Postoperative patient-controlled analgesia with intravenous tramadol, intravenous fentanyl, epidural tramadol and epidural ropivacaine+fentanyl combination

S. Aygun[1], *M.D., Specialist*; **H. Kocoglu**[1], *M.D., Assoc. Prof.*; **S. Goksu**[1], *M.D., Assoc. Prof.*; **M. Karaca**[2], *M.D., Assist. Prof.*; **U. Oner**[1], *M.D., Prof.*

[1]*Department of Anaesthesiology and Reanimation, Faculty of Medicine, University of Gaziantep*
[2]*Department of Obstetrics and Gynaecology, Gaziantep (Turkey)*

Summary

Purpose: The aim of this study was to compare the effects of IV tramadol, IV fentanyl, epidural tramadol, and an epidural ropivacaine+fentanyl combination in patient-controlled analgesia (PCA) after lower abdominal surgery.

Methods: Eighty adult patients undergoing lower abdominal surgery were randomly allocated to one of four groups to receive analgesics with PCA pumps. Patients in group I received IV tramadol, group II patients IV fentanyl, group III patients epidural tramadol, and group IV patients an epidural infusion of 0.125% ropivacaine + 2 μg ml^{-1} fentanyl combination. Analgesic effectiveness and side-effects were assessed at 1, 2, 3, 4, 5, 6, 8, 12, 16, 20, and 24 hours after surgery.

Results: Adequate analgesia was achieved in all groups. The analgesia was highest in group IV ($p < 0.05$), and lowest in group III patients ($p < 0.05$). Eleven patients (55%) in group I and eight patients (40%) in group II suffered from nausea/vomiting.

Conclusion: Although adequate pain relief was achieved with all regimens that were used in the study, intravenous tramadol and intravenous fentanyl are associated with high a incidence of nausea and vomiting.

Key words: Postoperative analgesia; Patient-controlled analgesia; Tramadol; Fentanyl; Ropivacaine.

Introduction

The treatment of pain after surgery is important not only to ensure patient comfort, but also to minimise complications. All relevant professionals, surgeons, anaesthetists and nurses must work together to optimise pain relief in the postoperative period [1].

Despite advances in knowledge of pathophysiology, pharmacology of analgesics, and the development of more effective techniques for perioperative analgesia, many patients continue to experience distressing pain postoperatively [2]. Many efforts and investigations have been established to find out the perfect combination and concentration of drugs, and the method of administration in order to achieve the best analgesia with minimal side-effects. However, there is no one consensus on the best drug regimen to be used for postoperative pain control. Patient-controlled analgesia (PCA) has been demonstrated to be an effective analgesic method after abdominal surgery, allowing for adequate pain relief with minimal impairment on recovery of normal functions [3].

The effectiveness of epidural local anaesthetics, like ropivacaine, with and without opioids in PCA have been studied by many investigators [4-8], and that of intravenous opioids by others [9, 10]. Tramadol, a synthetic opioid agonist, has also been used in PCA for pain relief after surgery [11-13]. The aim of this study is to compare the analgesic effectiveness and side-effects of intravenous tramadol and intravenous fentanyl as well as epidural tramadol, and an epidural ropivacaine and fentanyl combination using PCA for postoperative pain control after lower abdominal surgery.

Materials and Methods

Following institutional ethics committee approval and with informed patient consent, 80 ASA (American Society of Anesthesiologists) physical status I and II patients, aged between 18 and 60 years, and scheduled for elective lower abdominal surgery were randomly allocated to one of the four groups; intravenous tramadol group (Group I), intravenous fentanyl group (Group II), epidural tramadol group (Group III), and epidural ropivacaine plus fentanyl group (Group IV). Prior to surgery, patients were instructed how to use an Abbott Pain Management Provider®, and were told about the postoperative measurements that would be made together with a visual analogue scale (VAS). Patients with any contraindication to regional anaesthesia (epidural groups), with a history of allergies, and those unable to understand the use of PCA were not included to the study.

Patients were not premedicated. A lumbar epidural catheter was inserted at either the L_{2-3} or L_{3-4} intervertebral space using the loss of resistance technique before the induction of general anaesthesia in group III and group IV patients. Disposable 18 G Tuohy epidural needles and 20 G epidural catheters were used, and the catheters were inserted 3-4 cm into the epidural space. A test dose of 3 ml lidocaine (2%) was then administered.

Anaesthesia was induced with fentanyl (1 μg kg^{-1}) and propofol (1-2 mg kg^{-1}), and maintained with 0.6-1.5% isoflurane in a mixture of 65% nitrous oxide and 35% oxygen. A neuromuscu-

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lar blockade was achieved by vecuronium bromide (0.1 mg kg^{-1}, IV) and maintained by bolus administration (0.03 mg kg^{-1}) at 30 min intervals. At the end of surgery, patients were extubated after antagonism of the residual neuromuscular block with neostigmine (0.06 mg kg^{-1}) and atropine (0.02 mg kg^{-1}). No opioids were administered during the last 30 minutes of the operation.

