Tramadol Versus Low Dose Tramadol-paracetamol for Patient Controlled Analgesia During Spinal Vertebral Surgery

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Pain intensity may be high in the postoperative period after spinal vertebral surgery. The aim of the study was to compare the effectiveness and cost of patient controlled analgesia (PCA) with tramadol versus low dose tramadol-paracetamol on postoperative pain. A total of 60 patients were randomly divided into two groups. One group received 1.5 mg/kg tramadol (Group T) while the other group received 0.75 mg/kg tramadol plus 1 g of paracetamol (Group P) intravenously via a PCA device immediately after surgery and the patients were transferred to a recovery room, Tramadol was continuously infused at a rate of 0.5 mL/h in both groups, at a dose of 10 mg/mL in Group T and 5 mg/mL in Group P. The bolus and infusion programs were adjusted to administer a 1 mL bolus dose of tramadol with a lock time of 10 minutes. In Group P, 1 g of paracetamol was injected intravenously every 6 hours. The four-point nausea scale, numeric rating scale for pain assessment, Ramsey sedation scale, blood pressure, heart rate, respiration rate, peripheral oxygen saturation values and side effects were recorded at 0, 15 and 30 minutes, and at 1, 2, 4, 6, 12, 18 and 24 hours. The time to reach an Aldrete score of 9 was also recorded. A cost analysis for both groups was performed. In Group P, the numeric rating scale scores were significantly lower than that in Group T at 0 and 15 minutes. The number of side effects, additional analgesic requirement and the total dose of tramadol were lower in Group P than in Group T. However, the total cost of postoperative analgesics was significantly higher in Group P than in Group T ($p < 0.001$). We conclude that PCA using tramadol-paracetamol could be used safely for postoperative pain relief after spinal vertebral surgery, although at a higher cost than with tramadol alone.

Key Words: paracetamol, patient controlled analgesia, postoperative analgesia, spinal vertebral surgery, tramadol
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Postoperative pain is a nociceptive type of pain that develops as a result of tissue damage after surgical trauma, and is accompanied by central and peripheral sensitization. Approximately, 30–75% of patients experience moderate to severe pain in the postoperative period [1,2]. Inadequate analgesia in this period may

lead to functional deterioration caused by the pathophysiology of acute pain, and may trigger a sensitization process in the central and peripheral nervous systems, leading to chronic pain [1–5]. This ultimately increases the cost and the length of stay in a hospital [6,7]. Patient controlled analgesia (PCA) allows patients to administer their own analgesic medications when necessary. This reduces their anxiety and stress, both of which are major factors associated with postoperative pain [8].

The ideal analgesic agent used in PCA should have a rapid onset and a moderate duration. Furthermore, the agent should be free of side effects such as a ceiling dose, nausea, vomiting, respiratory depression and intestinal motility disorder. Opioids are commonly used as analgesics in intravenous (IV) PCA [9]. Nonsteroidal anti-inflammatory drugs (NSAIDs) are also commonly used for postoperative analgesia to avoid the side effects of opioids [10,11].

The aims of this study were to identify the effects of IV paracetamol on PCA tramadol use after spinal vertebral surgery and estimate the costs of the two types of treatment.

Methods

This prospective, randomized and controlled study was conducted after obtaining the approval of the Medical School Ethics Committee and informed consent from the patients.

A total of 60 patients who were scheduled for spinal vertebral surgery, and who were classified in the American Society of Anesthesiologists risk group I–II were admitted to the study. Their ages ranged from 18 to 60 years. Patients meeting any of the following criteria were excluded: (1) use of analgesics during the 24-hour period before surgery; (2) known allergy to any of the study drugs; (3) inability to use the PCA device due to lack of communication or muscle strength; (4) severe cardiopulmonary, renal or liver disease, morbid obesity (body mass index > 30 kg/m^2), or history of postoperative nausea and vomiting; (5) history of migraines; (6) current pregnancy, (7) history of alcohol abuse and convulsion anamnesis; (8) use of monoamine oxidase or serotonin reuptake inhibitors; or (9) history of complications during and after surgery.

