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Original Research Article

Assessment of Epidural Butorphanol, Nalbuphine and Fentanyl for Post-Operative Analgesia in Lower Abdominal Surgeries: A Comparative Study

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Abstract

Aim: The aim of this study to compare the epidural butorphanol, Nalbuphine, and fentanyl for post-operative analgesia in lower abdominal surgeries. **Methods:** This prospective randomized double-blind study was done the Department of Anaesthesia and Critical Care, Patna Medical College and Hospital**,** Bihar, India, from July 2019 to June 2020. A total of 60 patients were included in this study. Patients were randomly divided into three groups of 20 each. Group A - Butorphanol group, Group B - Fentanyl group and Group C - Nalbuphine group. 60 patients of age ranging from 20 to 60 years (20 in each group) of the American Society of Anesthesiologists (ASA) I and ASA II group were selected on the basis of inclusion and exclusion criteria outlined below. **Results:** The mean time of onset of analgesia was 11.88 minutes, 6.87 minutes, and 14.89 minutes in Groups A–C, respectively. Statistical analysis showed that onset of analgesia was faster in fentanyl group compared to other two groups ($p<0.05$). The mean duration of analgesia was 484.71 minutes in Group A, 181.55 minutes in Group B and 297.65 minutes in Group C. The duration was thus significantly longer in butorphanol group.There mean RR increased 6-8 hrs onward postoperatively in Group I, 4 hrs onward in Group B and immediately postoperatively in Group C. This hyperventilation was probably due to the onset of pain after analgesic effect of respective drugs curtailed off over time. The rate came down after administration of rescue analgesic, further confirming the assumption. The mean pain score recorded was significantly lower in Groups A and B than in Group C. All the patients in Groups B and C required analgesic supplementation within first 2-4 hrs and 4-6 hrs, respectively. Whereas 7 patients of Group A required supplementation within 6-8 hrs, 14 patients between 8 and 10 hrs. **Conclusion:** Opioid analgesics with local anesthetics are extremely safe, effective and reliable method of post-operative pain relief. The addition of fentanyl produces faster onset of analgesia with adverse effects like sedation and pruritus than butorphanol and nalbuphine when given epidurally along with 0.125% bupivacaine.

Keywords: Butorphanol, Opioid Analgesics, Epidural, Fentanyl.

Introduction

The popular technique for post-operative pain management is administration of analgesics through the epidural route because it can be used alone or in combination with general anesthesia[1]. Administration of analgesics via epidural route decreases stress response to surgery and pain, minimizes the need for systemic analgesics, and facilitates early rehabilitation[2]. Epidural analgesia with local anesthetics was found to be effective in pain management[3]. Opioids were used as an adjuvant to local anesthetics and this combination was found to be synergistic[3]. Better pain relief, motor sparing and reduced toxicity were the benefits of this combination.

Fentanyl, a μ opiate receptor agonist, has analgesic potency greater than morphine. When compared to morphine and pethidine it has shorter duration of action and lesser respiratory depressant effect[4].

Nalbuphine is a synthetically derived agonist-antagonist opioid analgesic which is equal in potency as an analgesic to morphine and is about one-fourth potent as nalorphine as an antagonist. It has a ceiling effect on respiratory depression. Sedation is commonly associated with it when used in post-operative period as an analgesic[3].

Butorphanol is also synthetically derived agonist- antagonist opioid analgesic. It is an agonist on κ receptor and either antagonist or partially agonist on μ receptor. It is considered safer than pure agonist opioids because of its ceiling effect on respiratory depression, lower addiction potential, lesser side effects like nausea, vomiting, pruritus, and urinary retention. It produces sedation more than that of morphine, which is desired in post-operative period[4]. This study was done to evaluate and compare the post-operative analgesic benefits in patients administered epidural butorphanol, nalbuphine, and fentanyl as adjuvants with local anesthetics postoperatively for surgeries under epidural anesthesia and to compare their post-operative efficacy with respect to increase in duration of analgesia, reduction in total requirements of analgesics postoperatively and study side effects and complications, if any attributable to these drugs.

