

KETAMINE VERSUS TRAMADOL AS AN ADJUNCT TO PCA MORPHINE FOR POSTOPERATIVE ANALGESIA AFTER MAJOR UPPER ABDOMINAL SURGERY: A PROSPECTIVE, COMPARATIVE, RANDOMIZED TRIAL

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Abstract

Background and aims: Patient-controlled analgesia (PCA) with morphine is commonly used to provide analgesia following major surgery, but is not sufficient as a monotherapy strategy. This study aimed to compare the adjunctive analgesic effect of ketamine versus tramadol on postoperative analgesia provided via PCA-morphine in patients undergoing major upper abdominal surgeries. **Methods:** Forty-two patients undergoing elective major upper abdominal surgery under general anesthesia were allocated to receive either ketamine (load dose of 0.5 mg kg⁻¹ followed by a continuous infusion of 0.12 mg kg⁻¹ h⁻¹ up to 48 postoperative hours; ketamine group, n = 21) or tramadol (load dose of 1 mg kg⁻¹ followed by a continuous infusion of 0.2 mg kg⁻¹ h⁻¹ up to 48 postoperative hours; tramadol group, n = 21) in addition to their standard postoperative analgesia with PCA-morphine. Postoperative data included morphine consumption, visual analog scale (VAS) scores, and side effects during the first 48 postoperative hours after PCA-morphine initiation. **Results:** There were no significant differences in patient demographic and intraoperative data between the two groups. Tramadol group had significantly less total morphine consumption during the first 48 postoperative hours (28.905 [16.504] vs 54.524 [20.846] mg [p < 0.001]) and presented significantly lower VAS scores at rest and mobilization (p < 0.05) than the ketamine group. No statistical difference was recorded between the two groups (p > 0.05) regarding postoperative cough, sedation, hallucinations, pruritus, urine retention, and postoperative nausea and vomiting. However, patients in the ketamine group reported dry mouth more frequently than patients in the tramadol group (p = 0.032). **Conclusions:** Postoperative administration of tramadol was superior to ketamine due to significantly reduced opioid consumption and better pain scores in patients receiving PCA-morphine after major upper abdominal surgery.

Keywords

Ketamine • tramadol • morphine • postoperative analgesia

Introduction

The upper abdominal procedures are accompanied by severe pain, which is commonly treated either with epidural analgesia or with intravenous (IV) morphine using patient-controlled analgesia (PCA) [1]. However, the epidural catheter in the case of hepatectomy is confronted with caution due to the possible coagulation abnormalities preoperatively and the bleeding predisposition after hepatectomy [2,3]. On the other hand, PCA morphine is not sufficient as a monotherapy strategy to effectively control postoperative pain after major upper abdominal surgery, indicating the need for a multimodal approach to pain management including paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) [4]. The use of NSAIDs in clinical practice, however, is limited due to their

several contraindications and potential adverse effects. Thus, investigating alternative effective analgesic schemes is crucial.

The successful combination of different drugs targets at improvement of analgesia, reduction of the side effects and exploitation of the pharmacodynamic advantages of each drug. For instance, tramadol acts as a μ -opioid receptor agonist, but it is also a serotonin and norepinephrine reuptake inhibitor [5,6]. Ketamine interacts with N-methyl-D-aspartate (NMDA) and non-NMDA glutamate receptors and cholinergic, monoaminergic, and opioid receptors [7–10]. Furthermore, the ceiling effect of many drugs reduces the drug efficiency. Thus, in the era of opioid-sparing analgesia, targeting at multiple, parallel pain pathways seems to be more effective in pain management.

The aim of the study is to make a comparison between ketamine and tramadol regarding their effect on postoperative analgesia in patients receiving PCA morphine after major upper abdominal

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surgeries. We investigated the hypothesis that the addition of tramadol continuous infusion to analgesia provided via PCA morphine compared to ketamine coadministration may improve postoperative analgesia by reducing postoperative morphine consumption and pain scores. The primary endpoint of the study was the total morphine consumption during the first 48 hours postoperatively.