In the preanesthetic evaluation, all patients were informed about the anesthesia method to be used. They were also trained on how to use the patient controlled analgesia device (Pain Management Provider, Abbott Laboratories, Chicago, IL, USA) and the 10-point numeric rating scale. We also collected verbal and written consent at this time. Thirty minutes before the patients were taken to the operation room, they were administered with 0.01 mg/kg atropine sulfate and 0.1 mg/kg midazolam intramuscularly.

In the operating room, patients were administered with 2 L/min oxygen (O_2) via a nasal cannula. Electrocardiograph, heart rate (HR), mean blood pressure (MBP) and peripheral O_2 saturation (SpO_2) were monitored using a Datex Ohmeda Cardiocap 5 (General Electric, Helsinki, Finland). Anesthesia was induced by 2 mg/kg propofol and 0.1 mg/kg vecuronium bromide. For analgesia, 0.05–2 μg/kg/min remifentanil hydrochloride was infused IV. Anesthesia was maintained with 50% O_2, 50% air and 1–1.5 minimum alveolar concentration (MAC) desflurane. Muscle relaxation was maintained by administering 0.03 mg/kg vecuronium bromide as needed.

In the study, hypotension (> 20% from the baseline systolic arterial blood pressure) was treated with IV boluses of 5 mg ephedrine repeated every 3 minutes, and bradycardia (heart rate <55 bpm) treated with atrophine 0.5/mg if occurs.

Patients were randomly divided into two groups using a random samples table. Group T received 1.5 mg/kg tramadol (100 mg/mL; Contramal ampoule, Abdi Ibrahim, Istanbul, Turkey) via one arm after remifentanil infusion via another arm, and Group P received 0.75 mg/kg tramadol plus 1 g paracetamol (Perfalgan®; Bristol-Myers Squibb, Istanbul, Turkey) intravenously via one arm, 15 minutes after stopping remifentanil infusion via another arm. Control values were recorded before the administration of the study drugs**.** The patients' vital signs were also taken and recorded afterwards. The duration of the surgical procedure and the total amount of remifentanil administered were recorded. Muscle relaxation was reversed by 0.05 mg/kg neostigmine and 0.01 mg/kg atropine.

The PCA device was inserted immediately after the patients were transferred to the postanesthesia recovery room and extubation. The tramadol dose for Group T was 10 mg/mL and continuous infusion was given at 0.5 mL/hr. In Group P, the tramadol dose was 5 mg/mL and continuous infusion was given at 0.5 mL/hr. In both groups, the bolus dose was 1 mL and the lockout time for the bolus and infusion

program was 10 minutes. In Group P, 1 g of paracetamol was administered intravenously over 15 minutes every 6 hours. The 4-hr dose limit was 300 mg.

In the recovery room, the patients' vital signs were monitored by Criticare 1100 (Criticare Systems Inc., Waukesha, WI, USA). The following parameters were recorded immediately after the patients were taken to the recovery room at 0, 15 and 30 minutes and at 1, 2, 4, 6, 12, 18 and 24 hours after commencing PCA: four-point nausea vomiting scale, numerical rating scale (NRS) for pain level, Ramsey sedation scale (1 = anxious, restless or both; 2 = cooperative, orientated and tranquil; 3 = responding to commands; 4 = brisk response to stimulus; 5 = sluggish response to stimulus; 6 = no response to stimulus), Aldrete score (Activity: voluntary movement of all limbs to command = 2 points, voluntary movement of two extremities to command = 1 point, unable to move = 0 points; Respiration: breathe deeply and cough = 2 points, dyspnea or hypoventilation = 1 point, apnea = 0 points; Circulation: BP ± 20 mmHg of the preanesthesia level = 2 points, BP ± 20–50 mmHg of the preanesthesia level = 1 point, BP > ± 50 mmHg of preanesthesia level = 0 points; Consciousness: fully awake = 2 points, arousable = 1 point, unresponsive = 0 points; Color: pink = 2 points, pale or blotchy = 1 point, cyanotic = 0 points), time needed to reach an Aldrete score of 9, MBP, HR, respiration rates, SpO_2 values and side effects.

