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Tramadol for Early Postoperative Analgesia in Abdominal Hysterectomy: Comparison of Different Administration Techniques

Abdominal Histerektomide Erken Postoperatif Analjezi için Tramadol: Farklı Uygulama Tekniklerinin Karşılaştırılması

Besim Haluk Bacanakgil, Işık Kaban

University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of Gynecology and Obstetrics, İstanbul, Turkey

ABSTRACT

Introduction: Tramadol is a centrally acting analgesic for control of postoperative pain. This study aimed to compare three different routes of administration of tramadol for early postoperative analgesia in abdominal hysterectomy.

Methods: Patients who were scheduled for abdominal hysterectomy with Pfannenstiel incision were divided into three groups according to the routes of administration of tramadol: incisional subcutaneous infiltration (group 1), subcutaneous infiltration plus intravenous administration (group 2), and slow intravenous administration (group 3), by sequential randomization. The analgesic effect was assessed using the revised face pain scale, and side effects such as nausea or hypotension were evaluated at 1, 2, 3, and 4 hours after surgery.

Results: A total of 90 cases were evaluated, including 30 cases in each group. In group 3, the pain score at the 1st hour was lower than the others (4.1±2.1 vs.5.2±1.9 and 5.6±2.3; p=0.040). Nausea more often occurred in group 2 at the second hour (33% vs 13% and 13%; p=0.017) and in group 1 at the fourth hour (20% vs 7% and 0; p=0.022). The mean arterial pressure in group 3 was lower at the first and second hours than those in the other groups at the same time points. The mean pulse rates of the groups were similar for each hour.

Conclusion: The results of this study showed that intravenous administration of tramadol is more effective for pain control in the first hour.

Keywords: Hysterectomy, postoperative, analgesia, tramadol

ÖZ

Amaç: Tramadol, postoperatif ağrının kontrolü için merkezi olarak etkili bir analjeziktir. Bu çalışmanın amacı, erken postoperatif analjezi için abdominal histerektomide tramadolün üç farklı uygulama yolunu karşılaştırmaktır.

Yöntemler: Pfannenstiel insizyonu ile abdominal histerektomi yapılacak olgular sıralı randomizasyon yöntemi ile insizyonel subkutan infiltrasyon (grup 1), infiltrasyon artı intravenöz (grup 2) ve intravenöz (grup 3) olmak üzere 3 gruba ayrıldı. Face pain skalası-revize ile analjezik etki ve mide bulantısı veya hipotansiyon gibi yan etkiler postoperatif 1., 2., 3. ve 4. saatlerde değerlendirildi.

Bulgular: Her grupta 30 hasta olmak üzere toplam 90 hasta değerlendirildi. Grup 3'ün ağrı skoru ilk saatte diğerlerinden daha düşüktü (4,1±2,1'e karşı 5,2±1,9 ve 5,6±2,3; p=0,040). Bulantı; grup 2'de 2. saatte (%33'e karşı %13 ve %13; p=0,017), grup 1'de 4. saatte (%20'ye karşı %7 ve 0; p=0,022) daha sıktı. Grup 3'te ortalama arter basıncı birinci ve ikinci saatte diğerlerine göre daha düşüktü. Grupların ortalama nabız hızı her saat için benzerdi.

Sonuç: Abdominal histerektomide postoperatif ilk saatte ağrı kontrolü için i.v. tramadol uygulaması, sc infiltrasyon ve sc infiltrasyon artı i.v. infüzyondan daha etkilidir ve tercih edilebilir.

Anahtar Kelimeler: Histerektomi, postop ağrı, tramadol, bulantı

Address for Correspondence/Yazışma Adresi: Işık Kaban MD, University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of Gynecology and Obstetrics, İstanbul, Turkey
Phone: +90 505 794 62 28 **E-mail:** drisikkaban81@gmail.com **ORCID ID:** orcid.org/0000-0001-5134-0513

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Introduction

Total abdominal hysterectomy (TAH) is the most common major non-obstetric surgical procedure for women and causes postoperative pain and discomfort. Tramadol, a centrally acting analgesic, consists of two enantiomers, both of which contribute to analgesic activity through different mechanisms (1,2). These two enantiomers act synergistically to provide analgesia. In addition to the weak opioid receptor agonist effect, tramadol inhibits presynaptic reuptake of noradrenaline and serotonin (5-HT), as well as stimulates 5-HT release. Thus, tramadol potentiates the endogenous analgesia system with both opioid agonist mechanism and monoaminergic effect (3). Tramadol is a synthetic medication that is structurally related to codeine and morphine (4).

