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Research Article

# Postoperative analgesia after major abdominal surgery: Fentanyl–bupivacaine patient controlled epidural analgesia versus fentanyl patient controlled intravenous analgesia



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## KEYWORDS

Postoperative analgesia;  
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**Abstract** *Background:* Major abdominal surgeries induce neurohumoral changes responsible for postoperative pain, various organ dysfunctions and prolonged hospitalization. Inadequate pain control is harmful and costly to patients thus an appropriate pain therapy to those patients must be applied.

*Methods:* One hundred patients (ASA I or II) of either sex aged from 20 to 60 years were scheduled for elective major abdominal surgery. Patients were allocated randomly into two groups (fifty patients each) to receive: patient-controlled epidural analgesia with bupivacaine 0.125% and fentanyl (PCEA group), or patient controlled intravenous analgesia with fentanyl (PCIA group). Postoperative pain was assessed over 24 h using Numerical Pain Rating scale (NPRS). The frequency of rescue analgesia, sedation score and overall patient satisfaction were recorded. Any concomitant events like nausea; vomiting, shivering, pruritus or respiratory complications were recorded postoperatively.

*Results:* There was a significant less pain in PCEA group at 2, 8 and 12 h. postoperative but PCIA group had less pain at immediate postoperative time. As regard sedation scale, patients of the PCEA group were significantly less sedated than PCIA group at immediate postoperative only. Overall patient satisfaction was significantly more in PCEA group.

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*Conclusion:* This study concluded that both PCEA and PCIA were effective in pain relief after major abdominal surgery but PCEA was much better in pain relief, less sedating effect and overall patient satisfaction.

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## 1. Introduction

Major abdominal surgeries induce neurohumoral changes responsible for postoperative pain, various organ dysfunctions and prolonged hospitalization. Inadequate pain control is harmful and costly thus an appropriate pain therapy must be used to those patients [1].

Patient-controlled analgesia (PCA) enables patients to self-titrate bolus doses of analgesics to their desired level of pain relief by using a programmable infusion pump. This individualizes the dose required to maintain adequate analgesia according to the patient's needs [2]. Opioids are commonly used epidurally but fentanyl, unlike morphine, is highly lipophilic and rapidly diffuses out of the epidural space. Respiratory depression is therefore, unlikely when fentanyl is given epidurally. However, much of fentanyl analgesic effect is mediated by systemic rather than spinal receptor binding [3].

Patient controlled analgesia (PCA) with intravenous opioids and patient-controlled epidural analgesia (PCEA) using an opioid either alone or in combination with a local anesthetic, are two methods in the management of pain after major surgery. PCA has been proposed as safe and effective technique for postoperative analgesia and is considered to be the "gold standard" for pain relief after major surgery [4].

In comparison with opioid analgesia by either intravenous or epidural routes, epidural administration of a local anesthetic and opioid mixture improved pain relief [5].

This study compares the analgesic effects of patient controlled epidural (fentanyl–bupivacaine) versus patient controlled intravenous fentanyl for postoperative analgesia in major abdominal surgery.

## 2. Patients and methods

This prospective randomized study was carried out on one hundred patients (ASA I or II) of either sex aged from 20 to 60 years. They were scheduled for elective major abdominal surgery at Gastroenterology surgical center, Mansoura University. The protocol was approved by responsible local research ethical authorities and written informed consent was obtained from all patients.

Preoperative exclusion criteria included patients under chronic treatment with analgesics or corticosteroids, with contraindications to epidural analgesia (coagulopathy, local infection), allergy to local anesthetic solutions or opioids. Patients whose ability to communicate was impaired were also excluded from the study.

Patients were allocated randomly (via closed envelop) into two groups (fifty patients each) to receive: patient-controlled epidural analgesia with fentanyl–bupivacaine (PCEA group), or patient controlled intravenous analgesia with fentanyl (PCIA group).

The day before surgery, all patients were instructed to describe pain on Numerical pain Rating scale (NPRS) and

how to use the PCA device (Abbott Pain Management Provider. S. No: 96450292. Abbott Laboratory, North Chicago. IL: 60064, USA).

