioid with both agonistic and antagonistic properties. Unlike morphine it is more lipid soluble and less water-soluble drug and it causes less late respiratory depression.[12]

This study was designed to evaluate the effect of epidural administration of fentanyl, buprenorphine, and local anaesthetic Bupivacaine.

In this study, all the Groups were comparable with respect to demographic variables.

Quality of Analgesia: Buprenorphine Group demonstrated less incidence of analgesic failure when compared with Bupivacaine and Fentanyl Group. This study was comparable to the study by Miwa, Yasuko, Yonemura, et al, which demonstrated longer duration of analgesia in Buprenorphine Group compared with control group of lignocaine 2%.[12]

Hypotension and Bradycardia: Statistically significant hypotension and bradycardia were observed in the Bupivacaine Group. These complications depend on the concentration of Bupivacaine.

Most studies using low Bupivacaine concentration have found no benefit. The 0.1% concentration of Epidural Bupivacaine is probably insufficient to offer pain relief of postoperative visceral pain.[13] Scott et al using epidural infusion of 0.5% Bupivacaine alone for postoperative analgesia following upper abdominal surgery did not provide adequate analgesia.[14]

Nausea and vomiting: Severe nausea and vomiting was observed in Groups II and III.

Though this was not statistically significant, but it was comparable to the study done by Miwa, Yasuko, MD et all no patients receiving Buprenorphine either 4µg/kg or 8µg/kg with 20 ml of 2% lignocaine had nausea and vomiting.[12]

Pruritus: It was observed in the Bupivacaine Group and Fentanyl Group.

Sedation: No sedation was observed in the Buprenorphine Group, as all the patients were alert during the study.

Overall, the study was comparable to the study by K. A. George, A. M. Chisakutu et al, where three out of ten patients receiving Bupivaicaine 0.2% (6-10mg/hr) as infusion had emetic symptoms, eight patients had sedation of grade-I and two patients had grade-II sedation, no patients had pruritus while in Fentanyl Group five patients out of ten receiving 30-50µg/hr of fentanyl had emetic symptoms, six patients had grade-I, three had grade-II, one had grade-III sedation, three patients had pruritus.[7]

In another study done by D. W. Cooper, D. M. Ryall et all

17% of patients receiving Bupivacaine 0.1% by patient controlled analgesia (PCA) had nausea and vomiting, 22% patients in Bupivacaine Group had sedation on the other hand no patients in Fentanyl Group receiving 4µg/ml Fentanyl by Patient Controlled Analgesia had nausea and vomiting, 37% patients had sedation.[15]

Similarly, in the study by T. A. Torda, P. Hann et al, 24 patients were studied in 4 groups. In one group, patients received only fentanyl 50 µg. In other group, patients received only Bupivacaine 50mg and in other two groups patients received fentanyl 50µg +Bupivacaine either 25mg or 12.5 mg. All patients received all four treatments. In only fentanyl group, itching was there in 2 patients while nausea was there in 12 patients while in only Bupivacaine group no patients were having itching but 10 patients were having nausea.[16]

Limitations: This study was limited by the OPD attendance of the patients requiring laparotomy, voluntary donor nephrectomy and renal surgeries. Therefore, the results of this study may not be generalized.

CONCLUSION

From this study, it can be effectively concluded that Buprenorphine is superior to Bupivacaine and Fentanyl as postoperative epidural anesthetic agent in terms of quality of analgesia and post-operative complications.

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