Methods

After obtaining an approval from the Ethics Committee of the University Hospital "Attikon" (protocol number 24/6/2011, 14th theme, Chairman Prof C. Liapis) and written informed consents from the subjects, 42 adult patients of American Society of Anesthesiologists (ASA) physical status I–II, aged 18–70 years, scheduled for elective major upper abdominal surgery under general anesthesia alone and postoperative analgesia with PCA morphine were enrolled in this study. The patients had an upper abdominal incision. Inclusion criteria included elective hepatectomies, gastrectomies, Whipple procedures, and peripheral pancreatectomies. The study was a prospective, randomized, single-blinded clinical trial registered at ClinicalTrials.gov (ID NCT02499341) and conducted in accordance with the ethical standards of the Helsinki Declaration.

Randomization and interventions

The aim of the study was to compare the efficacy of ketamine versus tramadol in the control of postoperative pain in patients receiving PCA morphine after major upper abdominal surgeries. For this reason, patients were randomized into two groups using a computerized random number generator, a computer method called Research Randomizer, as follows:

Ketamine group (n = 21): Thirty minutes before the expected end of surgery, ketamine was administered IV at a load dose of 0.5 mg kg⁻¹ followed by a continuous infusion of 0.12 mg kg⁻¹ h⁻¹ up to 48 postoperative hours.

Tramadol group (n = 21): Thirty minutes before the expected end of surgery, tramadol was administered IV at a load dose of 1 mg kg⁻¹ followed by a continuous infusion of 0.2 mg kg⁻¹ h⁻¹ up to 48 postoperative hours.

Exclusion criteria

The exclusion criteria were patient's refusal to participate in the study, performance of regional anesthesia, unsuitability for PCA, current opiate usage, drug addiction, chronic pain syndromes, psychiatric disorders, usage of monoamine oxidase inhibitor or selective serotonin reuptake inhibitor, sleep apnea syndrome, severe liver, kidney, or heart disease, and known allergy to ketamine, tramadol, or morphine.

Study design

The evening before the elective surgery, the patients, not aware of the group assignment, were instructed to use the PCA device and the visual analog scale (VAS) (0–10 cm, 0: no pain, 10: the worst pain), and they received oral premedication (ranitidine and hydroxyzine). All participants underwent the same protocol of general anesthesia. Anesthesia was induced with propofol 2 mg kg⁻¹, fentanyl 2 mcg kg⁻¹, and rocuronium 0.8 mg kg⁻¹ and maintained by propofol 1% continuous infusion. Before the surgical incision, 3 mcg kg⁻¹ fentanyl and 0.1 mg kg⁻¹ morphine were given IV, while repetitive doses of morphine 0.05 mg kg⁻¹ were administered IV in order to keep the systolic arterial pressure and the heart rate (HR) within the range of 20% of the baseline values. The intraoperative fluid management was guided by invasive hemodynamic monitoring.

Thirty minutes before the expected end of surgery, paracetamol 1 g was administered IV. Consequently, patients received either ketamine or tramadol according to the study group at the bolus doses and continuous infusions mentioned before. The pump remained attached to the IV line for 48 hours.

After recovery from anesthesia, patients were transferred to the Post-Anesthesia Care Unit (PACU), where pain was assessed using the VAS and treated with morphine bolus doses (2 mg IV) to achieve VAS scores <4. When a VAS score <4 was attained, a PCA morphine pump was connected to a peripheral IV line and was set to deliver morphine at a bolus dose of 1 mg with a lockout period of 8 minutes. The participants were instructed to use the button of PCA device upon an experience of pain. When the patients fully recovered, they were transferred to the wards.