Patients of both groups were premedicated with fentanyl 1.5 µg/kg and midazolam 0.05 mg/kg.

In PCEA group, under complete aseptic technique; 18G epidural catheter (Perifix, B. Braun Melsungen AG, Germany) was inserted through a midline approach in the lateral decubitus position at the T10–12 interspace using the loss of resistance technique (with air) after skin wheal of lidocaine local anesthetic 2%. The catheter was introduced approximately 5 cm into the epidural space. Appropriate catheter placement was confirmed by injection of a test dose of 3 ml lidocaine 2%.

General anesthesia was induced to all patients with propofol 2–2.5 mg/kg and rocuronium 0.9 mg/kg to facilitate tracheal intubation. Anesthesia was maintained with isoflurane (1–2%) in 50% oxygen air mixture. Controlled ventilation was achieved by (Drager-model (Primus), S. No: 5370893, Germany, 2006) ventilator to maintain end tidal carbon dioxide tension around 35 mm Hg.

ECG, noninvasive blood pressure, pulse oximetry and end tidal carbon dioxide (ETCO<sub>2</sub>) were monitored throughout surgery by (Datex-Omeda model (S/5) AN. S. No: 3422715, Finland, 1998) monitor. All patients received continuous intravenous fentanyl infusion 1 µg/kg/hr intraoperatively along with a bolus dose of fentanyl 0.5 µg/kg and 0.15 mg/kg rocuronium when needed. Fentanyl infusion was continued until shifting the patient to post anesthesia care unit (PACU).

At the end of surgery neuromuscular block was antagonized in all patients with neostigmine 0.04 mg/kg and atropine 0.02 mg/kg and trachea was extubated in the operating room and all patients were observed in the PACU for 24 h.

When the patients were awake enough to follow instructions after extubation, Patients in PCEA group received mixture of fentanyl 5 µg/ml along with bupivacaine 0.125% (1.25 mg/ml) and patients of PCIA group received fentanyl 20 µg/ml solutions through PCA pump.

PCA device was programmed to give a bolus dose 2 ml/dose with a minimal lockout interval of 10 min in both groups with no background infusion. Rescue analgesia of 0.5 µg/kg intravenous fentanyl was given to patients in both groups when NPRS > 3 at rest, despite three consecutive PCA boluses.

Postoperative pain was assessed over 24 h. using 10-cm Numerical Pain Rating scale (NPRS) where 0 = no pain and 10 = unbearable pain [6]. NPRS was recorded at times (immediate, 2, 8, 12, and 24 h postoperative). The frequency of rescue analgesia was also recorded.

Sedation was assessed postoperatively by 5 points Sedation score (at the same time intervals of NPRS) as follows 0 = aware-1 = drowsy-2 = asleep/easily respond to verbal command-3 = asleep/difficulty responding to verbal command-4 = asleep/no respond to verbal command [7].

Any concomitant events like nausea; vomiting, shivering, pruritus or respiratory complications were recorded postoperatively. The overall patient satisfaction with postoperative pain

management was assessed using 10-point scale with 0 representing extremely unsatisfied and 10 representing extremely satisfied [8]. This was determined by asking the patient one question at the end of the 1st 24 h postoperatively: how satisfied were you with your pain management over the past 24 h.

### 3. Statistical analysis

The statistical analysis of data was done by using *excel* program for figures and SPSS (SPSS, Inc., Chicago, IL) program statistical package for social science version 15. The description of the data was done in the form of mean  $\pm$  SD for parametric data and median (min–max) for nonparametric data. Frequency and percentage for Qualitative data. The analysis of data was done to test statistical significant difference between groups. Student *t*-test and Mann–Whitney test were used to compare between two groups while Chi square test was used for qualitative data. *P* was considered significant if  $\leq 0.05$  at confidence interval 95%.

The power of this clinical trial was retrospectively calculated using the G power analysis program version 3.1 (R). Using post hoc power analysis with accuracy mode calculations with numerical pain rating score as the primary objective and assuming an X error of 0.05 and an effect size convention of 0.8, a total sample size of 100 patients produced a powerful 0.97. [9].

