

# ORIGINAL PAPERS

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## The Effectivity of Fentanyl Versus Tramadol as Intravenous Patient-Controlled Analgesia After Cesarean Section\*

### Skuteczność fentanylu i tramadolu jako dożylnego znieczulenia kontrolowanego przez pacjentkę po cięciu cesarskim

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#### Abstract

**Background.** Patient-controlled analgesia (PCA) is the most widely used treatment method for post-cesarean section pain.

**Objectives.** To compare two different opioids with respect to analgesic quality and side effects.

**Material and Methods.** Sixty patients undergoing elective cesarean surgery were enrolled into two groups. Group F (n = 30) had postoperative IV PCA with fentanyl and Group T (n = 30) had IV PCA with tramadol. Postoperative pain scores, opioid requirements, side effects and patient satisfaction were compared.

**Results.** The patient demographics were similar in both groups. Group F patients consumed  $638.4 \pm 179$  µg of fentanyl, and Group T patients consumed  $559.5 \pm 207$  mg of tramadol. The number of patients requiring additional opioid was similar in both groups. Patient satisfaction did not differ in the two groups.

**Conclusions.** Both fentanyl and tramadol provide sufficient postoperative analgesia and patient satisfaction when used in PCA (*Adv Clin Exp Med* 2010, 19, 6, 739–743).

**Key words:** analgesia, patient-controlled; postoperative pain, cesarean section, fentanyl, tramadol.

#### Streszczenie

**Wprowadzenie.** Leczenie bólu kontrolowane przez pacjenta (PCA) jest najczęściej stosowaną metodą leczenia bólu po cesarskim cięciu.

**Cel pracy.** Porównanie dwóch różnych opioidów w odniesieniu do działania przeciwbólowego i działań niepożądanych.

**Materiał i metody.** Sześćdziesiąt pacjentek poddanych planowemu cięciu cesarskiemu zakwalifikowano do dwóch grup. W grupie F (n = 30) zastosowano dożylnie znieczulenie kontrolowane przez pacjentkę (PCA) fentanylem pooperacyjnie i w grupie T (n = 30) dożylnie PCA tramadolem. Porównano ocenę bólu pooperacyjnego, wymagania opioidów, skutki uboczne i zadowolenie pacjentek.

**Wyniki.** Wskaźniki demograficzne pacjentek były podobne w obu grupach. Grupa F otrzymała  $638,4 \pm 179$  µg fentanylu, a grupa T  $559,5 \pm 207$  mg tramadolu. Liczba pacjentek wymagających dodatkowych opioidów była podobna w obu grupach. Satysfakcja pacjentek nie różniła się w obu grupach.

**Wnioski.** Zarówno fentanyl, jak i tramadol użyty w PCA daje wystarczające znieczulenie pooperacyjne i zadowolenie matek (*Adv Clin Exp Med* 2010, 19, 6, 739–743).

**Słowa kluczowe:** znieczulenie kontrolowane przez pacjenta, ból pooperacyjny, cięcie cesarskie, fentanyl, tramadol.

\* The study was conducted at the Central Education and Research Hospital, Erzurum, Turkey.

Patient-controlled analgesia (PCA) is widely used for postoperative pain management [1]. As Prakash et al. wrote: "PCA allows patients to self-administer small predetermined doses of analgesic medication within limits prescribed by their physician, resulting in improved pain relief, avoidance of over- and undermedication, and greater patient satisfaction" [2]. Fentanyl, as a potent opioid, is commonly used to prevent postoperative pain. Traditionally, fentanyl is administered via the oral, IV or transdermal routes. As Roussier et al. noted: "Fentanyl is frequently preferred because of its high lipid solubility resulting in rapid onset of analgesia, a low incidence of side-effects and a low risk of delayed respiratory depression" [3]. Our goal in this prospective, double blind, randomized study was to compare postoperative pain scores and analgesic requirements for both kinds of opioids in patients following cesarean section, and we found that pain scores and opioid consumption levels were similar. Effectiveness was evaluated by comparing postoperative analgesic needs and side effects.