The following additional drugs were allowed: 1 mg/kg pethidine hydrochloride intramuscularly (50 mg/mL Aldolan ampoule) in the event of inadequate analgesia; 10 mg metoclopramide IV for nausea and vomiting; 45.5 mg pheniramine maleate for itching; an increased IV dose of naloxone for respiratory depression (< 10 breaths-per-min); and 5 mg of diazepam for convulsion. After 24 hours, the doses, total tramadol dose were recorded from the memory of the PCA device and the satisfaction score were recorded.

To estimate the total cost, we included the unit costs of tramadol, paracetamol, metoclopramide and pethidine. As of November 2009, the prices of one ampoule of tramadol (100 mg/mL), one flacon of paracetamol (1 g), one ampoule of metoclopramide and pethidine were 1.45 euro (€), 2.57€, 0.4€ and 0.51€, respectively.

A sample size of 56 patients was chosen to detect the difference of one unit on the NRS, with an α error = 0.05 and power at 80% [12]. Thus the 60 patients were enrolled in this study and they were allocated into two equal groups .

Statistical analyses were performed using SPSS version 10.0 (SPSS Inc., Chicago, IL, USA). Student's *t* test was used to compare age, weight, surgical duration, MBP, HR, respiration rate, SpO_2, NRS, Aldrete score, time to reach an Aldrete score of 9, total remifentanil and tramadol dose and the cost of administered drugs. American Society of Anesthesiologists risk group, sex, side effects, need for additional drugs and sedation level were compared using χ^2 tests.

Results

There was no significant difference between the groups with respect to the patients' demographic characteristics, American Society of Anesthesiologists risk group and surgical duration (Table 1). Similarly, there were no differences between the groups in terms of MBP, HR and SpO_2 values ($p > 0.05$) (Table 2).

The NRS values at 0 and 15 minutes were significantly higher in Group T than in Group P ($p < 0.05$) (Figure 1). There were no significant differences between the two groups in terms of Ramsey sedation scores, Aldrete scores or the time needed to reach Aldrete score of 9 ($p > 0.05$) (Table 3).

A comparison of the nausea scores revealed that they were significantly higher in Group T than in

Table 1. Demographic and clinical characteristics of patients administered with tramadol or tramadol-paracetamol

	Tramadol group ($n = 30$)	Tramadol-paracetamol group ($n = 30$)	*p*
Age (yr)	47.7 ± 8.7	44.5 ± 12.1	NS
Weight (kg)	78.2 ± 6.2	76.3 ± 6.9	NS
Sex, M/F	11/19	8/22	NS
ASA risk group (I/II)	17/13	18/12	NS
Duration of surgery (min)	174.2 ± 40.4	163.3 ± 38.1	NS
Number of laminectomies	2.9 ± 0.6	2.7 ± 0.7	NS

*Data presented as mean ± standard deviation or *n* (%). ASA = American Society of Anesthesiologists; NS = not significant.

Table 2. Changes in hemodynamic parameters in patients administered with tramadol or tramadol-paracetamol*