### 4. Results

Both groups were comparable with the respect to demographic data as seen in Table 1. We exclude one patient from the PCEA group from the study because of difficulty in insertion of the epidural catheter thus the group became 49 patients.

Patients in the PCEA group had significantly less pain when compared with patients in the PCIA group at 2, 8 and 12 h postoperative but patients in PCIA group had significantly less pain when compared with patients in the PCEA group at immediate postoperative time and no significant difference between both groups after 24 h as seen in Table 2.

As regard sedation scale, patients of the PCEA group were significantly less sedated than PCIA group at immediate postoperative time but no significant differences between both groups at 2, 8, 12 and 24 h as seen in Table 3. There were statistically no significant differences between both groups as regard number of patients needed additional analgesic injections Table 4.

Postoperative nausea, vomiting and respiratory complications (bradypnea–desaturation) were comparable in both groups Table 4.

**Table 1** Demographic data of the studied groups: values are mean  $\pm$  SD or number of patients (*n*).

Parameter	PCEA group ( <i>n</i> = 49 patients)	PCIA group ( <i>n</i> = 50 patients)	<i>P</i> value
Age (year)	44.45 $\pm$ 10.56	45.20 $\pm$ 10.61	0.725
Male/female	23/26	24/26	0.916
ASA1/ASA2	23/26	23/27	0.925

PCEA = patient controlled epidural analgesia, PCIA = patient controlled intravenous analgesia, (*n*) = number.

**Table 2** Postoperative average numerical pain rating score (0–10) in the studied groups: data are expressed in (median and range).

Postoperative time	PCEA group ( <i>n</i> = 49 patients)	PCIA group ( <i>n</i> = 50 patients)	<i>P</i> value
Immediate postoperative	3(2–4)	2(1–4)*	< 0.001
2 h Postoperative	2(1–3)*	3(1–4)	< 0.001
8 h Postoperative	2(1–3)*	3(1–3)	0.014
12 h Postoperative	2(1–3)*	3(1–3)	0.015
24 h Postoperative	2(1–3)	2(1–4)	0.544

PCEA = patient controlled epidural analgesia, PCIA = patient controlled intravenous analgesia, (*n*) = number.

\* Statistically significant in comparison to the other group (*P* < 0.05).

**Table 3** Postoperative average sedation score of the studied groups: data are expressed in (median and range).

Postoperative time	PCEA group ( <i>n</i> = 49 patients)	PCIA group ( <i>n</i> = 50 patients)	<i>P</i> value
Immediate postoperative	1(1–1)*	2(2–2)	0.001
2 h Postoperative	2(1–2)	2(1–2)	0.244
8 h Postoperative	2(1–2)	2(1–2)	0.943
12 h Postoperative	2(1–2)	2(1–2)	0.952
24 h Postoperative	2(1–2)	2(1–2)	0.954

PCEA = patient controlled epidural analgesia, PCIA = patient controlled intravenous analgesia, (*n*) = number.

\* Statistically significant in comparison to the other group.

As regard patient satisfaction score PCEA group were statistically more satisfied than PCIA group as seen in Table 5.

### 5. Discussion

This randomized clinical trial showed the effect of PCEA with fentanyl–bupivacaine compared with the effect of PCIA with fentanyl in patients undergoing major abdominal surgery.

Throughout the observation period (24 h) in this study, patients in the PCEA group had significantly less pain score and they were more satisfied by their pain therapy when compared with patients in PCIA group.

In the first hour postoperatively, the NPRS for pain score in PCIA group was significantly less than pain score in PCEA group because of the rapid onset of intravenous fentanyl than epidural fentanyl–bupivacaine combination. There are two possible explanations for this. The peak effect of intravenous fentanyl occurs 2–5 min after intravenous bolus administration [10], whereas the analgesic onset of fentanyl after epidural administration is delayed for 10–20 min [11]. This delay may be explained by the time taken for fentanyl to traverse the dura and cerebrospinal fluid and bind to opiate receptors in the neuraxis of the spinal cord. An alternative explanation may be the analgesic effects of epidural fentanyl appear largely mediated by systemic absorption [12].

