

The Postoperative Analgesic Effect of Tramadol When Used as Subcutaneous Local Anesthetic

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Recently, it has been shown that tramadol was an effective local anesthetic in minor surgery. In this study, its efficacy for relieving postoperative pain was evaluated. Forty patients undergoing minor surgery (lipoma excision and scar revision) under local anesthesia were included. The patients were randomly allocated into two groups: In group T ($n = 20$), 2 mg/kg tramadol, and in group L ($n = 20$), 1 mg/kg lidocaine were given subcutaneously. In both groups, the injection volume was 5 mL containing 1/200,000 adrenalin. The degree of the erythema, burning sensation, and pain at the injection site were recorded. Incision response, which is a degree of the pain sensation during incision, was recorded and graded with the visual analog scale (VAS) 0–10. After incision, VAS values were recorded at 15-min intervals. When the VAS score of the pain during surgery exceeded 4, an additional 0.5 mg/kg of the study drug was injected and this dosage was added to the total

amount. Patients were discharged on the same day. Subjects with VAS ≥ 4 were advised to take paracetamol as needed. No side effects were recorded in either group except for 1 patient complaining of nausea in group T at the 30th min of operation. After 24 h, patients were called and the time of first analgesic use and total analgesic dose taken during the postoperative period were recorded. During the 24 postoperative hours, 18 of 20 (90%) subjects did not need any type of analgesia in group T, whereas this number was 10 (50%) in group L ($P < 0.05$). The time span before taking first analgesic medication was longer (4.9 ± 0.3 h) in group T than that of group L (4.4 ± 0.7 h) ($P < 0.05$). We propose that tramadol can be used as an alternative drug to lidocaine for minor surgeries because of its ability to decrease the demand for postoperative analgesia.

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Tramadol is a centrally-acting drug, which is effective in the treatment of moderate to severe pain (1,2). In addition to its systemic action, the local anesthetic effect of tramadol on peripheral nerves has been shown in both clinical and laboratory studies (3,4). In our previous study, we found that tramadol had a local anesthetic effect similar to that of prilocaine after intradermal injection. However, tramadol had an increased incidence of local reaction (rash) when compared with prilocaine.

The aim of this study was to evaluate the effect of tramadol on the degree of postoperative pain and amount of postoperative analgesic consumed. In addition, the value of combining tramadol with epinephrine to lessen side effects such as burning and erythema was also assessed. In the present study, the

local anesthetic and postoperative analgesic effect of tramadol were compared with that of lidocaine for minor surgery performed using local anesthesia.

Methods

The study was approved by the Ethics Committee of the ZKU Research Hospital and written informed consent was obtained from all subjects. Forty patients, ASA physical status I–II, aged 18–60 yr, undergoing lipoma excision and scar revision, were included. The lesions were situated on the extremities and body, and the required incision was not more than 4 cm. Patients who had lesions requiring extensive tissue undermining, and lesions situated on the face were not included. Other exclusion criteria were opioids, tramadol, or clonidine use and known tramadol allergy.

The patients were randomly assigned to receive either 2 mg/kg tramadol (Contramal[®]; Abdi Ibrahim Ltd., Istanbul, Turkey) (group T, $n = 20$), or 1 mg/kg lidocaine (Jetokain[®]; Adeka Ltd., Samsun, Turkey) (group L, $n = 20$). Randomization was provided by

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shuffled, sealed, opaque, numbered envelopes. In both groups, the studied drug was prepared by an independent anesthesiologist who was not involved in the medication or surgery. Both of the solutions, which were diluted to 5 cc containing 1/200,000 adrenaline, had a similar appearance and viscosity. No perioperative sedation was given. The same surgeon, who also was not aware of the consistency of the given medication, performed all the injections with a 25-gauge needle mounted to the syringe. The patients were instructed to inform the investigator about the intensity of pain during injection and incision (incision response), pinprick sensation, and the degree of pain every 15 min. The responses were evaluated with a verbal analog scale (VAS), in which no pain was graded as zero and the most excruciating pain as 10. The first incision was performed 2 min after injection of the drug. When the VAS score exceeded 4 points during surgery, an additional 0.5 mg/kg of the same solution was injected and this dosage was added to the total amount. Bleeding during surgery was assessed by the same surgeon and graded between zero and 3. Local reactions (no reaction = zero, mild rash = 1, erythema = 2, urticaria = 3) were also recorded. Patients were discharged on the same day. When the patients experienced pain postoperatively, they were allowed 1 g of paracetamol, orally bid. After 24 h, patients were called and the time of first analgesic use and total dose after operation were recorded.