Postoperative analgesia consisted of PCA morphine and continuous infusion of either ketamine or tramadol according to the study group. Supplementary administration of NSAIDs was not allowed until the end of the study period. If analgesia was not adequate and VAS was >5, a bolus dose of morphine 2 mg was given IV as the rescue dose. If the repetitive morphine doses were not efficient, the interval time of the PCA morphine pump was set at 6 minutes. In case of persistent pain despite the aforementioned interventions, NSAIDs were administered and the patient was removed from the study. Also, metoclopramide 10 mg was given IV twice a day to prevent postoperative nausea and vomiting (PONV). PONV was assessed with a 4-point scale (0–3: 0, none; 3, more than three episodes of vomiting). If the PONV was >2, dexamethasone 8 mg was given IV as the first-line treatment, while ondansetron 4 mg was used as the second-line treatment.

Data recording

The study period was 48 hours (1, 2, 4, 6, 12, 18, 24, 36, and 48 hours), considering as zero time the time of the connection

of the PCA morphine pump to the patient. At these time points, morphine consumption, VAS scores, oxygen saturation, respiratory rate, HR, mean arterial pressure (MAP), patient's mobilization, ability to cough, and the drugs' side effects (itching, seizures, confusion, sense of dry mouth, urinary retention, sedation, quality of sleep, PONV) were assessed. Additionally, patient's overall satisfaction with their analgesia management was assessed at 48 hours with a 5-point scale (1 = excellent, 5 = very bad). The postoperative total intrahospital stay was also recorded.

Outcomes

The primary outcome of the study was the total morphine consumption during the first 48 hours postoperatively. The secondary outcomes included VAS scores at rest and mobilization, vital signs, side effects, overall patient satisfaction, and duration of postoperative intrahospital stay.

Statistical analysis

Shapiro–Wilk test was performed to test for normal distribution of continuous variables. The results are given as mean \pm standard deviation (SD) or as median and interquartile range [IQR] according to the normality of continuous variables. All qualitative variables are presented as absolute or relative frequencies. Student's *t*-test or its nonparametric equivalent Mann–Whitney *U* test was used to compare the continuous variables between the groups under study. Fisher's exact test was employed for comparison of categorical variables (or Pearson's chi-square where Fisher's exact was not applicable). Vital parameters and PCA dosing were compared using the repeated-measures analysis of variance (ANOVA) and Bonferroni post hoc test. Mixed linear model analysis was performed in order to assess analgesic outcome (VAS score) between the groups over time and ANOVA with Bonferroni post hoc test for the identification of time points with differences between groups.

All tests were two-tailed and statistical significance was established at 5% ($p < 0.05$). Data were analyzed using Stata™ (version 10.1 MP; Stata Corporation, College Station, TX, USA).

Power analysis

The difference in morphine consumption between the two study groups was considered clinically relevant if it was at least 20%. In order to calculate the necessary number of patients in the study, we employed a known published method [11]. Based on this methodology and using $\alpha = 0.05$, a desired power of the study 0.90, and setting SD (in morphine consumption in 48 hours) at 0.20, we estimated that 42 patients would be needed in total (21 in each group).

Results

All 42 participants completed the study protocol (Figure 1). The population under study was homogenous concerning somatometric characteristics, type of surgery, and surgery duration ($p > 0.05$). Groups displayed a trend toward age difference, which, however, did not reach statistical significance ($p = 0.058$; Table 1).