## Material and Methods

The study protocol was approved by the regional ethics committee. After providing written informed consent for this randomized, prospective, double-blind study, 60 patients undergoing elective cesarean surgery for pregnancy were enrolled. Exclusion criteria included patient refusal to join the study, allergy to opioids, a history of chronic pain, an American Society of Anesthesiologists (ASA) physical status grade more than 3, inability to understand how to use the PCA device, age less than 18 years, and extreme obesity (body mass index > 40). All surgical procedures were performed by one of three surgeons. The anesthetists that collect the data were not aware of the patient groups. Patients were monitored by finger pulse oximetry, electrocardiogram and non-invasive blood pressure monitoring in the operating room. The patients were randomly assigned to receive either intravenous fentanyl (Group F, n = 30) or tramadol (Group T, n = 30) by PCA. The patients were randomly allocated according to a computer-generated randomization list. All the patients were premedicated with atropin 0.01 mg kg<sup>-1</sup> im 45 minutes before the surgical procedure. The use of the PCA system and a standard visual analogue scale (VAS) for pain was explained to the patients the day before the operation; in the VAS, 0 would mean "no pain" and 100 would mean "worst possible pain imaginable". General anesthesia was induced by propofol 2 mg kg<sup>-1</sup> and atracurium 0.4 mg kg<sup>-1</sup>.

The patients' lungs were mechanically ventilated and ventilation was adjusted to maintain end-expiratory CO<sub>2</sub> between 32–36 mm Hg. After the baby was born, anesthesia was maintained by sevoflurane with an end-tidal concentration of 1.5% in oxygen–nitrous oxide (FI<sub>O<sub>2</sub></sub> = 0.5). Isotonic saline was used for intraoperative fluid maintenance.

Postoperatively, patients in Group F received an initial dose of 1 µg kg<sup>-1</sup> fentanyl IV. For the PCA, 1 mg of fentanyl was diluted in 100 ml of isotonic saline. The PCA boluses were 20 mcg, and the lockout interval was 8 minutes without an infusion rate. Patients in Group T received 1 mg kg<sup>-1</sup> tramadol as an initial dose, and 1 g of tramadol was diluted in 100 ml of isotonic saline for the PCA device. The demand dose was 20 mg; the lockout interval was 8 minutes without basal infusion. The patients began to receive analgesic medication via PCA immediately after the initial doses.

For 24 hours following the surgery, pain scores were recorded using the VAS at rest and after coughing. The intensity of pain was assessed at 0, 1, 2, 4, 8, 12 and 24 hours by the 100-point VAS, and the pain scores were recorded. If the VAS score was more than 30, the physician in charge could give a 2-cc bolus via PCA without changing the bolus dose and lockout interval. The time interval to the first analgesia requirement was recorded, as were side effects like pruritus, nausea and vomiting: 0 = no episode; 1 = at least one episode. The level of sedation was assessed by the Ramsey scale (1 = anxious, agitated, restless; 2 = cooperative, oriented, tranquil; 3 = responds to comments only; 4 = brisk response to light glabellar tap or loud noise; 5 = sluggish response to light glabellar tap or loud noise; 6 = no response).

Nausea and vomiting were treated with metoclopramide 10 mg IV. Pruritus was treated with diphenhydramine 25 mg IV. All patients were given a questionnaire at the end of the 24th hour, asking if they would accept the same anesthetic procedure and the same analgesic method in the future. The answers and the related reasons were noted and accepted as the criteria for satisfaction. All the patients were interviewed about their level of satisfaction by a blinded interviewer.

The Statistical Package for Social Sciences (SPSS) for Windows 10.0 program was used for statistical analysis. Group size was selected by using proportions sample size estimates ( $\alpha$ : 0.05,  $\beta$ : 0.09). Values were expressed as mean  $\pm$  SD. The paired t-test was used for comparisons between groups with normal distribution parameters, and the unpaired t-test was used for abnormally distributed parameters. Qualitative data were compared by using the  $\chi^2$  test ( $p < 0.05$ ). A  $p$ -value < 0.05 was considered significant.