Material and methods

This prospective randomized double-blind study was done the Department of Anaesthesia and Critical Care, Patna Medical College and Hospital**,** Bihar, India, from July 2019 to June 2020, after taking the approval of the protocol review committee and institutional ethics committee.

A total of 60 patients were included in this study.

The study was confined to the hospital inpatients only who were scheduled for surgeries of lower abdomen. 60 patients of age ranging from 20 to 60 years (20 in each group) of the American Society of Anesthesiologists (ASA) I and ASA II group were selected on the basis of inclusion and exclusion criteria outlined below.

Inclusion criteria

- ASA I and II patients.
- Surgeries of the lower abdomen.
- Patients were eligible for enrolment in the study if they were >18 years old, within ±50% of their ideal body weight, had no clinically significant cardiovascular or central nervous system diseases.

Exclusion criteria

- Pregnant patients
- Breastfeeding patients
- ASA III and IV patients
- Local infection
- Known allergy to study drugs
- Coagulopathies
- Vertebral anomalies
- Neurological disease

Patients were randomly divided into three groups of 20 each.

- Group A - Butorphanol group
- Group B - Fentanyl group
- Group C - Nalbuphine group.

Pre-anesthetic evaluation

Patients were visited on the previous day of the surgery. A detail clinical history was taken, Detail general and systemic examinations were done. Basic laboratory investigations such as complete hemogram, bleeding time, clotting time, blood sugar, blood urea, serum creatinine and urine analysis, electrocardiography (ECG), and chest X-ray were carried out routinely in all patients. The patients were explained about the epidural technique with catheter in situ and its advantages and disadvantages. They were also educated about the usage of linear visual analog scale (VAS) for assessment of the intensity of post-operative pain and were instructed to mark on the scale at the point which he/she felt was representative of their level of discomfort.

Premedication

To allay the anxiety and apprehension, all patients were premedicated with Tablet Alprazolam 0.25 mg on the night before the surgery. The patients were also kept nil orally for 6 hrs before surgery.

Anesthesia

Epidural technique was adopted for surgery of the lower abdomen for all patients with 0.5% bupivacaine. The patient was made to lie supine on the operation table. An intravenous line was secured with 18G canula and infusion of 5% Ringer lactate was started. Routine monitors such as ECG, noninvasive blood pressure (NIBP), and pulse oximetry were connected for every case, and basal vital signs were recorded before starting the epidural technique. Drugs and equipment necessary for resuscitation and general anesthesia administration were kept ready.

An autoclaved epidural tray was used. The patient was placed in sitting or lateral position. 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 18 G disposable Tuohy needle with loss of resistance technique. Then, 20 G catheter was passed through the epidural needle till about 2-3 cm of the catheter was in the space. The needle was withdrawn keeping the inserted epidural catheter in situ and was fixed to the back using adhesive tape. 3 ml of 2% lignocaine with adrenaline 1:2,00,000 was injected through the catheter as a test dose and observed for any untoward reactions including drug interactions as well as intravascular or intrathecal injection. After confirming correct placement of the catheter, epidural anesthesia was activated using 16-18 ml bolus dose of 0.5% bupivacaine. Subsequent top up doses were given depending on the duration of surgery and intensity of pain. No narcotics were administered throughout the intraoperative period.

The intensity of pain and pain relief was assessed using VAS at 5,10,15,30,60 minutes and thereafter hourly for 8 hrs and then at 4 hrs interval for 24 hrs postoperatively. As and when the patient complained of 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 >5, an intramuscular non-opioid analgesic as per the institutionally approved protocol was given.

VAS consisted of a 10 cm line, marked at 1 cm 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.

Table 1: Quality of analgesia

VAS score	Intensity of pain
0-2	No pain to slight pain
2-5	Mild pain
5-7	Moderate pain
7-9	Severe pain
10	Worst possible pain (intolerable)

Quality of analgesia was assessed during the duration of analgesia using pain score and compared between all the three groups.