We considered a 30% increase in total postoperative analgesic efficacy to be clinically important. From preliminary data, we calculated with α set at 0.05 that 15 patients per group would give a statistical power of 95% between groups. Power analysis used an online calculator for sample size (<http://www.powerandprecision.com>). The data obtained were normally distributed as assessed by the Kolmogorov-Smirnov test. Data were shown as mean (SD) or median.

The data were analyzed and compared by using Student's *t*-test, χ^2 , and Fisher's exact χ^2 tests, with a *P* value of < 0.05 considered as statistically significant.

Results

The age, sex, body weight, and length of surgical times were comparable between groups (Table 1).

Arterial blood pressure, heart rate, and peripheral oxygen saturation remained stable during the study. One patient in group T experienced nausea at the 30th min of operation. Except for this patient, none of the patients had postoperative nausea and vomiting in either group throughout the remainder of the study.

There was no significant difference between groups with respect to injection pain (group T 1.15 ± 0.7 , group L 1.25 ± 0.4 , *P* = 0.43), pinprick test (group T 0.30 ± 0.05 , group L 0.45 ± 0.1 , *P* = 0.77), local

Table 1. Patient Characteristics

	Group T (n = 20)	Group L (n = 20)
Male/female	11/9	12/8
Age (yr)	32.7 (17-57)	39.5 (24-60)
Weight (kg)	66.6 (11)	65.4 (10)
Duration of surgery (min)	34.5 (15-45)	30 (15-45)

Data are mean (number, SD, or range).
 Group T = tramadol group, group L = lidocaine group.

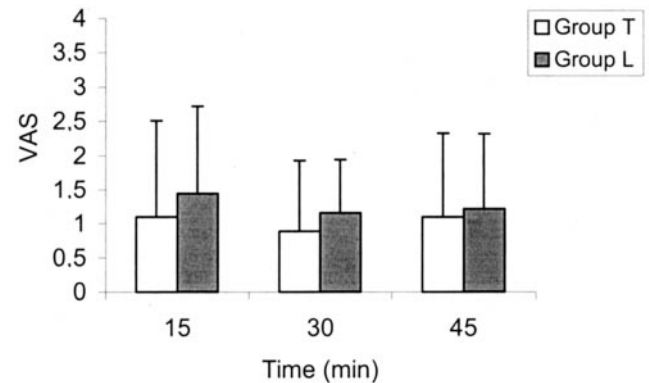


Figure 1. Intraoperative pain scores in both groups (not significant) (mean \pm SD). VAS = visual analog scale.

reaction at the injection site (group T 0.10 ± 0.06 , group L 0.15 ± 0.1 , *P* = 0.99), and bleeding quantity (group T 0.6 ± 0.1 , group L 0.7 ± 0.1 , *P* = 0.83).

Surgical incision was performed at the second minute in all patients. An additional dose of local anesthetic was needed in 5 patients in group T (mean dose 150.0 mg) and 2 patients in group L (mean dose 80.0 mg). The number of patients who required additional injection did not differ significantly between groups (*P* = 0.22).

The VAS score did not differ significantly between groups at 15 and 30 min (Fig. 1). During the 24 postoperative hours, 18 of 20 (90%) subjects did not need paracetamol in group T, whereas this number was 10 (50%) in group L (*P* = 0.02). The length of time to first analgesic medication was longer in group T than that of group L (*P* = 0.01) (Table 2). When cumulative doses of paracetamol were compared, this amount was significantly less in group T than in group L (*P* = 0.005) (Table 2).

