ORIGINAL RESEARCH

THE EFFICACY OF INTRAVENOUS PATIENT-CONTROLLED ANALGESIA USING TRAMADOL FOLLOWING SUPRATENTORIAL TUMOR RESECTION WITH CRANIOTOMY

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ABSTRACT

Objective: The aim of this study was to evaluate the analgesic efficacy of intravenous PCA using tramadol in patients, undergoing supratentorial tumor resection with craniotomy.
Material and Method: One hundred and fifty patients with ASA I-II between 18 and 70 years of age scheduled for an elective supratentorial craniotomy for tumor resection, were assigned to receive standardized general anesthesia. Postoperative pain was assessed at standard time intervals using a visual analogue scale (VAS) score. When the VAS score was >3, 1 to 1.5 mg/kg of tramadol was administered intravenously and PCA using tramadol was started. For 48 h postoperatively, the VAS, Glasgow coma, sedation, comfort, and nausea and vomiting scores were assessed.
Results: During the first 48 hours, 46% of the patients needed analgesic therapy and PCA with tramadol was adequate for these patients. Most patients needed analgesic drugs at 2 hours and their mean analgesic usage was higher at that point than at other periods in the first 2 h ($p<0.05$).
Conclusion: PCA with tramadol can be used effectively for postoperative pain management after craniotomy.

Keywords: Tramadol, Pain, Craniotomy

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HASTA KONTROLLÜ ANALJEZİ YÖNTEMİ İLE UYGULANAN TRAMADOLÜN SUPRATENTORİYAL KRANİYOTOMİ SONRASI AĞRI TEDAVİSİNDE ETKİNLİĞİNİN ARAŞTIRILMASI

ÖZET

Amaç: Bu çalışmada, hasta kontrollü analjezi yöntemi ile uygulanan tramadolün supratentoriyal kraniyotomi sonrası ağrı tedavisinde etkinliğinin araştırılması amaçlanmıştır.
Gereç ve Yöntem: Elektif supratentoriyal kraniyotomi operasyonu planlanan, ASA I-II grubundan, 18-70 yaş arasında 150 hasta çalışmaya dahil edilerek, propofol ve remifentanil ile standart genel anestezi uygulandı. Bupivakain ve epinefrin ile çivili başlık noktalarına ve cerrahi insizyona skalp infiltrasyonu uygulandı. Hastalar tam olarak uyandıktan sonra ekstübe edilerek, postoperatif ağrı skorları, vizüel analog skalası (VAS) skoru kullanılarak değerlendirildi. VAS skoru >3 olduğunda, tramadol 1-1.5 mg/kg titre edilerek intravenöz olarak uygulandı ve intravenöz hasta kontrollü analjezi yöntemi ile tramadol (20 mg bolus ve 8 dakika kilitli kalma süresi) uygulanmaya başlandı. Postoperatif 48 saat süresince VAS, Glasgow koma, sedasyon, konfor, bulantı ve kusma skorları takip edildi.
Bulgular: Postoperatif 48 saat süresince hastaların %46`sının analjezik ihtiyacı oldu ve bu hastalarda intravenöz hasta kontrollü analjezi yöntemi ile uygulanan tramadol ile yeterli analjezi sağladı. Postoperatif ilk 2 saatte analjezik ihtiyacının daha yüksek olduğu belirlendi ($p<0.05$).
Sonuç: İntravenöz hasta kontrollü analjezi yöntemi ile uygulanan tramadolün kraniyotomi operasyonu sonrası ağrı tedavisinde etkin olduğu sonucuna varılmıştır.

Anahtar Kelimeler: Tramadol, Ağrı, Kraniyotomi

INTRODUCTION

The ideal analgesic method for postcraniotomy headaches should consist of analgesic agents with short duration of action and few side effects. But there is no standard pain therapy and different approaches were used by different groups after craniotomy[1-3]. Most studies concluded that morphine provides more effective analgesia than other compounds, which is to be expected from a drug with a long duration of action. However, its depressive effects on respiration and neurologic responses and the possibility that pain can be treated with less potent drugs has led to the use of other opioids. Several investigators have reported that adequate analgesia can be achieved in neurosurgical patients with drugs such as codeine or nalbuphine[2,3]. Acetaminophen, COX-2 inhibitors, and ketoprofen alone are insufficient, but they may play supplementary roles and, in addition to narcotics, seem suitable for pain control after craniotomy[1,3-5]. Non-steroidal anti-inflammatory drugs may be contraindicated in some settings because of the potential for intracranial bleeding[6]. Incisional bupivacaine is helpful in the immediate postoperative phase to achieve pain control[7].