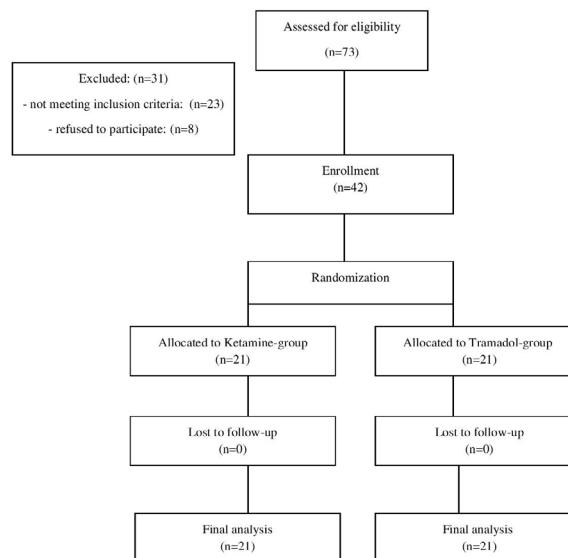


Figure 1: Flow diagram

No statistical difference was detected in time (minutes) between the groups regarding tramadol or ketamine pump start ($p > 0.05$, data not shown) and PCA morphine pump start ($p > 0.05$; Table 2). During the first 48 hours after surgery, patients in the tramadol group received significantly less morphine ($p < 0.001$; Table 2), although intraoperatively, the groups received indifferent amounts of morphine (Table 2). Patients in the ketamine group requested and were administered more doses from the PCA morphine pump over the study period (Figure 2). In particular, the morphine doses given from the PCA pump were higher in the ketamine group from the sixth hour after surgery and for the rest of the observation period. Mixed model analysis revealed statistical difference between the two groups over time for VAS at rest ($p < 0.001$) and VAS at movement ($p = 0.001$; Figure 3). Specifically, the ketamine group had higher VAS at rest at the 6th, 12th, and 24th hour and VAS at mobilization at the 6th and 24th hour ($p < 0.05$) compared to the tramadol group. In regard to the vital signs, MAP and HR were significantly higher in the ketamine group compared to the tramadol group

Table 1. Somatometric and intraoperative data of the study population, by group

	Study group		p Value	
	Ketamine group (n = 21)	Tramadol group (n = 21)		
Somatometric characteristics of the study group				
Age (years)		57 [50–60]	62 [56–66]	0.058
Gender (female vs male)	11 (52.38%) versus 10 (47.62%)		8 (38.1%) versus 13 (61.9%)	0.268
BMI (kg/m ²)		23.38 (2.78)	25 (3.37)	0.097
Intraoperative data				
Type of surgery				
Pancreatectomy		2 (9.52%)	6 (28.57%)	0.175
Whipple		5 (23.81%)	8 (38.1%)	
Cholopeptic anastomosis		2 (9.52%)	-	
Hepatectomy		6 (28.57%)	5 (23.81%)	
Gastrectomy		6 (28.57%)	2 (9.52%)	
Duration of surgery (minutes)		155 [120–190]	159 [115–185]	0.899

Note: Results are presented as mean (SD) or as median [IQR] according to the normality of continuous data and as absolute/relative frequencies for categorical data. Tests employed are paired *t*-test, Mann–Whitney *U* test, and Fisher's exact test. Key: BMI, body mass index; IQR, interquartile range; SD, standard deviation.

Table 2. Intraoperative and postoperative morphine administration and PCA morphine pump initiation, by group

Morphine administration	Study group		p Value
	Ketamine group (n = 21)	Tramadol group (n = 21)	
Intraoperative (bolus, mg)	16.614 (5.22)	15.79 (4.59)	0.59
PACU (bolus, mg)	4 [0–6]	2 [0–4]	0.341
Ward (bolus, mg)	0 [0–0]	0 [0–0]	0.146
Time to PCA morphine pump start from tramadol/ ketamine pump start (minutes)	95.62 (46.14)	87.24 (44.81)	0.554
PCA administration (mg)	54.524 (20.846)	28.905 (16.504)	<0.001
Total morphine (mg)	60.714 (20.03)	32.428 (18.17)	<0.001

Note: Results are presented as mean (SD) or as median [IQR] according to the distribution of continuous data. Tests employed are paired *t*-test and Mann–Whitney *U* test.

Key: IQR, interquartile range; PACU, post-anesthesia care unit; PCA, patient-controlled analgesia; SD, standard deviation.

(for MAP: overall $p < 0.001$; for HR: overall $p = 0.032$ between groups; Figure 4). In particular, the MAP was higher in the ketamine group at all time points compared to the tramadol group, whereas the HR was higher at 1, 18, 24, and 36 hours in the ketamine group compared to the tramadol group, which reveals a rather sustained difference in cardiovascular effects between the two medications. The respiratory rate was normal and did not differ between the groups statistically (in all patients $\geq 10 \text{ min}^{-1}$, data not shown).