For approximately 30 years, tramadol drug has been used for the control of postoperative pain. Its efficacy for the treatment of moderate to severe postoperative pain has been demonstrated in patients who underwent surgery. Tramadol may be administered orally, rectally, intravenously (IV), intramuscularly, or subcutaneously (SC) (5,6).

In this study, different routes of administration of tramadol were compared in terms of pain control and side effects in the early postoperative period in patients who underwent abdominal hysterectomy with a Pfannenstiel incision for benign diseases.

Methods

This prospective, randomized, patient-blinded, evaluator-blinded, observational trial study included 90 female patients (mean age: 49 years) with American Society of Anesthesiologists (ASA) physical status I/II scheduled to undergo elective TAH with or without bilateral salpingo-oophorectomy through Pfannensteil incision under general anesthesia for benign diseases. The exclusion criteria were presence of giant fibroids, severe intra-abdominal adhesion, and malignancy, history of chronic pain, history of regular analgesic drug use, and contraindications to tramadol. In addition, those who had undergone abdominal surgery, those using narcotic analgesics or psychotropic drugs, and those with alcohol dependence were excluded.

For postoperative analgesia, patients were randomly allocated into one of the three groups according to the routes of administration of tramadol: incisional SC infiltration (group 1), SC infiltration plus IV administration (group 2), and slow IV administration (group 3) by sequential randomization. In all three groups, tramadol was administered immediately following the closure of the Pfannenstiel incision.

In group 1, 2 mg/kg tramadol was diluted with 20 mL of sterile saline and applied equally to the SC tissue on both sides of the incision. In group 2, half of the tramadol dose calculated as 2 mg/kg was diluted with 20 mL of sterile saline and applied SC; the other half was administered by slow IV infusion. In group 3, 2 mg/kg tramadol was administered by slow IV infusion.

All cases were either ASA I or ASA II. In all patients, procedures were performed under general anesthesia. During the induction period, pentothal 6 mg/kg, rocuronium 0.6 mg/kg, and midazolam 2 mg were also administered. Following orotracheal intubation, anesthesia was continued with 1%-2% sevoflurane and NO_2%50 + O_2%50 mixture.

Patients' pain was evaluated using the revised face pain scale (FPS-R) on the first, second, third, and fourth hours after surgery. The FPS-R is commonly used for measuring pain intensity in pediatric and adult populations (7). The FPS-R consists of six face pictures that depict different degrees of pain from "no pain" to "most pain possible." A numerical value ranging from 0 to 10 (i.e., 0, 2, 4, 6, 8, 10) is assigned to each face [visual analog scale, (VAS)].

Blood pressure and pulse values were measured. The mean blood pressure was taken into consideration while analyzing blood pressure values. Occurrences of nausea and vomiting were recorded. The study was double-blind. The physician who evaluated using FPS-R did not know which group the patient belonged to. The patients did not know which drug was used for analgesia. The operation time was defined as the time period from skin incision to closure of the incision. In patients who had a pain score ≥4 or could not tolerate pain, an additional 75 mg diclofenac sodium was administered IV.

The study was approved by the Local Ethics Committee University of Health Sciences Turkey, İstanbul Training and Research Hospital (approval number: 1175/2018). Informed consent form was obtained from all patients for the inclusion and publication of their data.

Statistical Analysis

Data were analyzed using SPSS 22.0 program. Mean and standard deviation, median and minimum-maximum values, frequencies, and ratios were used for descriptive analysis. The Shapiro-Wilk test was used to analyze normality distribution of data. The Kruskal-Wallis test was used in the analysis of quantitative independent data. The chi-square test was used for the analysis of qualitative independent data. A p-value <0.05 was considered to indicate significance.

