Brief Reports

Wound closure tramadol administration has a short-lived analgesic effect

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Purpose: To evaluate the effects of tramadol administration at wound closure on postoperative pain and analgesic requirements in patients undergoing laparoscopic cholecystectomy.

Methods: In a prospective, randomized, double-blind study 80 patients were allocated into two groups (n = 40 in each) to receive either 200 mg tramadol or placebo *iv* at the time of wound closure. Postoperatively, all patients received tramadol from a patient-controlled analgesia (PCA) device. Pain, analgesic consumption, vital signs and side effects were recorded postoperatively for 24 hr.

Results: Administration of 200 mg tramadol at the time of wound closure was associated with a short-lived (60 min) reduction in pain scores and PCA consumption compared with placebo. Although the time to first request for analgesia after surgery was longer in patients who received tramadol at wound closure, there was no difference between the two groups with respect to pain scores or to the requirements of postoperative analgesia over the next 23 hr. The cumulative PCA consumption of tramadol in 24 hr was 139.4 ± 108 and 102.4 ± 106 mg in the placebo and tramadol groups, respectively ($P = 0.06$).

Conclusions: Wound closure administration of 200 mg tramadol had a short-lived (60 min) analgesic effect but did not affect the long-term pain scores or analgesic requirements after laparoscopic cholecystectomy.

Objectif : Évaluer les effets de l'administration de tramadol, lors de la suture de la plaie chirurgicale, sur la douleur postopératoire et les besoins analgésiques chez des patients qui subissent une cholécystectomie laparoscopique.

Méthode : Il s'agit d'une étude prospective, randomisée et en double aveugle auprès de 80 patients, répartis en deux groupes de 40, qui ont reçu 200 mg de tramadol ou un placebo *iv* au moment de la suture de la plaie. Après l'opération, tous les patients ont reçu du tramadol sous forme d'analgésie contrôlée par le patient (ACP). La douleur, la consommation d'analgésique, les signes vitaux et les effets secondaires ont été enregistrés pendant 24 h après l'intervention.

Résultats : L'administration de 200 mg de tramadol, comparé au placebo, lors de la fermeture cutanée, a été associée à une brève (60 min) diminution des scores de douleur et de la consommation d'ACP. Même si le temps écoulé avant la première demande d'analgésie postopératoire a été plus long chez les patients qui ont reçu du tramadol au moment de la suture de la plaie, il n'y a pas eu de différence intergroupe quant aux seuils de douleur ou aux besoins d'analgésie postopératoire pendant les 23 h suivantes. La consommation totale de tramadol en ACP pendant 24 h a été de $139,4 \pm 108$ et $102,4 \pm 106$ mg dans les groupes placebo et tramadol, respectivement ($P = 0,06$).

Conclusion : L'administration de 200 mg de tramadol lors de la suture de la plaie chirurgicale a un effet analgésique de courte durée (60 min), mais ne modifie pas les scores de douleur ou les besoins analgésiques à long terme qui suivent la cholécystectomie laparoscopique.

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TRAMADOL hydrochloride is an analgesic combining mainly μ -opioid and monoaminergic actions through indirect activation of postsynaptic $\alpha 2$ -adrenoceptors. Several studies have demonstrated that tramadol was equally effective in controlling postoperative pain as morphine.^{1,2} The synergy of monoaminergic and opioid activity achieves analgesic effects.³ Administering analgesics before the patient emerges from general anesthesia may result in an "acceptable" comfort level for the patient in the early postoperative period. This would be considered preventative analgesia.⁴

This study was designed to evaluate the effects of tramadol administration at wound closure on postoperative pain and analgesic requirements.

Methods

After obtaining informed consent and approval from the local Ethics Committee, we studied 80 ASA group I or II patients undergoing elective laparoscopic cholecystectomy. None of the patients were pregnant or lactating, abusing centrally acting drugs, consuming monoamine oxidase inhibitors, or allergic to study drugs. Lorazepam, 2 mg *po*, was given as premedication 90 min preoperatively.

Anesthesia was induced with 5 mg·kg⁻¹ thiopental and 2 μ g·kg⁻¹ fentanyl. Anesthesia was maintained with nitrous oxide 70% and isoflurane in oxygen 30%. Tracheal intubation was facilitated with 0.5 mg·kg⁻¹ atracurium. Standard monitoring was used. Additional doses of fentanyl were administered as required.

At the time of wound closure, patients were randomly allocated into two groups to receive either 200 mg tramadol *iv* ($n = 40$) or placebo ($n = 40$). Tramadol and placebo (normal saline) was prepared by a pharmacist to a fixed volume of 10 ml and marked only with a coded label to maintain the double-blind nature of the study. Duration of anesthesia and surgery and the total dose of fentanyl administered were noted for all patients.

Postoperative analgesia

Patients in both groups received tramadol from a PCA device (Abbott Pain Management Provider) for postoperative analgesia (100 ml containing 400 mg tramadol). The PCA parameters were: No background infusion; Demand dose = 4 ml (16 mg tramadol); lockout time = 5 min; 4 hour limit = 100 ml (400 mg tramadol).