After the first postoperative hour the analgesic effect of the epidural fentanyl–bupivacaine combination was significantly more than the analgesic effect of intravenous fentanyl as the

**Table 4** Postoperative complications and number of patients need rescue postoperative analgesia. Values are expressed as number (*n*) and percentage (%).

Complications	PCEA group ( <i>n</i> = 49 patients)	PCIA group ( <i>n</i> = 50 patients)	<i>P</i> value
Number of patients developed nausea	4 (8.2%)	5 (10%)	0.751
Number of patients developed vomiting	2 (4.3%)	3 (6%)	0.663
Number of patients developed pruritus	1 (2%)	2 (4%)	0.570
Number of patients developed shivering	4 (8.2%)	5 (10%)	0.751
Number of patients need rescue analgesia PO	1 (2%)	4 (8%)	0.176

PCEA = patient controlled epidural analgesia, PCIA = patient controlled intravenous analgesia, (*n*) = number.

**Table 5** Overall postoperative patient satisfaction score. Data are expressed in median and range.

	PCEA group ( <i>n</i> = 49 patients)	PCIA group ( <i>n</i> = 50 patients)	<i>P</i> value
Patient satisfaction score	9(7–10)*	7(7–10)	<0.001

PCEA = patient controlled epidural analgesia, PCIA = patient controlled intravenous analgesia, (*n*) = number.

\* Statistically significant in comparison to the other group.

local anesthetic works on nerve roots and the plasma concentration of fentanyl was attained the threshold level to control pain. Other investigators also observed that, after the first postoperative hour, the pain was less intense after epidural fentanyl than after intravenous fentanyl administration, despite the similar or even lower plasma fentanyl concentrations in epidural fentanyl group [13].

At the end of the 24 h postoperatively there was no significant difference in NPRS between both groups as the plasma level of fentanyl was constant in controlling pain in both groups. Epidural analgesia has been shown to provide superior analgesia compared with systemic opioids in systematic reviews [14,15]. In a study comparing epidural versus intravenous fentanyl for postoperative analgesia following orthopedic surgery Privado et al. [13] found that epidural fentanyl is more efficient than intravenous fentanyl administration and the same result also reported in another study [16]. Welchew and Breen [17] found that both routes of fentanyl administration resulted in equally satisfactory analgesia but the total dose of fentanyl in intravenous group was twice the total dose of fentanyl in epidural group during the first 24 h postoperatively. The application of opioids by epidural analgesia delivers the drug close enough to the spinal cord so that the opioids can inhibit pain transmission from afferent nerves to the central nervous system through interaction with pre- and postsynaptic opioid receptors in the dorsal horn [18,19]. When the same amount of an opioid is used, epidural application of PCA should achieve more effective analgesia than systemic administration [20].

In this study an epidural combination of fentanyl and bupivacaine was made thus the dose of fentanyl is lesser than its intravenous dose and this explains the significantly lower sedation score in the PCEA group.

Postoperative pain in PCEA group is lower than PCIA group thus the overall patient satisfaction were significantly better in PCEA group. Based on previously published literature, epidural analgesia using a local anesthetic combined

with an opioid was not only superior in relieving pain at rest and on coughing, but also led to a higher rating of well-being or satisfaction after operation than intravenous opioid analgesia [20].

In this study no significant difference in other parameters like number of patient needs analgesics, nausea, vomiting, pruritus, shivering and respiratory complications.

Although not investigated in this study, shorter hospital stay and earlier full diet were other positive effects of the epidural PCA [21]. Van Boerum et al. reported that the patients in the epidural PCA group could start a full diet earlier and were discharged earlier in one and half days on average than the PCIA group [22,23]. Also, patients in the epidural PCA group started ambulation earlier than in the PCIA group [23]. Moreover, patients in the PCEA group were significantly more satisfied with pain therapy [24].

## 6. Conclusion

This study concluded that both PCEA and PCIA were effective in pain relief after major abdominal surgery but PCEA was much better in pain relief, less sedating effect and overall patient satisfaction.

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## Conflict of interest

No conflict of interest emerged during the implementation of this work. The paper had not been presented at any congress before.

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