	MBP (mmHg)		HR (beats/min)		SpO_2 (%)	
	Tramadol group ($n=30$)	Tramadol-paracetamol group ($n=30$)	Tramadol group ($n=30$)	Tramadol-paracetamol group ($n=30$)	Tramadol group ($n=30$)	Tramadol-paracetamol group ($n=30$)
Control	87.3±17.6	89.1±10.5	76.0±6.5	74.3±7.9	99.1±0.7	99.5±0.6
After ind	89.2±8.9	84.9±8.7	74.8±6.7	72.7±8.8	98.9±0.9	99.4±0.7
0 min	87.8±9.8	89.3±10.5	80.8±6.6	77.5±7.0	97.8±0.7	98.3±0.8
15 min	87.6±9.4	89.9±11.0	77.6±8.5	77.2±9.8	97.3±0.9	98.0±1.1
30 min	90.4±9.4	90.5±11.8	77.9±7.1	77.8±10.2	97.3±1.1	97.9±0.9
1 hr	87.7±9.0	91.1±11.9	72.9±6.7	74.8±8.9	97.3±0.9	97.5±1.0
2 hr	88.4±9.0	89.7±9.7	75.0±9.1	77.0±9.3	97.2±0.9	97.4±0.9
4 hr	86.8±10.2	93.2±11.1	74.8±9.2	74.3±6.8	97.1±1.3	97.5±1.0
6 hr	92.4±8.8	90.5±11.8	75.5±9.4	76.1±9.5	97.3±0.9	97.6±0.8
12 hr	90.7±7.7	91.5±10.3	76.9±7.9	76.1±9.9	96.7±1.1	97.4±0.9
24 hr	92.6±9.8	89.1±8.8	75.7±7.9	76.0±7.1	97.2±0.9	97.5±0.7

*Data presented as mean±standard deviation. MBP=mean blood pressure; HR=heart rate; SpO_2=peripheral oxygen saturation; After ind=after analgesia induction.

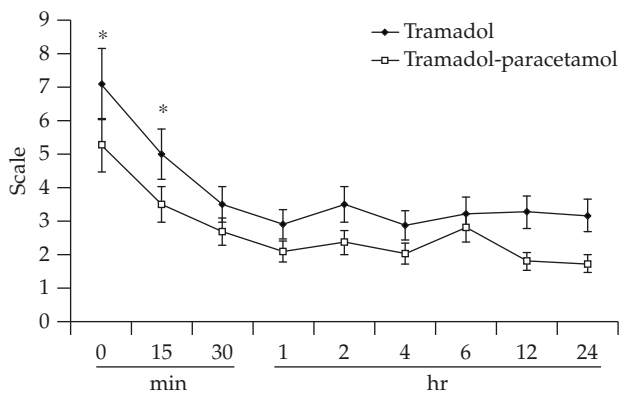

Figure 1. *Changes in the numeric rating scale in patients administered with tramadol or tramadol-paracetamol. *$p<0.05$.*

Group P at 0, 15 and 30 minutes, and at 1, 4, 6 and 12 hours ($p<0.05$) (Figure 2). All subjects who experienced severe nausea responded to treatment. In Group T, vomiting occurred at 0 minutes in one patient, at 15 minutes in five patients, at 30 minutes in five patients, 1 hour in two patients, at 4 and 6 hours in one patient each and at 12 hours in two patients. On the other hand, in Group P, vomiting occurred at 0 minutes in two patients, at 15 minutes in one patient and at 4 hours in one patient. The rate of vomiting was significantly lower in Group P than Group T at 30 minutes ($p=0.02$). There were no stastical difference in rate of vomiting in other time points between two groups, and no subject suffered from persistent vomiting.

In Group T, perspiration was observed at 1 and 2 hours in two patients each, and at 4, 6 and 12 hours in one patient each. There was not perspiration in any patient in Group P. The rate of perspiration was not significantly different between the two groups. In addition, no subject suffered from respiratory depression, bradycardia or hypotension.

None of the subjects in either group needed additional drugs such as ephedrine, atropine and naloxone after the control or infusion of the study drugs. The total doses of pethidine hydrochloride ($p=0.006$) and metoclopramide ($p<0.001$) used in Group T were significantly higher than those used in Group P (Table 4). The mean dose of remifentanil used during the operation was not significantly different between the two groups (Table 4). The mean required and administered amounts of tramadol, and the total dose of tramadol were significantly higher in Group T than in Group P ($p<0.01$) (Table 4).

The total cost of tramadol, metoclopramide and pethidine was significantly higher in Group T than in Group P (4.5±0.5€ *vs*. 2.3±0.4€; $p<0.001$). However, because the mean cost of paracetamol was 10.3€ per patient in Group P ($p<0.001$ *vs*. Group T), the total cost of drugs, including paracetamol, was significantly higher in Group P than in Group T (12.6±0.4€ *vs*. 4.5±0.5€; $p<0.001$).