After total recovery from anaesthesia, whenever patients complained of pain, pain relief was provided to all patients by using PCA with a standard PCA pump (Abbott Pain Management Provider, Chicago, IL, USA). Analgesic solutions were prepared as 100 ml saline solutions in all groups in a double-blind fashion by one of the authors not taking further part in data collection. The solution contained 5 mg ml^{-1} tramadol in group I and III, 10 μg ml^{-1} fentanyl in group II, and 0.125% ropivacaine+2 μg ml^{-1} fentanyl in group IV.

Patients in group I received intravenous tramadol with a continuous infusion rate of 5 mg h^{-1} after the bolus dose of 20 mg. The loading dose was 50 mg, and the lock-out time was 15 minutes. Group II patients received intravenous fentanyl with the continuous infusion rate of 10 μg hr^{-1} after a 25 μg of bolus dose. The loading dose was 15 μg, and the lock-out time was ten minutes in this group. Epidural tramadol was infused continuously to Group III patients with a basal infusion rate of 10 mg/hr^{-1}, a loading dose of 25-mg, and a lock-out time of 15 minutes after a 20-mg bolus dose. Group IV patients received an epidural infusion of ropivacaine+fentanyl solution as a 6-ml bolus dose, 10-ml loading dose, 2 ml/hr^{-1} infusion rate, and 10-minute lock-out time.

Non-invasive arterial blood pressure, heart rate, respiratory rate, peripheral oxygen saturation and occurrence of untoward events such as hypotension (blood pressure < 90 mm Hg), bradycardia (heart rate < 45 bpm), urinary retention or incontinence, pruritis, abdominal pain, and back pain were noted at 1, 2, 3, 4, 5, 6, 8, 12, 16, 20, and 24 hours after the end of surgery. At the same times the dynamic pain score, motor block (in epidural groups), and sedation were also evaluated. Motor block was assessed by using the modified Bromage scale (0 = no motor block, 1 = hip blocked, 2 = hip and knee blocked, and 3 = hip, knee and ankle blocked). Dynamic pain was assessed by VAS (0 = no pain, 10 = most severe pain). The degree of sedation was measured by using a five-point scale (0 = awake and alert, 1 = weak sedation, tendency to sleep, 2 = mild sedation, easy to wake up when spoken to, 3 = moderately sedated, easy to wake up when slightly shaken, and 4 = deeply sedated and difficult to wake up when shaken).

Statistical analyses were performed using a statistical package for social sciences (SPSS, Chicago, IL) for windows (version 8.0). The one-way ANOVA test was used to compare the results of groups. A p value of < 0.05 was considered to be statistically significant.

Results

There were no significant differences between the groups in terms of demographic and surgical data (Table 1). Most of the patients were gynaecological patients in all groups. Adequate analgesia was achieved in all groups within the first hour of application, and continued for 24 hours. The VAS values were highest in the first measurement (1st hr), and lowest in the last measurement (24th hr) in all groups. The analgesic level was highest in group IV patients ($p < 0.05$) and lowest in group III patients between the 1st and 20th hour ($p < 0.05$) (Table 2).

Table 2. — *The level of pain relief determined by visual analogue scale (VAS) in groups (mean ± SD).*

	Group I (n = 20)	Group II (n = 20)	Group III (n = 20)	Group IV (n = 20)
Control	6.9 ± 1.2	7.4 ± 1.1	7.2 ± 0.4	7.0 ± 0.5
1st hour	4.0 ± 1.1	3.9 ± 1.7	4.7 ± 1.3	0.4 ± 0.3*
2nd hour	2.0 ± 1.2	1.9 ± 1.3	2.8 ± 0.9	0*
3rd hour	0.8 ± 0.8	0.9 ± 0.8	2.1 ± 0.8	0*
4th hour	0.5 ± 0.4	0.5 ± 0.3	1.8 ± 1.0	0*
5th hour	0.4 ± 0.3	0.2 ± 0.1	1.2 ± 1.0	0*
6th hour	0.4 ± 0.2	0.2 ± 0.1	0.6 ± 0.5	0
8th hour	0.2 ± 0.1	0.1 ± 0.1	0.5 ± 0.4	0
12th hour	0.1 ± 0.1	0	0.4 ± 0.3	0
16th hour	0.1 ± 0.1	0	0	0
20th hour	0.1 ± 0.1	0	0	0
24th hour	0	0	0	0

*p < 0.05, between groups.

The number of loading doses given was highest in group III and lowest in group IV. These differences were statistically significant ($p < 0.05$) (Table 1). The amount of drugs that was given to patients was significantly higher in the intravenous tramadol group than the epidural tramadol group (470.0 ± 121.4 mg vs 346.4 ± 49.8 mg, respectively) ($p < 0.05$).