All patients were observed for two hours in the recovery room before returning to the ward. Heart rate, pulse oximetry were monitored continuously and blood pressure was monitored every five minutes by an electronic oscillometer. When the patient was alert

in the recovery room, objective pain assessments, side effects (such as nausea, vomiting, dizziness, sedation dry mouth, sweating, headache were checked from a check list), PCA demand and PCA consumption were recorded. Assessments were made at 15 min intervals for the first hour, 30 min intervals for the second hour and 3, 4, 5, 6, and 24 hr after recovery from anesthesia. Pain intensity was assessed on each occasion using a four-point scale (0 = no pain or asleep; 1 = slight pain; 2 = moderate pain; 3 = severe pain). The patient was asked to assess his own pain using a visual analog score along a 10-cm line marked from "no pain" to "most severe pain imaginable". All observations were recorded by one anesthesiologist who had been instructed in the study design and score system and who was unaware of the patients' group assignments.

Sample size

A sample size of 39 in each group was estimated to have 80% power to detect a difference of 40 mg in means in the tramadol PCA consumption, assuming that the common standard deviation is 70 using a two group *t* test with a 0.05 one-sided significance level. The average tramadol PCA consumption was derived from our previous study.¹

Statistical analysis

Differences between groups were analyzed with unpaired Student's *t* test, Kruskal-Wallis test, Mann-Whitney test or Fisher's Exact test as appropriate. Repeated measures analysis of variance was performed to detect changes over time in hemodynamic variables (within group comparison). The times at which first PCA demand was requested were treated as being analogous to survival data. "Survival" curves were plotted to indicate the proportion of patients in each group who had received no analgesia by a given time after operation. These times were compared using Mantel-Cox log-rank test. Results were expressed as means and SD and were considered significant when $P < 0.05$.

TABLE I Patient characteristics (mean $\pm$ SD or (range)).

	Saline ($n = 40$)	Tramadol ($n = 40$)
Age (yr)	36.3 (20-61)	36.45 (20-63)
Weight (kg)	70.7 (10.3)	72.4 (11.4)
Height (cm)	160.2 (5.9)	161.5 (6.5)
Sex (M/F)	5/35	6/34
Intraoperative fentanyl (μ g)	166.3 $\pm$ 28	155 $\pm$ 25.4
Surgical time (min)	85.3 (19.4)	79.5 (16.6)

TABLE II Incidence of side effects (% of patients).

	Saline (n = 40)	Tramadol (n = 40)
Nausea and vomiting	18 (45)	26 (65)
Tachycardia	1 (2.5)	2 (5)
Hypertension	0	4 (10)
Tachypnea	1 (2.5)	0
Drowsiness	1 (2.5)	1 (2.5)

FIGURE 1A The number of demands made by patients on the PCA pump (mean and SD) at different times postoperatively. * $P = 0.01$ or less.
 FIGURE 1B PCA tramadol consumption (mean and SD). * $P = 0.01$ or less.
 FIGURE 1C Log rank test. Proportion of patients not requesting PCA analgesia. The graph steps down when patients requested analgesia.

Results

The groups were comparable with respect to patient characteristics, doses of fentanyl administered intraoperatively and duration of surgery (Table I).

FIGURE 2 Visual analogue pain score in saline group (Figure 2A) and tramadol group (Figure 2B) during the first 24 hr after surgery. At 30, 45, and 60 min postoperatively, patients in saline group reported higher pain score ($P = 0.01$ or less).

Postoperative analgesia was achieved in all patients. The number of demands made by patients on the PCA pump and the PCA drug consumption were not different between groups except at 30, 45 and 60 min where patients in the saline group requested more analgesia ($P < 0.05$) (Figures 1A,1B). The cumulative PCA consumption of tramadol in 24 hr was 139.4 ± 108 and 102.4 ± 106 mg in the saline and tramadol groups, respectively ($P = 0.06$). Time to first postoperative PCA analgesic demand and proportion of patients required no analgesia were different ($P < 0.03$) between the two groups (Figure 1C). There were no differences in visual analogue pain score during the first 24 hr postoperatively between the groups except at 30, 45 and 60 min where patients in saline group reported higher pain scores ($P = 0.01$) (Figures 2A,2B). Observer pain score was also different between the two groups at 30 and 45 min ($P = 0.01$).

The incidence of side effects (Table II) was similar in both groups ($P = \text{NS}$). There were no differences in respiratory rate or hemodynamic variables between the two groups.

Discussion

In this study, administration of 200 mg tramadol at the time of wound closure was associated with a short-lived (60 min) reduction in pain scores and PCA consumption as compared to placebo. Although the time to first request for analgesia after surgery was significantly longer in patients who received tramadol at wound closure, there was no difference between the two groups with respect to pain scores or to the requirements of postoperative analgesia over the next 23 hr.

Coetzee *et al.*⁵ reported that 50% of their patients required supplementary analgesia during their 90-min stay in the recovery room whether they had received 3 mg·kg⁻¹ tramadol or 0.2 mg·kg⁻¹ morphine at wound closure. Brennan *et al.*⁶ reported that, in animals, early treatment strategies did not necessarily modify later hyperalgesia. In accordance with Brennan's observation, the present study and other studies⁵ have demonstrated that there was no evidence that timing of analgesic treatment had an impact on postoperative pain or analgesic requirements.

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