In Group T, the satisfaction score was rated as good by four (13.3%) patients and as very good by 26 (86.7%) patients. In Group P, the satisfaction score was rated as good by two (6.7%) patients and as very good by 28 (93.3%) patients. There was no significant different between the two groups in terms of the general satisfaction scores ($p>0.05$).

Table 3. Changes in Ramsey and Aldrete scores in patients administered with tramadol or tramadol-paracetamol*

	Aldrete scores		Ramsey scores	
	Tramadol group ($n=30$)	Tramadol-paracetamol group ($n=30$)	Tramadol group ($n=30$)	Tramadol-paracetamol group ($n=30$)
0 min	7.8±0.4	7.8±0.3	2.5±0.5	2.3±0.4
15 min	9.7±0.4	9.8±0.4	2.1±0.3	2.0±0.2
30 min	10.0±0.0	10.0±0.0	2.0±0.2	2.0±0.0
60 min	10.0±0.0	10.0±0.0	2.0±0.2	2.0±0.0
Time to Aldrete score of 9 (min)	7.3±1.3	5.9±1.3		

*Data presented as mean±standard deviation.

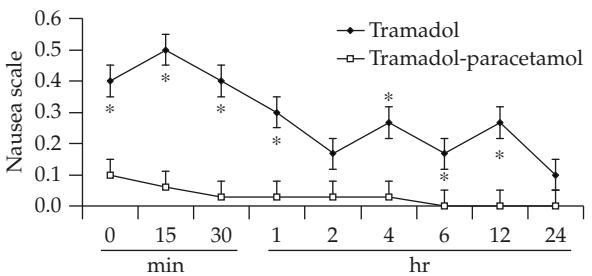

Figure 2. *Changes in the nausea score in patients administered with tramadol or tramadol-paracetamol. *p<0.05.*

Discussion

Effective postoperative analgesia prevents many of the negative effects associated with pain. Thus, all authorities agree that postoperative pain needs to be managed effectively [13]. McHugh et al [14] reported that approximately 82% of patients undergoing day surgery leave the operating room reporting pain.

Studies have shown the many advantages of IV patient controlled postoperative analgesia. The PCA method minimizes fluctuations in plasma drug concentrations that would otherwise have an adverse effect on the effectiveness of postoperative analgesic agents and exacerbate their side effects. Thus, adequate analgesia can be provided with smaller drug doses and fewer side effects [15]. The ideal postoperative analgesic treatment should have a rapid onset of effect, low incidence of side effects and a minimal effect on major organs. The use of opioids in the treatment of postoperative pain dates back to the early days of modern surgery. However, opioids have dose dependent side effects, which limit their use and may prevent adequate pain control [16].

Perioperative paracetamol and other NSAIDs reduce the dose needed for opioids and the incidence of side effects [17–19]. Although, non-opiate drugs have less analgesic effect than opioids, they may have better outcomes and may increase the effectiveness of opioids when used for somatic-visceral pain [20]. Because of their synergistic effects, adjuvant drugs in combination with opioids decrease the incidence of side effects associated with opioids [6]. NSAIDs constitute one part of a multi-factorial approach for pain control. NSAIDs primarily inhibit prostaglandin synthesis at peripheral sites of inflammation. In addition they may exert their analgesic effect by acting within the central nervous system (CNS). The central effect of NSAIDs increases their peripheral mechanism of action, due to interference with the formation of prostaglandin within the CNS. The central mechanism may be mediated by endogen opioids peptides or blockade of the release of serotonin. Inhibition of excitatory amino acids of NMDA activation has also been proposed [21]. Besides the arachidonic acid cascade in peripheral tissue is affected by NSAIDs, their use in combination with opioids is quite effective in specific receptors due to their central effect [22]. It has been shown that paracetamol in combination with tramadol is more effective than the use either drug alone, because their mechanisms of action and pharmacokinetics complement each other [22,23].