Results

A total of 90 patients were evaluated, with 30 patients in each group. The mean age, body mass index, gravidity, and parity of the groups were comparable (Table 1).

In the first hour, the VAS score was lower in group 3 than in other groups ($p=0.040$) (Figure 1). Nausea tended to improve in later hours, especially in group 3 (Figure 2). No vomiting was observed in group 3 at the fourth hour postoperatively. Additionally, group 3 showed significance in the binary comparisons (Table 2 and Figure 3). The pain scores in the second hour postoperatively in group 3 were acceptable, although not significant ($p=0.069$). The pain scores of the other groups at the third and fourth hours postoperatively were comparable. The mean arterial pressures in group 3 were lower at the first and second hours postoperatively than those in the other groups at the same time points ($p=0.013$, $p=0.023$, respectively). The pulse rates of the three groups were comparable. Nausea more often occurred in group 2 at the second hour and in group 1 at fourth hour postoperatively (respectively, $p=0.017$, $p=0.022$).

Table 1. Characteristics of patients according to the method of tramadol administration

	Group 1 (SC) (n=30)	Group 2 (SC + IV) (n=30)	Group 3 (IV) (n=30)	p
Age (mean ± SD)	49.3±6.2	50.4±6.9	49.9±6.0	0.825
BMI* (mean ± SD)	29.5±5.2	30.6±5.7	30.5±6.7	0.899
Gravida [median (min-max)]	3 (0-6)	3 (1-6)	4 (2-10)	0.128
Parity [median (min-max)]	2 (0-6)	2 (1-4)	3 (2-6)	0.052
OD* [minute (mean ± SD)]	135±50	119±31	133±34	0.782
Pulse rate (mean ± SD)				
Postoperative 1st hour	78±10	75±14	77±8	0.982
2nd hour	80±12	77±12	79±8	0.897
3rd hour	79±8	80±14	77±6	0.620
4th hour	80±10	79±16	78±5	0.892
MAP* (median, 95% CI)				
Postoperative 1st hour	100 (93.0-103.0)	95.0 (91.6-98.2)	83.3 (83.3-93.3)	**0.013**
2nd hour	99.3 (90.8-99.7)	93.3 (86.6-100.0)	90 (86.6-96.0)	**0.023**
3rd hour	96.6 (88.6-103.0)	93.3 (91.6-96.6)	86.6 (84.1-90.3)	0.061
4th hour	96.6 (90.0-101.6)	93.3 (90.3-96.6)	93.3 (87.3-95.8)	0.288
VAS* scores (median, 95% CI)				
Postoperative 1st hour	6.0 (4.0-8.0)	6.0 (4.0-6.0)	4.0 (4.0-6.0)	**0.040**
2nd hour	4.8 (2.4-7.2)	5.0 (2.8-6.9)	3.6 (2.1-5.7)	0.069
3rd hour	4.1 (2.1-6.0)	4.0 (2.0-6.0)	3.2 (1.2-4.0)	0.250
4th hour	3.0 (1.0-4.1)	2.5 (1.5-3.9)	2.5 (1.0-3.0)	0.570
Nausea [n (%)]				
Postoperative 1st hour	6 (20%)	14 (47%)	12 (40%)	0.083
2nd hour	4 (13%)	10 (33%)	4 (13%)	**0.017**
3rd hour	4 (13%)	8 (27%)	2 (7%)	0.096
4th hour	6 (20%)	2 (7%)	0	**0.022**
Vomiting (n)				
Postoperative 1st hour	4 (13.3%)	2 (6.6%)	0	0.120
2nd hour	0	0	0	-
3rd hour	0	0	0	-
4th hour	2 (6.6%)	0	0	-

To calculate the mean arterial pressure, double the diastolic blood pressure and add the sum to the systolic blood pressure, and then divide by 3.