Tramadol is a parenteral opioid, and may be used for postoperative pain. It has not yet been studied effectively for its efficacy in patient controlled analgesia (PCA) after a craniotomy for tumor resection. Tramadol is a synthetic analogue of codeine that binds to mu opiate receptors and inhibits norepinephrine and serotonin reuptake. It is commonly used to treat mild to severe postoperative pain[8]. Tramadol may have advantages over conventional opioids in terms of side effects. Other potential advantages of administering tramadol include a long duration of action, rapid recovery, and limited depression of respiratory function[9-]. The purpose of the present study was to evaluate the potency, efficacy, and side effects of tramadol and patient satisfaction regarding pain management after supratentorial craniotomy for tumor resection.

MATERIAL AND METHOD

For this study, we obtained approval from the ethics committee of the Ministry of Health of Turkey and each patients` written consent. We prospectively enrolled 150 patients between 18 and 70 years of age with an American Society of Anesthesiologists (ASA) physical status of I-II, who were scheduled for elective supratentorial craniotomy for tumor resection in the supine position. Demographic data and the location of the tumor were recorded in each patient. The PCA technique and the visual analogue scale (VAS) were explained to patients during the preoperative visit.

Before the induction of general anesthesia, standard monitorization devices were applied (electrocardiogram, blood pressure cuff, and pulse oximeter probe). After the induction of anesthesia, a 20-gauge catheter was placed in the radial artery and the esophageal temperature and end-tidal carbon dioxide concentration were monitored. The anesthesia protocol was standardized for all patients. General anesthesia was induced with 2-3 mg/kg propofol and muscle relaxation was achieved with 0.15 mg/kg cis-atracurium and remifentanil titrated in doses of 0.5-1 µg/kg. After tracheal intubation, the lungs were ventilated with an air/oxygen mixture (FiO_2 0.5). Anesthesia was maintained with the titration of 0.1-0.25 µg/kg/min remifentanil and propofol infusion (100-200 µg/kg/min). The scalp infiltration was done with bupivacaine (0.25%) and epinephrine (1:200.000) for skeletal fixation, skin incision, and wound closure. Drugs such as furosemide, dexamethasone, phenytoin, and antibiotics were administered intravenously as required by the surgeon.

After tracheal extubation, patients were transferred to the post anesthetic care unit and were equipped with PCA pumps (Abbott Pain Management Provider, North Chicago, IL). Postoperative pain was assessed in the fully-awake patient after extubation using a VAS score (0 = no pain, 10 = worst pain imaginable). When the VAS score was greater than 3, 1 to 1.5 mg/kg tramadol hydrochloride (Grünenthal GmbH, Stolberg, Germany) was slowly administered intravenously in 2 minutes. The PCA solution contained 5 mg/mL of tramadol and the PCA device was set to deliver 20-mg bolus with an 8-min lockout time and no background infusion. The demand dose was increased to 30 mg if analgesia was inadequate after 1 hour. In patients with pain (VAS >3), the initial dose of tramadol was injected. We administered 0.1 mg/kg morphine intravenously when the previously described analgesia techniques were not sufficient. Postoperative assessment included the GCS score, the VAS score, the efficacy of analgesic treatment scores (0: complaint, 1: dissatisfactory/poor, 2: satisfactory, 3: good/excellent), the nausea and vomiting score (0: no nausea or vomiting, 1: nausea but no vomiting, 2: retching but no vomiting, 3: vomiting) at the initial visit, and whether the patient had informed staff about the presence of pain. These factors were assessed at 5., 10., 20., 30., and 45. minutes and 1, 2, 4, 6, 12, 24, 36 and 48 hours after surgery. The incremental and cumulative tramadol consumption at these times was also recorded from the PCA device. At the patients' request, or in the presence of nausea and vomiting, ondansetron (4mg IV) was administered. The number of patients receiving antiemetics and the doses of antiemetics administered were recorded. Any episodes of pruritus, dizziness, dry mouth, epigastric discomfort, bradypnea, hypoxia or other adverse effects were also noted.

The results of these analyses were expressed as the mean ± standard deviation. Statistical analysis was performed with the t-test for unpaired data, the chi-square, and Fischer tests when appropriate ($p<0.05$).