There was no significant difference within and between groups in haemodynamic changes. Hypotension and bradycardia were not seen in any group at any time. Two patients (10%) had grade 2 motor blockade in group IV which disappeared after the 12-hour assessment time. In no case was the level of sedation higher than grade 1. Eleven patients (55%) in group I, and eight patients (40%) in group II suffered from nausea/vomiting which was treated with metoclopramide (10 mg, IV). No patient developed respiratory complications, and SpO_2 did not decrease below 90% in any patient. We did not observe any other complications in any group at any time.

Table 1. — *Demographic and surgical data of patients, and number of loading doses in groups (mean ± SD).*

	Group I (n = 20)	Group II (n = 20)	Group III (n = 20)	Group IV (n = 20)
Age (years)	40.2 ± 11.7	39.8 ± 11.5	38.1 ± 9.9	38.5 ± 10.4
Gender (m/f)	6/14	6/14	4/16	5/15
Weight (kg)	71.0 ± 12.3	72.7 ± 10.3	69.0 ± 8.3	68.2 ± 9.2
Type of surgery	Gynaecological: 11 Inguinal herniation: 8 Other: 1	Gynaecological: 11 Inguinal herniation: 7 Other: 2	Gynaecological: 10 Inguinal herniation: 8 Other: 2	Gynaecological: 11 Inguinal herniation: 6 Other: 3
Time of operation (min)	110 ± 46.1	92.7 ± 37.4	98.7 ± 35.3	84.0 ± 26.3
Number of loading doses	17.4 ± 5.8	31.1 ± 8.2	30.5 ± 9.9*	16.7 ± 3.9**

*p < 0.05, compared to group I and group IV. **p < 0.05, compared to group II and III

Discussion

The main finding of this study is that we achieved adequate analgesia with all therapeutic regimens including the epidural tramadol group. Although tramadol has been used extensively for postoperative pain relief, its epidural usage is not common. Siddik-Sayyid *et al.* [14] reported adequate and safe postoperative analgesia with epidural tramadol after caesarean section operations without respiratory depression. They compared the effects of 100 mg and 200 mg epidural tramadol, and obtained no difference between groups concerning all parameters studied including side-effects. However, the highest VAS score in the epidural tramadol group in our study can be contributed to the effectiveness of the epidural way of tramadol, that is to say that intravenous tramadol is more effective than epidural tramadol in PCA for postoperative pain control.

Fentanyl is a lipid soluble opioid, and used extensively in anaesthetic practice. Most of the time it is combined with another drug in postoperative pain control. We used fentanyl alone in PCA, and found that it causes adequate pain relief after lower abdominal operations. Tramadol is an opioid-like substance used commonly for postoperative pain control. Fentanyl and tramadol have mostly been compared with morphine in PCA. Howell *et al.* [15] compared intravenous fentanyl with morphine in patient-controlled analgesia, and reported similar analgesic effects with both drugs. They also reported that more patients in the fentanyl group required supplementary boluses. In another study intravenous tramadol was compared with morphine for post-thoracotomy pain control, and found to have similar effects on pain relief [16]. Unlugenc *et al.* [17] reported similar results about tramadol versus morphine used after major abdominal surgery for pain control. In our study there was no statistically significant difference in analgesic effects between intravenous tramadol and intravenous fentanyl, nor in side-effects although patients in the tramadol group had a slightly higher rate of nausea. This high rate of nausea is similar to the report of Pang *et al.* [18] who has also compared tramadol with morphine in patient-controlled analgesia after surgery.

Local anaesthestics provide good analgesia, but often undesired side-effects, such as motor block or haemodynamic instability, may develop due to higher doses required to produce sufficient analgesia [19, 20]. The combination of low doses of epidural opioids with a local anaesthetic solution has been suggested to reduce the incidence of side-effects of both opioids and local anaesthetics with clinical potentiation of analgesia provided by patient-controlled epidural analgesia (PCEA) [21]. A ropivacaine-fentanyl combination has been reported to be used successfully in postoperative PCEA. Pirbudak *et al.* [22] reported safe and adequate pain relief for labour with the epidural usage of the ropivacaine-fentanyl combination. On the other hand Berti *et al.* [4] investigated the effects of 0.2% ropivacaine with and without fentanyl for PCEA after surgery, and reported no significant difference between the two groups. In our study, although a small degree of motor block was observed in a small number of patients, the ropivacaine-fentanyl combination produced the best analgesia postoperatively.

In conclusion, intravenous tramadol, intravenous fentanyl, epidural tramadol, and an epidural ropivacaine and fentanyl combination can all provide adequate pain relief in patient-controlled analgesia after surgery. Although the intravenous use of tramadol or fentanyl avoids the necessity of placing an epidural catheter, both drugs are associated with a disturbingly high incidence of nausea and vomiting.

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Address reprint requests to:
H. KOCOGLU, M.D.
Gaziantep University,
Faculty of Medicine
Department of Anesthesiology
and Reanimation
27310 Gaziantep (Turkey)