## Results

All 60 patients who were enrolled in the study were included in the analyses. The patients' ages, weights, heights, ASA physical status and operating room time were similar in the two groups (Table 1). There were no major anesthetic or surgical complications. In Group F, 76% of the parturients were ASA1 and 24% were ASA2; in Group T 80% of parturients were ASA1 and 20% of them were ASA2 (Table 1). Group F patients consumed  $638.4 \pm 179.10$  mcg fentanyl and Group T patients consumed  $559.5 \pm 207.04$  mg tramadol (Table 2) ( $p > 0.05$ );  $44 \pm 26.471$  mcg additional fentanyl

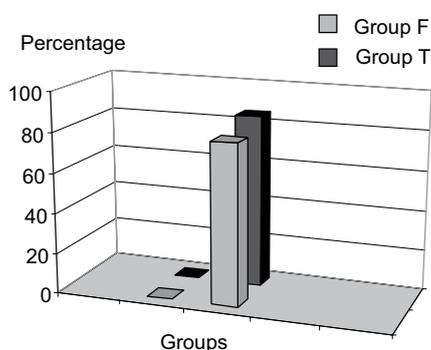
**Table 1.** Patients' demographics and duration of surgery (Values are mean)

**Tabela 1.** Dane demograficzne pacjentów oraz czas trwania operacji (wartości średnie)

	Group F (Grupa F)	Group T (Grupa T)
Age – years (Wiek – lata)	$26.32 \pm 8.69$	$28.06 \pm 11.47$
Weight – kg (Masa ciała – kg)	$73.58 \pm 10.42$	$74.96 \pm 10.21$
Height – cm (Wzrost – cm)	$65 \pm 10.02$	$64 \pm 18.38$
Duration of surgery – min (Czas operacji – min)	$124.87 \pm 58.16$	$121.25 \pm 38.27$
ASA	76% ASA1, 24% ASA2	80% ASA1, 20% ASA2

Group F (n = 30): Fentanyl PCA group. Group T (n = 30): Tramadol PCA group.

Grupa F (n = 30): PCA fentanylem. Grupa T (n = 30): PCA tramadolem.



**Fig. 1.** Additional opioid consumption of groups (%). Group F (n = 30): Fentanyl PCA group. Group T (n = 30): Tramadol PCA group.  $P > 0.05$

**Ryc. 1.** Dodatkowe spożycie opioidów w grupach – %. Grupa F (n = 30): PCA fentanylem. Grupa T (n = 30): PCA tramadolem.  $P > 0,05$

and  $62.6 \pm 32.688$  mg additional tramadol was required (Table 2). The number of patients requiring opioids in the first 24 hours was similar in both groups. In Group F, 24 patients (80%) required additional opioid; in Group T, 22 patients (86%) received an additional opioid bolus dose (Figure 1). Postoperative pain was compared at 1, 2, 4, 8, 12 and 24 hours after surgery. There was no significant difference between the two groups' pain scores in the postoperative period (Table 3). Postoperative nausea and vomiting scores were similar in both groups ( $p > 0.05$ ). Antiemetics were necessary for 10 patients in Group F and 11 in Group T (Figure 2). The time to the first analgesic requirement was also significantly shorter for the general anesthesia group as compared with spinal anesthesia ( $p < 0.05$ ). All patients received paracetamol 1 g IV

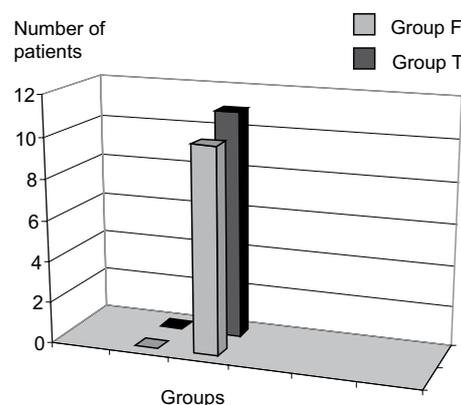
**Table 2.** Opioid consumption values of groups (Values are mean)

**Tabela 2.** Spożycie opioidów w grupach (wartości średnie)

	Group F – $\mu$ g (Grupa F)	Group T – mg (Grupa T)
Total opioid consumption (Całkowita ilość podanych opioidów)	$638.4 \pm 179.10$	$559.5 \pm 207.04$
Additional opioid consumption (Dodatkowa ilość podanych opioidów)	$44 \pm 26.471$	$62.6 \pm 32.688$

Group F (n = 30): Fentanyl PCA group. Group T (n = 30): Tramadol PCA group.

Grupa F (n = 30): PCA fentanylem. Grupa T (n = 30): PCA tramadolem.