RESULTS

Table I shows the demographic characteristics of the 150 patients included in the study (age, sex, height, weight, and ASA status) as well as the location of the tumor. After surgery, all patients were extubated safely . Side effects of surgery and anesthesia were observed.

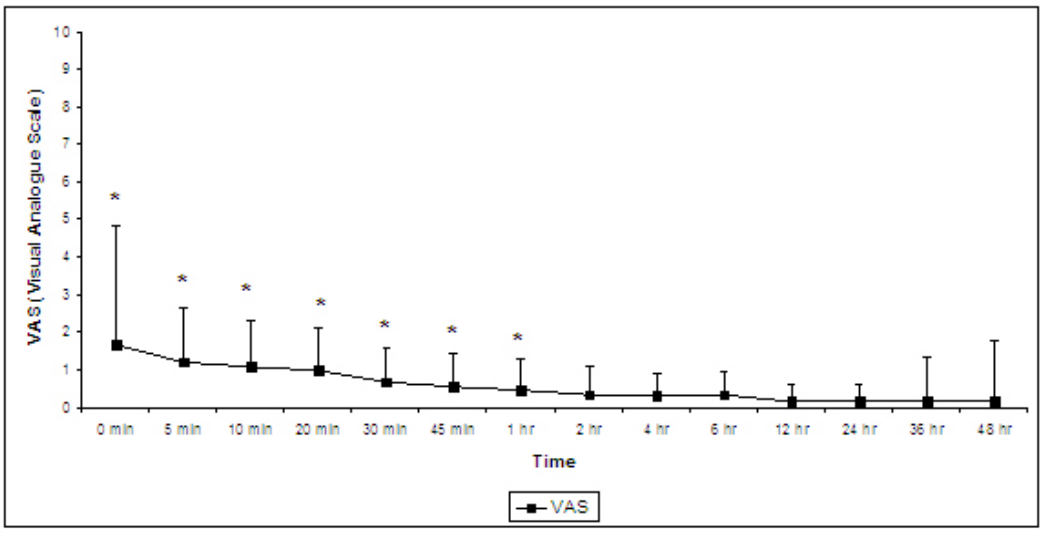
During 48 hours after surgery, 46% (n= 69) of patients complained of pain and required analgesia. All of these patients were able to

use the PCA device when they suffered pain. The number of patients who used the PCA device was significantly higher in the first 2 hours after surgery than during other time periods ($p<0.05$) (Figure 1). PCA with tramadol offered adequate pain relief for these patients and none of the patients required morphine. The efficacy of analgesic treatment showed a statistically significant increase after 1 hour ($p<0.05$) and was determined by all patients to be satisfactory or good (Figure 2). Incremental and cumulative tramadol consumption is shown in Table II. Incremental and cumulative tramadol consumption was similar ($p<0.05$).

The incidence of nausea and vomiting was 40% (n: 60) postoperatively in all patients. Nausea occurred in 27% of the patients (n= 41) after surgery. Tramadol was administered to 26 of these patients. Retching and vomiting occurred in 13% (n= 19). Of these, 13 patients had been administered tramadol. The incidence of tramadol-related postoperative nausea and vomiting was 57% (n= 39). Nausea and vomiting scores were significantly higher in the first 30 minutes than in the other periods ($p <0.05$). There were no episodes of decreasing GCS scores, pruritis, bradypnea, hypoxia, or major adverse effects.

Table I. Demographic characteristics of patients (n=150).

Age (years), mean ± SD	52 ± 15
Sex (Female/Male)	71/79
Height (cm), mean ± SD	168 ± 10
Weight (kg), mean ± SD	74 ± 11
ASA status (I/II)	92/58