The onset of analgesia is faster with IV than oral paracetamol and the time to reach maximum pain relief is shorter. Thus, IV paracetamol is more effective in reducing pain intensity within the 1st hour of treatment [24]. Hence, IV paracetamol was preferred in this study because of these characteristics.

In a study to determine whether the addition of IV paracetamol would reduce daily morphine consumption in patients with postoperative pain after orthopedic surgery, 60 patients were randomly selected to

Table 4. Use of total metoclopramide, pethidine, remifentanil and tramadol doses*

	Tramadol group ($n=30$)	Tramadol-paracetamol group ($n=30$)	p
Metoclopramide (mg)	5.7 ± 5.0	1.3 ± 3.4	< 0.001
Pethidine (mg)	45.4 ± 33.8	20.8 ± 32.8	0.006
Remifentanil (μg)	1,207.9 ± 340.1	1,113.6 ± 403.5	–
Required amount of tramadol (mg)	67.7 ± 25.9	47.7 ± 16.5	0.010
Administered amount of tramadol (mg)	62.8 ± 23.5	39.2 ± 12.8	0.010
Total dose tramadol (mg)	276.0 ± 45.1	153.0 ± 15.6	< 0.001

*Data presented as mean ± standard deviation.

receive IV paracetamol or placebo [25]. All patients were given 15-minute IV infusions every 6 hours after surgery. All patients received morphine via PCA (1 mg bolus; 15-minute lockout interval; basal rate, 0.5 mg/hr). The total morphine dose per 24 hours and the number of bolus doses were determined. In that study, morphine consumption was significantly in the IV paracetamol group, and the number of bolus doses per 24 hours decreased by 37% [25] versus morphine alone.

Another study was conducted to assess the analgesic effectiveness and the incidence of side effects for the addition of IV paracetamol or placebo to morphine in patients who underwent spinal fusion surgery [26]. In that study, both groups administered morphine PCA morphine, and reduction in morphine dose was 46%. The sedation level was mild for all patients; however, 3 days after surgery, the sedation level was significantly lower in the IV paracetamol group than the placebo group. Thus, adding IV paracetamol to opioids in patients suffering from orthopedic postoperative pain was found to be safe and effective, and reduced the required opioid dose [26].

In a study [17] comparing 1 g IV paracetamol, 2 g propacetamol and placebo on postoperative pain after major orthopedic surgery (knee replacement surgery) in 151 patients, the initial drug request time was significantly longer in the group given the two active drugs. Evaluation of the 24-hour pain intensity revealed that the pain scores were significantly lower in this group in comparison with the other group. This study showed that IV paracetamol is efficient and safe for pain relief after knee replacement surgery [17].

Another study compared paracetamol, paracetamol-tramadol and paracetamol-nalbuphine for analgesia after supratentorial craniotomy performed under propofol-remifentanil anesthesia. One hour before surgery was completed, all subjects were administered IV with 30 mg/kg paracetamol, followed by 30 mg/kg every six hours. The paracetamol-tramadol group was also given 1.5 mg/kg tramadol at the same time. The authors concluded that paracetamol alone was inadequate to suppress craniotomy pain, and that tramadol or nalbuphine were needed in combination with paracetamol for adequate analgesia [27].

Similarly, in the present study, the NRS scores reported by patients in Group P were significantly lower at 0 and 15 minutes than those in Group T. The NRS scores remained lower at all times in Group P than in Group T. It was found that the tramadol demand and administration amounts, and the total tramadol dose were lower in Group P than in Group T. In this study, we allowed the use pethidine in both groups to provide additional analgesia for patients with a NRS score exceeding 4. In fact, the mean pethidine dose was significantly lower in Group P than in Group T.

Although tramadol has minimal cardiovascular affects, it has been reported to cause a slight but clinically insignificant increase in HR and blood pressure [28]. On the other hand, paracetamol does not affect the cardiovascular system at therapeutic doses [29]. In the present study, we found no significant differences between the two groups in terms of systolic, diastolic and MBP, and HR at any time-point. The decrease in MBP and HR values did not exceed 20% and no additional treatment was deemed necessary in any subject.