SC: Subcutaneously, IV: intravenously, SD: standard deviation, BMI: body mass index, min: minimum, max: maximum, OD*: operation duration, MAP: mean arterial pressure, CI: confidence interval, VAS: visual analog scale

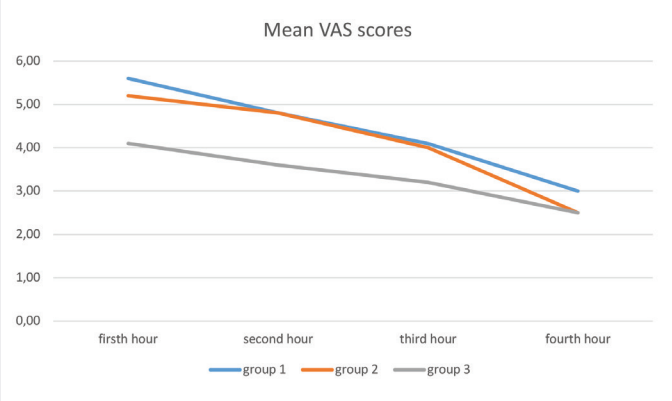

Figure 1. Graph of the mean visual analog scale scores of the patients by groups

VAS: Visual analog scale

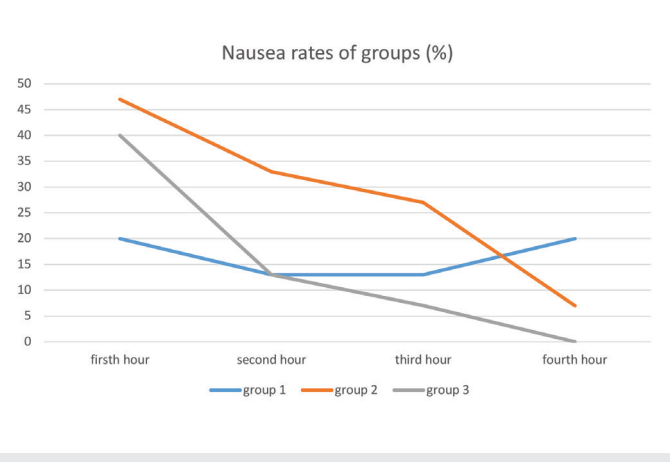

Figure 2. Graph of percent rates of nausea of the patients by groups

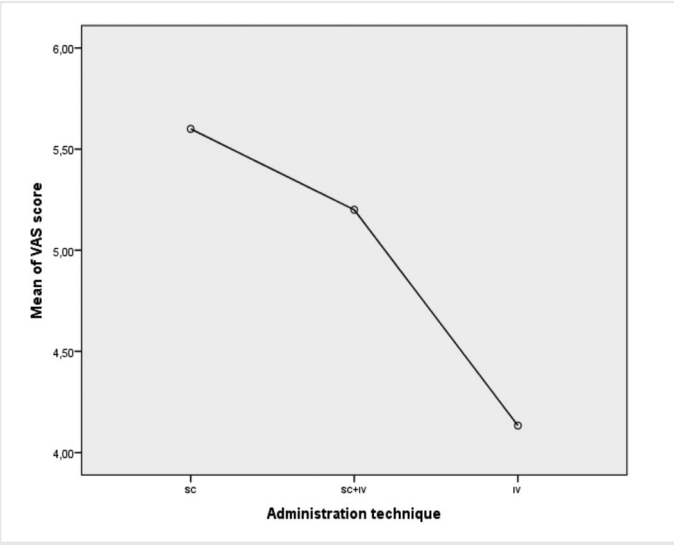

Figure 3. Graph of the visual analog scale scores for the first-hour postoperatively

Table 2. Binary comparisons for first-hour VAS scores

Groups	p
Subcutaneous and subcutaneous plus intravenous	0.480
Subcutaneous and intravenous	**0.040**
Subcutaneous plus intravenous and intravenous	0.070

VAS: Visual analog scale

Discussion

In this randomized trial, the effectiveness of different routes of tramadol administration to control pain in the early postoperative period of abdominal hysterectomy was compared. At the first-hour postoperatively, the analgesic effect of IV administration was significantly higher than those of other routes of administration. The results of this study imply that IV administration of tramadol was more advantageous for the control of postoperative pain. However, when tramadol was given IV, patients should be monitored carefully for low blood pressure. Blood pressure was significantly lower in the IV group, especially during the first-hour postoperatively. In addition, nausea more often occurred with IV intravenous administration than with SC infiltration, especially in the first-hour postoperatively. Side effects such as low blood pressure and nausea were less common with SC administration. However, the pain score was higher with SC administration than with IV administration of tramadol.