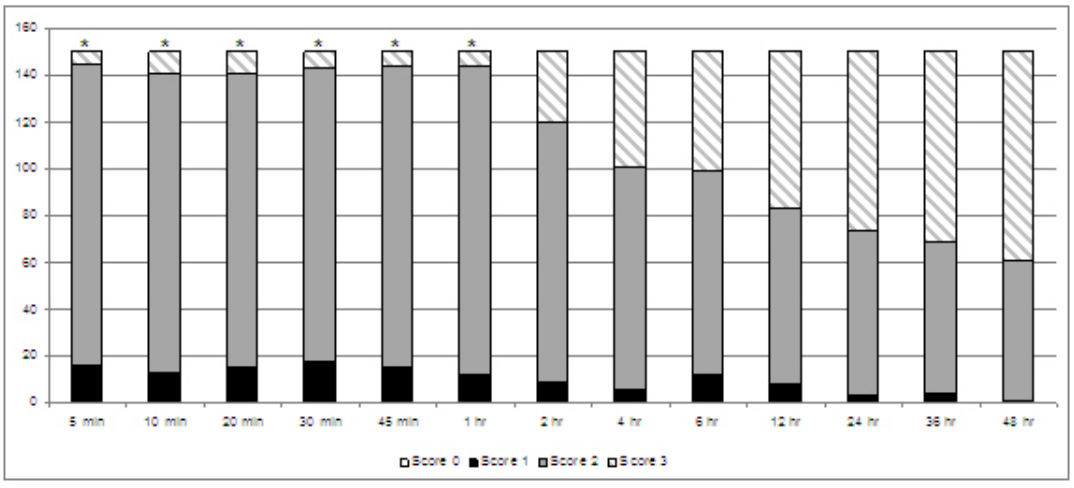
* p <0.05 when compared with other periods.

Figure 1: Visual analog scale (VAS) pain scores during the first 48-h period after surgery.

Table II. Incremental and cumulative tramadol consumption and incidence of PCA use for each of the indicated times during the postoperative 48 hours

Time after surgery	Incremental tramadol consumption (mg)	Cumulative tramadol consumption (mg)	Number of patients who used PCA (n=150)
5 min	28 ± 10	133 ± 29	37*
10 min	33 ± 18	156 ± 50	31*
20 min	40 ± 22	191 ± 66	27*
30 min	40 ± 20	218 ± 93	26*
45 min	43 ± 20	257 ± 113	28*
1 h	45 ± 20	299 ± 133	26*
2 h	44 ± 20	325 ± 162	23*
4 h	48 ± 27	371 ± 188	6
6 h	51 ± 29	409 ± 223	10
12 h	51 ± 29	442 ± 259	4
24 h	51 ± 29	490 ± 287	1
36 h	51 ± 29	541 ± 317	1
48 h	54 ± 35	590 ± 349	5

Data are mean ± SD or number of patients.
* p <0.05 when compared with other periods.



* p <0.05 when compared with other periods.

Figure 2: Patient satisfaction score. Values are shown as the number of patients.

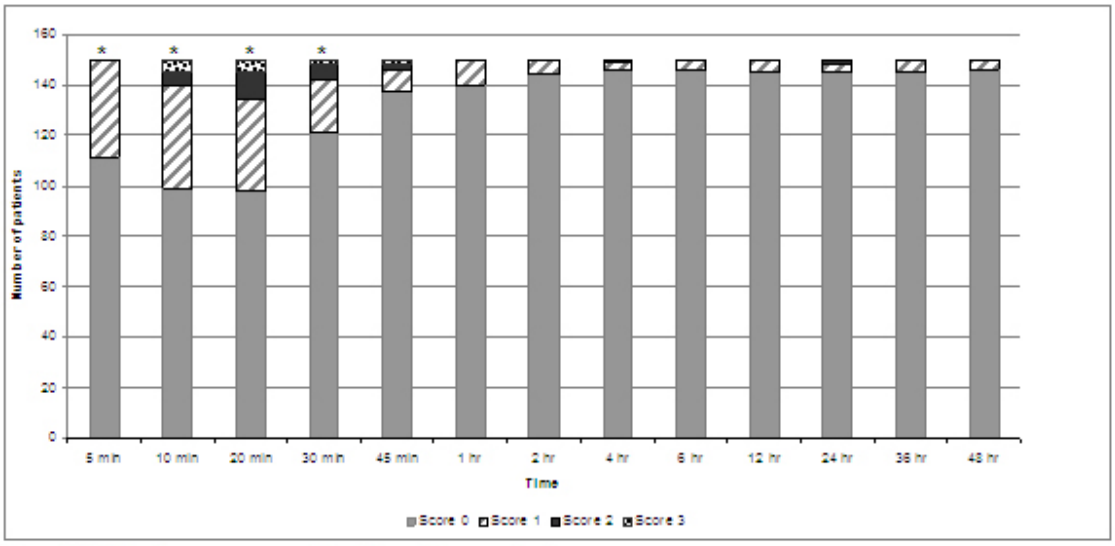


Figure 3: Postoperative nausea and vomiting scores during the first 48-h period after surgery. Values are shown as the number of patients.