Table 2: Quality of analgesia

Pain score	Pain relief
0	No pain relief
1	Poor pain relief
2	Fair pain relief
3	Good pain relief
4	Excellent pain relief

Side effects

Sedation - quality of sedation after giving the study drug was based on sedation scoring.

- Grade 0 - No sedation, patient wide awake.
- Grade 1 - Mild sedation, patient awake but drowsy.
- Grade 2 - Moderate sedation, sleepy but arousable.
- Grade 3 - Severe sedation, unarousable.

Statistical analysis

All data recorded was analyzed using statistical package for social sciences (SPSS version 21.0). Data are expressed as mean with a standard deviation. Discreet data are expressed as frequency with percentage of total. ANOVA with post hoc test was used to compare continuous variables. A $p<0.05$ was considered significant.

Results

All the three groups were comparable in terms of age, sex and weight, duration and type of surgery (Tables 3 and 4).

Onset of analgesia

The mean time of onset of analgesia was 11.88 minutes, 6.87 minutes, and 14.89 minutes in Groups A–C, respectively.

Table 3: Demographic data

	Group A	Group B	Group C
Age in years	35.4±10.9	34.8±9.53	35.67±9.80
Sex (female: male)	18:2	18:2	18:2
Weight (kg)	53.97±5.5	53.98±6.89	52.29±5.88
Duration of surgery (minutes)	97±52.56	95±51.54	97±51.78

Table 4: Block characteristics

Time (minutes)	Group A	Group B	Group C
Onset of analgesia	11.88±3.2	6.87±3.98	14.89±2.78
Range	7-17	5-8	10-18
Level of analgesia	T9	T10	T9
Duration of analgesia (minutes)	484.71	181.55	297.65

Statistical analysis showed that onset of analgesia was faster in fentanyl group compared to other two groups ($p<0.05$).

Duration of analgesia

The mean duration of analgesia was 484.71 minutes in Group A, 181.55 minutes in Group B and 297.65 minutes in Group C. The duration was thus significantly longer in butorphanol group.

All the three groups there was no change observed in pulse rate and mean arterial pressure. The mean RR increased 6-8 hrs onward postoperatively in Group I, 4 hrs onward in Group B and immediately postoperatively in Group C. This hyperventilation was probably due to the onset of pain after analgesic effect of respective drugs curtailed off over time. The rate came down after administration of rescue analgesic, further confirming the assumption. The mean pain score recorded was significantly lower in Groups A and B than in Group C. All the patients in Groups B and C required analgesic supplementation within first 2-4 hrs and 4-6 hrs, respectively. Whereas 7 patients of Group A required supplementation within 6-8 hrs, 14 patients between 8 and 10 hrs.

Table 5 shows, in this study, 15% patients in Group A, 20% patients in Group B and 50% patients in Group C had nausea and vomiting. The high female proportion in the study group and the fact that pain and opioids themselves are emetogenic may be the underlying reasons. This was the main side effect in butorphanol group which constituted 30% and 15% of the patients in fentanyl group had sedation. The majority of the patients had mild sedation, patient awake but drowsy. This was statistically significant ($p<0.001$) as compared to nalbuphine group. In this study, no patients in nalbuphine group and butorphanol group had pruritus whereas 6 patients in fentanyl group had pruritus. Pruritus induced by epidural opioids is likely due to interaction with trigeminal nucleus in medulla.

Table 5: Complications

Complication	Group A (%)=20	Group B (%)=20	Group C (%)=20	p value
Nausea and vomiting	3 (15)	4 (20)	10(50)	0.42
Urinary retention	3(15)	1 (5)	0 (0.0)	0.58
Respiratory depression	0 (0.0)	0 (0.0)	0 (0.0)	-
Sedation	6 (30)	3 (15)	2 (10)	0.001
Pruritus	0	6	0	<0.001

Discussion

Post-operative pain is acute pain, which starts with the surgical trauma and usually ends with tissue healing. It diminishes with time after surgery and responds to analgesics. The effective relief of pain to the patients undergoing surgery is essential and is of paramount importance both on humanitarian grounds and also in reducing post- operative morbidity, hence should be duly imparted by the treating anesthesiologist.