Several studies have reported on the postoperative effects of tramadol on obstetrics and gynecologic surgery. In patients who underwent cesarean section, Haliloglu et al. (8) and Sahmeddini et al. (9) have reported that SC infiltration of tramadol may be a useful technique to reduce postoperative pain (8). Altunkaya et al. (10) suggested that tramadol can be used as a local anesthetic agent (11). However, in these studies, SC infiltration was not compared with the IV administration. In our study, both SC infiltration and SC plus IV administration of tramadol were not as effective as IV administration in early postoperative analgesia. These patients may need additional analgesics in the early postoperative period.

Study limitation

A potential limitation of this study was the lack of a placebo group. However, a placebo group is unlikely in patients who underwent surgery. This study showed that IV administration of tramadol was more advantageous in controlling early postoperative pain. However, in this application, low blood pressure and nausea in the first-hour postoperatively appeared to be a disadvantage.

Conclusion

This study showed that IV administration of tramadol is more effective than SC infiltration or SC infiltration plus IV infusion to control pain in the first hour after abdominal hysterectomy. However, the mean arterial pressure of patients who received tramadol via the IV route becomes lower for the first 2 hours postoperatively; thus, patients should be closely monitored for hypotension.

Ethics Committee Approval: The study was approved by the Local Ethics Committee University of Health Sciences Turkey, İstanbul Training and Research Hospital (approval number: 1175/2018).

Informed Consent: Informed consent form was obtained from all patients for the inclusion and publication of their data.

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References

1. Grond S, Sablotzki A. Clinical pharmacology of tramadol. Clinical Pharmacokinet 2004; 43: 879-923.
2. Boora K. Tramadol. In: xPharm: The Comprehensive Pharmacology Reference. 2011.
3. Scott LJ, Perry CM. Tramadol: A review of its use in perioperative pain. Drugs 2000; 60: 139-76.
4. David J. Skinner, Jonathan Epstein, Marco Pappagallo. Chapter 69 - Tramadol. In: Smith HS, editor. Current Therapy in Pain. Elsevier Ltd; 2009. pp. 508-12.
5. Miotto K, Cho AK, Khalil MA, Blanco K, Sasaki JD, Rawson R. Trends in Tramadol: Pharmacology, Metabolism, and Misuse. Anesth Analg 2017; 124: 44-51.
6. Smith AB, Ravikumar TS, Kamin M, Jordan D, Xiang J, Rosenthal N; CAPSS-115 Study Group. Combination tramadol plus acetaminophen for postsurgical pain. Am J Surg 2004; 187: 521-7.
7. Hicks CL, von Baeyer CL, Spafford PA, van Korlaar I, Goodenough B. The faces pain scale - revised: toward a common metric in pediatric pain measurement. Pain 2001; 93: 173-83.

8. Haliloglu M, Bilgen S, Menda F, Ozcan P, Ozbay L, Tatar S, et al. Analgesic efficacy of wound infiltration with tramadol after cesarean delivery under general anesthesia: Randomized trial. J Obstet Gynaecol Res 2016; 42: 816-21.

9. Sahmeddini MA, Azemati S, Motlagh EM. Local infiltration of tramadol versus bupivacaine for post cesarean section pain control: A double-blind randomized study. Iran J Med Sci 2017; 42: 235-41.

10. Altunkaya H, Ozer Y, Kargi E, Babuccu O. Comparison of local anaesthetic effects of tramadol with prilocaine for minor surgical procedures. Br J Anaesth 2003; 90: 320-2.

11. Altunkaya H, Ozer Y, Kargi E, Ozkocak I, Hosnuter M, Demirel CB, et al. The postoperative analgesic effect of tramadol when used as subcutaneous local anesthetic. Anesth Analg 2004; 99: 1461-4.