DISCUSSION

This study shows that tramadol with PCA is efficacious and has minimal side effects for treating pain after supratentorial tumor resection craniotomy.

Our study showed that tramadol with PCA has adequate analgesic effects for postcraniotomy headache. The PCA settings were not changed in 46% of patients needing treatment during the first 48 hours after surgery. However, the VAS scores and analgesic requirements were high during the first 2 hours compared with other periods. This phenomenon seemed to be related to the timing of the first dose of tramadol. The patients were extubated and, after ensuring their cooperation, the first dose was administered and the patients were questioned with respect to their pain. In fact, the peak effect of tramadol injected intravenously was observed approximately 60 min after a 100-mg bolus[12]. For this reason, the VAS scores may appear to be high within the first 2 hours[13]. The VAS scores of patients who initially scored higher than 3 decreased gradually after the injection of the bolus tramadol dose. After 2 hours, their analgesic requirements were markedly lower.

Another reason for higher pain scores within the first 2 hours was the use of remifentanil peroperatively. The short-lived analgesic effect of remifentanil infusion used to maintain anesthesia does not carry over to the postoperative period[14-16]. A peroperative loading dose of tramadol might provide better postoperative pain relief in patients who were administered remifentanil peroperatively and to whom tramadol analgesia was to be administered postoperatively[12,17,18]. In a limited number of studies of tramadol for treating postcraniotomy pain, tramadol was used intramuscularly[5] or administered intermittently intravenously[19]. In only one of these studies tramadol was administered through the PCA[19]. With regard to depressed respiration and sedation, Sudheer and colleagues found no differences between tramadol, codeine and morphine, but codeine and morphine provided better pain relief[19]. Sudheer's study included a total of 60 patients, with subgroups for each operative procedure comprising 4 to 6 patients. Information about the patients' use of tramadol was not collected. Nonetheless, the study revealed important information about the respiratory effects of tramadol use with

PCA. Tramadol was started during the postoperative phase, as was the case in our study, and because of the delayed peak concentration levels, the analgesic requirements of patients were higher. Furthermore, because of the late injection of the bolus dose, treatment was insufficient. Moreover, with an average duration of surgery of 5.4 hours, the nerve block applied in the form of bupivacaine before surgery did not contribute to the ability of tramadol to relieve pain[7,20,21]. On the other hand, the patients may have benefited from the anti-inflammatory effects produced by the intraoperative administration of dexamethasone.

The most common side effects of tramadol, nausea and vomiting, may occur in patients after intracranial surgery but may also be due to the manipulation of intracranial structures, increases in intracranial pressure, as a consequence of general anesthesia, or as a side effect of perioperative opioid administration[1]. The literature shows that the parenteral use of tramadol is associated with more nausea and vomiting than the use of either morphine or codeine[19,22]. The rate of nausea induced by tramadol has been reported to range from 32% to 50%[5,12,19,23]. The rate of postoperative nausea and vomiting (PONV) in our study was 40% after supratentorial craniotomy. However, in our study the incidence of the tramadol-related postoperative nausea and vomiting was 57%. The reason for the higher rate, compared to what has been reported in the literature, may be that prophylactic antiemetic therapy was not applied. Since nausea and vomiting may increase intracranial pressure after a craniotomy, the prophylactic use of an antiemetic, as stated in the literature, is an important way to decrease PONV following tramadol usage[8]. Pain itself may also be a cause of postoperative nausea. For that reason, treating pain and controlling nausea and vomiting are important in preventing an increase in intracranial pressure.

Wound infiltration with a local anesthetic is another technique used to decrease postoperative pain[7]. In our study, the mean duration of surgery was 5.4 hours, and the preoperative use of bupivacaine could affect postoperative pain. Beneficial effects of bupivacaine seemed to last longer than expected. In fact, this long-acting effect of bupivacaine could occur because of the prevention of inflammatory responses that accompany the early postoperative period.

A limitation of the present study is that it is not controlled, and consequently not randomized. However, we aimed to understand the efficacy of tramadol on postcraniotomy pain, and we did not compare tramadol with different analgesic drugs. During the study period, if the patient required any additional analgesic therapy following tramadol, we planned to administer morphine, and none of the patients required any additional analgesic drug during the study period.

In conclusion, our study supports patient-controlled analgesia with tramadol as an effective analgesic method for postoperative pain management after supratentorial craniotomy. However, further studies should be designed with randomized, controlled groups for comparison of the different analgesic drugs on postcraniotomy pain therapy.

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