Previous studies of IV PCA, particularly using opioids, have reported low rates of the most feared side effect, respiratory depression [30–32]. Tramadol has been reported to provide adequate analgesia without causing changes in the respiratory rate, SpO_2 and blood gases, or causing hypoxia, and is thought to

have a clear advantage over opioids [28,30,32]. Unlike opioids, tramadol is not related to central side effects that occur as a result of paracetamol binding to receptors in the CNS. Hence, tramadol is not associated with nausea, vomiting, sedation or respiratory depression [28,33,34]. The respiratory rates were recorded in this study because they could indicate the presence of respiratory depression as a result of the drugs used. However, none of the subjects developed a respiratory rate below 10 breaths/min, which could indicate respiratory depression. Furthermore, the respiratory rates and SpO_2 values were not significantly different between the two groups. We did not expect any instances of respiratory depression at the doses of tramadol used in this study.

Side effects of tramadol have been reported to include nausea, vomiting, perspiration, headache, fatigue, dryness of the mouth, and urinary retention [28]. The most commonly observed side effects of tramadol are nausea and vomiting, which are caused by chemoreceptor trigger zone stimulation [28]. Although paracetamol may cause nausea, vomiting, loss of appetite, stomach ache and hypoglycemic coma at high doses, it is well-tolerated at therapeutic doses [34]. In our study, the nausea scores were significantly higher in Group T than in Group P, which is consistent with findings in other studies. Accordingly, the mean dose of metoclopramide, an antiemetic, was significantly higher in Group T than that in Group P. Another side effect of tramadol, perspiration, was observed more frequently in Group T than in Group P. This may be attributed to the significantly higher dose of tramadol in Group T.

Previous studies have shown that tramadol is associated with a lower risk for sedation and dependency than traditional opioids. This was claimed to be due to its weak affinity and potency for μ receptors, blockade of noradrenalin reuptake, and its slow onset of action [28,35]. The Ramsey sedation scale was used to measure the level of sedation in this study and the scores were similar in both groups. Notably, an increase in sedation did not occur in any patient. Thus, the treatments used in both groups did not increase sedation. The patients' postanesthesia levels were assessed using the Aldrete postanesthesia score. No significant difference was found between the two groups in terms of Aldrete score and the time needed to reach an Aldrete score 9. Thus, the postanesthesia levels were not prolonged in any patient.

A study on the use of propacetamol and ketorolac in addition to PCA morphine in gynecology patients showed no significant difference in patient satisfaction levels between the two groups [36]. Similarly, there was no difference in the number of patients who reported their satisfaction with the pain treatment at 24 hours as "very good" or "good" in our study. Thus, the PCA method, which allows active patient management of analgesia, is an effective control method that requires lower drug doses, alleviates patient fear of pain and gives patients the confidence that pain can be relieved without depending on clinical staff.

Controlling the cost of analgesia is very important, because the prices of new analgesic agents are generally high [37]. However, few studies have compared the cost of tramadol versus low dose tramadol-paracetamol for postoperative PCA. In our study, we found that the cost of low-dose tramadol-paracetamol was higher than that of tramadol alone. However, the costs of anesthesia may differ between countries and may even vary in the same country over time, which should be considered [37].

In conclusion, we compared low-dose PCA tramadol-paracetamol with tramadol for pain control after spinal vertebral surgery. We found that low-dose tramadol-paracetamol decreased the amount and increased the effectiveness of analgesics administered in the postoperative period. This combination reduced the incidence of side effects and provided effective analgesia. The combined paracetamol-tramadol regimen was superior to tramadol alone in reducing the intensity of pain during the 1st hour of treatment. The cardiovascular, respiratory and postanesthesia effects of tramadol and paracetamol-tramadol were similar. Taken together, the PCA paracetamol-tramadol combination regimen could be used safely for postoperative pain management after spinal vertebral surgery. However, the cost of the paracetamol-tramadol combination was higher than that of tramadol alone.

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