**Fig. 2.** Antiemetic drug requirements of groups. Group F (n = 30): Fentanyl PCA group. Group T (n = 30): Tramadol PCA group.  $P > 0.05$

**Ryc. 2.** Zapotrzebowanie na leki przeciwwymiotne w grupach. Grupa F (n = 30): PCA fentanylem. Grupa T (n = 30): PCA tramadolem.  $P > 0,05$

**Table 3.** Postoperative VAS scores of groups (values are mean)**Tabela 3.** Pooperacyjne ocena VAS dwóch grup (wartości średnie)

Hours (Godziny)	Group F (Grupa F)	Group T (Grupa T)
0	50 ± 15.3	52.6 ± 10.48
1	31.6 ± 14.8	36.6 ± 15.3
2	20.3 ± 16.5	28.6 ± 14.07
4	19 ± 10.2	22 ± 13.2
8	24 ± 13.5	20.6 ± 11.7
12	28 ± 15.8	22.6 ± 10.1
24	15.3 ± 7.7	11.3 ± 10.0

Group F (n = 30): Fentanyl PCA group. Group T (n = 30): Tramadol PCA group. P > 0.05.

Grupa F (n = 30): PCA fentanylem. Grupa T (n = 30): PCA tramadolem. P > 0,05.

postoperatively every six hours as a prophylactic analgesic. Two patients from Group F and three patients from Group T stated that they would not accept the same analgesic procedure in the future, because of incidences of nausea and vomiting.

## Discussion

As Karamanlioğlu et al. wrote: “IV PCA is effective for individual pain relief in the postoperative period. Is generally well tolerated, the most common adverse events being nausea and vomiting” [13]. Several opioids or local anesthetics are used for PCA. Morphine, meperidine, fentanyl, tramadol or remifentanyl are the most preferred opioids [5–7]. In the 1998 study by Baraka et al., tramadol was “associated with a high incidence of intraoperative maternal recall [and] lower umbilical vein PO<sub>2</sub> and higher PCO<sub>2</sub>” than fentanyl [8], but in that study the opioids were given preoperatively, as preemptive analgesia. Preemptive analgesia is a recommended technique for postoperative pain treatment [9], but there is always a potential risk of respiratory depression for the newborns when parturients receive opioids as a preemptive analgesic agent. For this reason, the authors of the current study did not use opioids in the preoperative period.

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Postoperative treatment of acute pain by multimodal analgesia is an effective method [10]. In this method, nonsteroidal anti-inflammatory drugs or paracetamol reduce the consumption of opioids [11]. As Karamanlioğlu et al. pointed out, “Reuben and Connelly [12] demonstrated significant opioid-sparing effects with celecoxib and rofecoxib when used in conjunction with PCA morphine after spinal fusion surgery” and they themselves observed “a significant analgesic benefit with regard to postoperative pain relief and a decrease in opioid requirement after thyroid surgery” using the same procedure [13]. The authors of the current study gave paracetamol 1 g to all patients 4 times a day. The first dose was given before the surgical process ended. This provided both preemptive analgesia and multimodal analgesia at the same time. In the current study, there were no differences in adverse effects in the two groups during the first 24 postoperative hours.

Sudheer et al. compared the analgesic efficacy and side effects of tramadol with morphine after craniotomies, and reported: “Morphine produced significantly better analgesia than tramadol at all time points” [14]. The analgesic effect of morphine is of long duration, so it is a better choice for major cranial operations. While cesarean section is not a minor type of surgery it was the authors’ assessment that both tramadol or fentanyl provided sufficient analgesia and the doses used via PCA were not overdoses. This also limited the incidence of side effects.

Other studies have demonstrated that tramadol is as effective as morphine for PCA pain control after major surgery [15, 16]. In another study, researchers demonstrated that tramadol can also be used as an additional agent with other opioids, with better results than in single opioid usage [17]. PCA Fentanyl has also been found to be safe and efficient for postoperative analgesia for children [18].

The present study comparing fentanyl with tramadol did not find a significant difference in postoperative pain scores. The pain scores and PCA opioid consumption during the first 24 hours after surgery in patients who had undergone cesarean section were similar. Further studies can be performed with different types of opioids by IV, epidural or transdermal PCA.

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