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 post-operative 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 is mainly involved with the mediation of visceral pain. After this, achieving satisfactory post-operative 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 post-operative pain in recent times. However, there are disadvantages associated with narcotics as they are not always simple to use and may be associated with some unpleasant adverse effects such as nausea and vomiting (post-operative nausea and vomiting), 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, acts as a mu (μ) agonist/antagonist and kappa agonist, also produces analgesia, associated with fewer side effects and also low abuse potential. Its 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 such as 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 hrs.

Nalbuphine is an agonist - antagonist, equipotent to morphine also has a low abuse potential. It is known to produce profound analgesia and is known to be associated with side effects like sedation. It commonly finds its place in clinical practice as it has a ceiling effect on respiratory depression.

This study is a prospective randomized controlled clinical comparative study done to assess the efficacy and safety of epidural butorphanol, epidural fentanyl and epidural nalbuphine, each combined with 0.125% bupivacaine for the management of post-operative pain. A total of 60 patients belonging to age groups 18-60 years were taken, out of which majority of patients belonged to 20-50 years of age. The patients undergoing elective lower abdominal surgeries in general surgery, gynecology, urology, and plastic surgery were selected.

The mean time of onset of analgesia was 11.88 minutes, 6.87 minutes, and 14.89 minutes in Groups A–C, respectively. This could be correlated with the studies conducted by Mok and Tsai[5] who did a study to evaluate the analgesic efficacy and safety of epidural butorphanol (4 mg) in comparison to that of epidural morphine 5 mg in patients with post-operative pain. In their study, it was observed that the onset of pain relief with epidural butorphanol appeared at 15 minutes and peaked at 30 minutes. Kaur et al.[6] also studied epidural butorphanol and fentanyl as adjuvants in lower abdominal surgeries and demonstrated earlier onset with fentanyl when used with bupivacaine epidurally (mean 10.80 minutes) than with butorphanol used with bupivacaine epidurally (mean 11.08 minutes).

As regarding the duration of analgesia, the duration was thus significantly longer in butorphanol group. The above observation correlates with the works of Malik et al.[7] who used 2 mg butorphanol epidurally for post-operative analgesia after orthopedic surgeries and found duration to be 5.59±1.15 hrs after the first dose. Abboud et al.[8] noted

the duration of analgesia to be 4.82±0.77 hrs, 5.53±0.86 hrs, 8.05±0.97 hrs after use of the first dose of 1 mg, 2 mg, and 4 mg butorphanol used epidurally. Chatrath et al.[9] used 10 mg epidural nalbuphine along with 0.25% bupivacaine and found the duration to be 380±11.4 minutes after lower limb and hip surgeries. Kaur et al.[6] noted the duration of epidural fentanyl 100 µg with 20 ml bupivacaine was 3-9 hrs, mean duration being 5.96 hrs. Their study demonstrated that the duration was significantly greater in butorphanol group with a mean duration of 7.64 hrs.

Side effects of opioids include sedation, nausea, vomiting, pruritus, urinary retention, and respiratory depression. Pruritus was seen in 6 patients of fentanyl group. This is in accordance with findings of Abboud et al.[8] who found paucity of side effects with epidural butorphanol given after cesarean section and attributed this to high lipid solubility of butorphanol thus limiting its cephalic spread to the brainstem. Chatrath et al.[9] studied the effects of epidural nalbuphine and tramadol for post-operative analgesia in orthopedic surgeries and concluded that patients were more comfortable after nalbuphine epidurally since they complained of lesser side effects. Sedation was observed in butorphanol group consistent with the study of Venkatraman et al.[10] who observed sedation in patients receiving epidural butorphanol.

Conclusion

Opioid analgesics with local anesthetics are extremely safe, effective and reliable method of post-operative pain relief. The addition of fentanyl produces faster onset of analgesia with adverse effects like sedation and pruritus than butorphanol and nalbuphine when given epidurally along with 0.125% bupivacaine. Butorphanol administered epidurally has advantage of longer duration of analgesia than fentanyl or epidural nalbuphine with side effects like nausea vomiting and sedation.

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