No statistical difference in side effects (sedation, PONV, others) were detected between the groups at all time points ($p > 0.05$; Table 3). A notable exception was detected in dry

mouth, which patients in the ketamine group reported more frequently than patients in the tramadol group (Table 3).

No statistical difference was detected between the groups in mobilization, ability to cough, sleep quality, and postoperative analgesia satisfaction score ($p > 0.05$, data not shown). Most patients in both groups were highly satisfied with the provided analgesic scheme. Moreover, no statistical difference was detected in dexamethasone administration between the groups and in postoperative hospitalization days ($p > 0.05$, data not shown). No patient received ondansetron during hospitalization, and there was no need for PCA pump change in any of the participants.

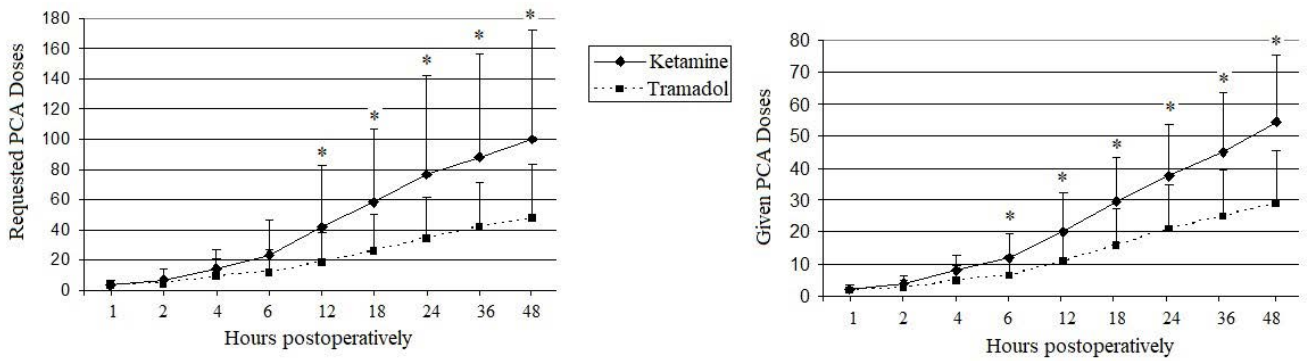


Figure 2: Requested and given PCA morphine over the study period, by group. Key: PCA, patient-controlled analgesia.

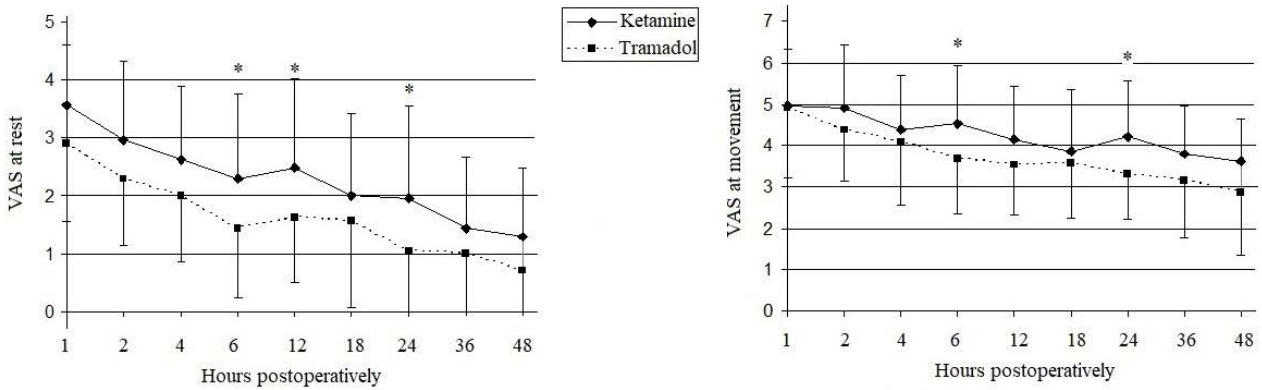


Figure 3: VAS at rest and VAS at movement over the study period, by group. Key: VAS, visual analog scale.