Discussion

In this study, subcutaneously administered tramadol provided local anesthesia equal to lidocaine. This result is in accordance with our previous study (3). Moreover, tramadol extended the pain-free period after operation and significantly decreased the need for postoperative analgesia.

Table 2. Comparison of First Analgesic Time and Total Postoperative Paracetamol Consumption (mg) in the Tramadol (Group T) and Lidocaine (Group L) Groups

	Group T (n = 20)	Group L (n = 20)
First analgesic medication time (h)	4.9 (4.7-5.4)*	4.4 (4.0-4.7)
Total postoperative paracetamol consumption (mg)	100 (-44-244)†	500 (259-740)

Data are mean (95% confidence interval).

* $P = 0.01$ versus group L; † $P = 0.005$ versus group L.

Initially, it was thought that tramadol produced its antinoceptive and analgesic effects through spinal and supraspinal sites rather than via a local anesthetic action (5). However, several clinical studies have shown that it might have peripheral local anesthetic type properties (3,4,6,7). By direct tramadol application to the sciatic nerve in rats, it was proven that tramadol exerts a local anesthetic type effect (6). In the present study, tramadol had a local anesthetic action similar to that of lidocaine, and because of its antinoceptive effect, it could extend the postoperative pain-free period.

When extracellular sodium concentration decreases, the nerve fiber becomes sensitive to local anesthetics (8). Jou et al. (2) suggested that tramadol affects sensory and motor nerve conduction by a similar mechanism to that of lidocaine, which acts on the voltage-dependent sodium channel leading to axonal blockage. However, Mert et al. (9) proposed that tramadol might have a mechanism different from that of lidocaine for producing conduction blocks; the presence of a large Ca^{+2} concentration in the external medium increases tramadol's activity whereas decreasing lidocaine's activity.

Tramadol is structurally related to codeine, which is, in fact, a methyl-morphine (7,10). Tramadol exerts its action on central monoaminergic systems and this mechanism may contribute to its analgesic effect (10). After IM injection, tramadol was rapidly and almost completely absorbed and peak serum concentrations were reached in 45 minutes on average (11,12). Serum concentrations adequate for the treatment of slight pain were already achieved after about 7 minutes on average (12). The recommended IM daily dose is between 50 and 100 mg every 4-6 hours (10,12). The elimination pharmacokinetics of tramadol are appropriately described by a two-compartment model, with a reported elimination half-life of $5.1(\text{SD} \pm 0.8)$ hours for tramadol, and 9 hours for the metabolite 1 derivative after a single oral dose of 100 mg (10). In this study, the duration of postoperative analgesia provided by subcutaneous tramadol was significantly longer when compared with lidocaine injection (group T 4.9 ± 0.3 , group L 4.4 ± 0.7 hours). Additionally, the total amount of the consumed analgesic in the postoperative period was considerably less in group T.

Again, no difference was found between groups in arterial blood pressure, heart rate, and respiratory depression. This finding is comparable to that of other studies in which tramadol was used IM, IV, or by patient-controlled analgesia (11).

Nausea and vomiting have been major side effects of tramadol used for postoperative analgesia (10). The incidence of these side effects seems to be related mainly to the peak serum concentrations, as an initial IV loading dose of 3 mg/kg caused more symptoms than a subsequent infusion or patient-controlled analgesia (10,11). In our study, 1 patient complained of nausea at the 30th minute of the operation, but vomiting was not observed.

We studied the local anesthetic and postoperative analgesic effects of tramadol given subcutaneously. Because there was no previous study evaluating the use of tramadol as a local anesthetic, we did not have a reference dose; therefore, we gave 2 mg/kg tramadol, which was used safely in IM injections for analgesia. In 5 cases, an additional 0.5 mg/kg tramadol was needed.

As a result, with tramadol, the postoperative pain-free period was significantly prolonged and less analgesics were required. We conclude that tramadol may be a good choice for minor surgery using local anesthesia because of its sufficient local anesthetic and analgesic effects.

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