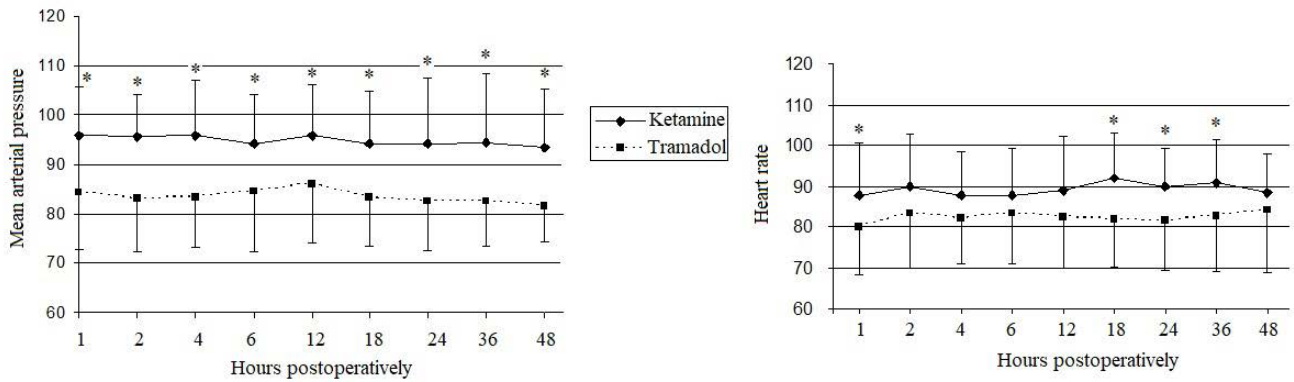


Figure 4: Mean arterial pressure and heart rate over the study period, by group

Table 3. Side effects related to analgesia protocol, by group

	Study group		p Value
	Ketamine group (n = 21)	Tramadol group (n = 21)	
Sedation (1, awake; 2, medium sedation/wakes up easily; 3, mostly sedated does not wake up easily; 4, unarousable)			
1st hour (1/2/3)	3 (14.29%)/14 (66.67%)/4 (19.05%)	1 (4.76%)/13 (61.9%)/7 (33.33%)	0.408
2nd hour (1/2/3)	3 (14.29%)/15 (71.43%)/3 (14.29%)	4 (19.05%)/12 (57.14%)/5 (23.81%)	0.671
4th hour (1/2/3)	5 (23.81%)/15 (71.43%)/1 (4.76%)	7 (33.33%)/12 (57.14%)/2 (9.52%)	0.616
6th hour (1/2)	12 (57.14%)/9 (42.86%)	12 (57.14%)/9 (42.86%)	0.999
12th hour (1/2)	16 (76.19%)/5 (23.81%)	13 (61.9%)/8 (38.1%)	0.505
18th hour (1/2)	16 (76.19%)/5 (23.81%)	17 (80.95%)/4 (19.05%)	0.999
24th hour (1/2)	18 (85.71%)/3 (14.29%)	18 (85.71%)/3 (14.29%)	0.999
36th hour (1/2)	18 (85.71%)/3 (14.29%)	19 (90.48%)/2 (9.52%)	0.999
48th hour (1/2/3)	20 (95.24%)/1 (4.76%)-	18 (85.71%)/2 (9.52%)/1 (4.76%)	0.606
PONV (0, none; 1, nausea; 2, less than three episodes of vomiting; 3: more than three episodes of vomiting)			
1st day (0/1/2)	17 (80.95%)/2 (9.52%)/2 (9.52%)	17 (80.95%)/2 (9.52%)/2 (9.52%)	0.999
2nd day (0/2)	19 (90.48%)/2 (9.52%)	18 (85.71%)/3 (14.29%)	0.999
Other side effects			
Pruritus (no/yes)	19 (90.48%)/2 (9.52%)	18 (85.71%)/3 (14.29%)	0.999
Hallucinations (no/yes)	15 (71.43%)/6 (28.57%)	20 (95.24%)/1 (4.76%)	0.093
Confusion (no/yes)	19 (90.48%)/2 (9.52%)	21 (100%)-	0.488
Seizures (no/yes)	21 (100%)-	21 (100%)-	-
Dry mouth (no/yes)	12 (57.14%)/9 (42.86%)	19 (90.48%)/2 (9.52%)	0.032
Bradycardia (no/yes)	21 (100%)-	21 (100%)-	-
Uterine retention (no/yes)	21 (100%)-	21 (100%)-	-
Hypotension (no/yes)	21 (100%)-	20 (95.24%)/1 (4.76%)	0.999

Note: Results are presented as absolute and relative frequencies. Test employed: Fisher's exact test. Key: PONV, postoperative nausea and vomiting.

Discussion

Our study demonstrated that the addition of tramadol continuous infusion to PCA morphine compared to coadministration of ketamine provided better postoperative analgesia in patients undergoing major abdominal surgery with less morphine consumption, lower VAS scores, and better hemodynamic response. However, except the sensation of "dry mouth", which was more frequently reported by patients receiving ketamine, no other difference was found between the two groups with respect to other side effects, sleep quality, mobilization of patients, satisfaction with postoperative analgesia, and postoperative stay in the hospital.

To the best of our knowledge, so far, there is no other published study comparing these two analgesics regarding their effect on PCA morphine-provided postoperative analgesia, although there are several studies investigating the postoperative opioid-sparing effect of each drug in different surgical populations.

Tramadol has been used as an adjunct to postoperative opioid analgesia following major surgery and was administered at different time points and/or in different doses and regimens. Notably, although tramadol via PCA has been found to effectively control postoperative pain following abdominal surgery, it is associated with increased incidence of nausea [12–15] and is rarely used in the clinical practice as a monotherapy approach. Preoperative pre-emptive administration of tramadol is questionable, since it has not consistently been found to be superior to intraoperative use [16,17]. Also, the addition of systemic administration of 100 mg tramadol given IV every 6 hours to PCA morphine was not found to improve pain relief after total knee arthroplasty [18]. On the contrary, the addition of a tramadol infusion to PCA morphine resulted in improved analgesic efficacy and reduced morphine consumption in patients undergoing abdominal surgery [19,20]. Webb et al. administered tramadol at an intraoperative initial loading dose of 1 mg kg⁻¹ at the end of surgery followed by postoperative infusion at 0.2 mg kg⁻¹ h⁻¹ for the first postoperative 48 hours in patients undergoing major upper abdominal surgery and receiving PCA morphine

to control postoperative pain [19]. They found that the addition of tramadol infusion to PCA morphine improved analgesia and reduced morphine requirements compared with morphine PCA alone (72.8 vs 103 mg over 48 hours). Similar beneficial effects were found by Kocabas *et al.* who used the same regimen of tramadol for the first 24 postoperative hours in patients undergoing abdominal hysterectomy and reported reduction in PCA morphine requirements (27 vs 40.5 mg over 24 hours) and improved patient satisfaction with pain relief [20]. In our study, we tested the same regimen of tramadol in patients undergoing major abdominal surgery and found that the addition of tramadol to PCA morphine was associated with a very low mean total PCA morphine consumption (28.905 mg) over 48 postoperative hours, less than that reported in the previous studies. It is worth mentioning that our study design allowed the use of ondansetron only as a rescue dose in case of persistent PONV, and that no patient needed to receive ondansetron during the study period. Therefore, we can assume that in our study, tramadol exhibited its maximum pharmacological analgesic efficacy, since serotonin antagonists were not used that have been shown to inhibit the analgesic effects of tramadol [21,22].

Ketamine has also been investigated as a supplement analgesic in patients undergoing different types of surgery and receiving PCA morphine to relieve their postoperative pain. Carstensen *et al.*, in their qualitative review of randomized trials on this topic, concluded that “for thoracic surgery the addition of ketamine to PCA morphine is superior to PCA alone providing better postoperative analgesia with a significant reduction in pain score and cumulative morphine consumption, but for abdominal surgery this beneficial effect remains unclear” [23]. Reeves *et al.* have shown that adding ketamine to morphine for PCA after major abdominal surgery did not improve pain relief or minimize opioid consumption [24]. Similarly, Murdoch *et al.* did not find any beneficial effect related to the addition of ketamine to PCA morphine in patients undergoing total abdominal hysterectomy [25]. In contrast, adjunctive ketamine with PCA morphine was found to provide superior analgesia after major abdominal surgery when administered as a continuous infusion of 0.15 mg kg⁻¹ h⁻¹ for the first 48 postoperative hours, with a significant decrease in morphine consumption (28 vs 54 mg) [26]. Also, Guillou *et al.* found a significant morphine-sparing effect (55 vs 75 mg) using a different regimen of ketamine in patients undergoing major abdominal surgery [27]. The provided regimen included a loading dose of ketamine of 0.5 mg kg⁻¹ followed by a continuous infusion of 0.12 mg kg⁻¹ h⁻¹ for the first 24 postoperative hours and then with a lower flow of 0.06 mg kg⁻¹ h⁻¹ for the next 24–48 hours [27]. In our study, using the same initial loading dose of ketamine (0.5 mg kg⁻¹) as in the aforementioned study, which, however, was followed by a constant continuous infusion of 0.12 mg kg⁻¹

h⁻¹ during the first 48 hours after major abdominal surgery, we found that the mean total PCA morphine consumption was 54.524 mg. This amount is similar to that reported by Guillou, but it is almost twofold higher than that observed in patients receiving adjunctive tramadol in our study. However, the increased consumption of morphine observed in the ketamine group was not associated with increased incidence of opioid-related side effects. Patients in both groups did not develop uterine retention, respiratory depression, severe sedation, or persistent PONV that needed to be treated with ondansetron. In our study, supplemental administration of tramadol to PCA morphine was found to achieve more sufficient postoperative pain control than that provided by adjunctive ketamine, since patients in the tramadol group reported constantly lower pain scores at rest and mobilization. We should underline, however, that this difference reached a statistical significance only at the 6th, 12th, and 24th hour at rest and at the 6th and 24th hour during mobilization, respectively. We would also like to emphasize that no difference was found between the two study groups in postoperative satisfaction scores, while most patients expressed increased satisfaction with their analgesic regimen. Therefore, we can assume that the concomitant administration of ketamine to PCA morphine, although inferior to tramadol, might be used to relieve pain following major upper abdominal surgery, particularly in patients in whom tramadol is contraindicated.

Also, we found that patients receiving ketamine showed significantly higher blood pressure and HR compared to tramadol-treated patients. In particular, MAP was higher in the ketamine group at all time points of the postoperative study period, even in cases where the patients did not complain of pain. Thereby, this hemodynamic response appears to be associated with the sympathomimetic properties of ketamine. Finally, it is worth noting that all participants in our study did not receive NSAIDs during the postoperative period; therefore, superior analgesia observed in the tramadol group is exclusively related to supplemental administration of tramadol to PCA morphine. Consequently, tramadol regimen investigated in the present study appears to play an important role in the postoperative analgesia of patients who are contraindicated for the use of NSAIDs or in patients with hypertensive disorders.

Limitations of our study were: single blinding, exclusion of elderly patients aged >70 years, and exclusion of patients with severe cardiovascular disorders or other systemic diseases.

Conclusions

In conclusion, we found that supplemental administration of tramadol compared to coadministration of ketamine provided superior postoperative analgesia in patients who underwent

major upper abdominal surgery and were treated with PCA morphine. An intraoperative single load dose of tramadol followed by continuous infusion achieved lower morphine consumption and VAS scores with better hemodynamic control than ketamine administration. However, patients in the ketamine group expressed similar satisfaction with their analgesic regimen and did not show any significant difference in the side effects other than dry mouth, which was more commonly reported by patients receiving ketamine.

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Conflicts of interest: nothing to declare.

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