

Effects of Paracetamol and Tenoxicam on Postoperative Pain and Need for Rescue Analgesia in Root Canal Treatments Performed Under General Anesthesia: A Retrospective Study

Genel Anestezi Altında Tamamlanan Kök Kanal Tedavilerinde Parasetamol ve Tenoksikamın Postoperatif Ağrı Düzeyi ve Kurtarma Analjezisi Gereksinimi Üzerine Etkisinin Değerlendirilmesi: Retrospektif Bir Araştırma

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Keywords

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Abstract

Objective: This study aimed to investigate the effects of parenterally administered paracetamol and tenoxicam on early postoperative pain regarding analgesia in healthy adults who had completed root canal treatments (RCTs) in a single visit under standard general anesthesia protocols.

Materials and Methods: In this retrospective study, the data of 83 adult patients who underwent RCTs under general anesthesia in a single visit due to severe nausea reflex and/or anxiety were analyzed. Patients were divided into two groups according to the intravenous administration of 15 mg/kg paracetamol (P group) or 0.5 mg/kg tenoxicam (T group) 30 min before the end of general anesthesia to meet their analgesia requirements. Thereafter, early postoperative period visual analog scale (VAS) scores were recorded at the 5th minute after the patients were taken to the recovery room and at the subsequent 2nd hour. After 2 h, rescue analgesia was given to patients with VAS scores >4 in both groups and recorded. Data were analyzed statistically.

Results: A total of 68 patients who met the inclusion criteria were evaluated. Regarding postoperative pain values, the average VAS score was significantly lower in the T group at both the 5th minute and 2nd hour than in the P group. In both groups, the mean VAS scores were decreased by the same amount over time, and the differences between the groups were not significant (p=0.452). Moreover, no significant difference was found between the two groups in terms of the need for rescue analgesia (p=0.571).

Conclusion: Tenoxicam, administered parenterally, provides more effective analgesia for postoperative pain management compared with paracetamol when it is used in RCTs under general anesthesia.

Öz

Amaç: Bu çalışmanın amacı, standart genel anestezi protokolleri altında tek seansta kök kanal tedavileri tamamlanan sağlıklı erişkinlerde analjezi amacı ile parenteral uygulanan parasetamol ve tenoksikamın erken dönem postoperatif ağrı üzerine etkinliklerinin araştırılmasıdır.

Gereç ve Yöntemler: Bu retrospektif çalışmada, şiddetli bulantı refleksi ve/veya anksiyete sebebiyle genel anestezi altında kök kanal tedavileri tek seansta gerçekleştirilen 83 yetişkin hastanın verileri incelenmiştir. Hastalar, analjezi gereksinimlerinin sağlanması için genel anestezi sonlanmadan 30 dakika önce 15 mg/kg parasetamol (grup P) veya 0,5 mg/kg tenoksikamın (grup T) intravenöz olarak uygulanmasına göre iki gruba ayrılmıştır. Sonrasında, hastaların derlenme odasına alındıktan sonra 5. dakikadaki ve takip eden 2. saatteki erken postoperatif dönem vizüel analog skala (VAS) ölçümleri kayıt edilmiştir. Her iki grupta da 2 saat sonunda VAS skorları 4 üzerinde olan hastalara kurtarma analjezisi uygulanmış ve kayıt edilmiştir. Veriler istatistiksel olarak analiz edilmiştir.

Bulgular: Dahil edilme kriterlerini karşılayan toplam 68 hasta değerlendirmeye alınmıştır. Postoperatif ağrı değerleri açısından hem 5. dakikada hem de 2. saatte grup T'de grup P'ye göre istatistiksel olarak anlamlı olarak daha düşük VAS skor ortalamaları gözlenmiştir. Her iki grupta da VAS skor ortalamaları zamanla aynı ölçüde azalmıştır ve gruplar arası fark istatistiksel olarak anlamlı değildir ($p=0,452$). Ayrıca, kurtarma analjezi ihtiyacı bakımından da iki grup arasında anlamlı fark görülmemiştir ($p=0,571$).

Sonuç: Genel anestezi altında uygulanacak kök kanal tedavilerinde postoperatif ağrı yönetimi açısından parenteral olarak uygulanan tenoksikam, parasetamole kıyasla daha etkin analjezi sağlamaktadır.

Introduction

Dental anxiety is defined as an undescribable state of intense unease that develops due to fear and anxiety related to dental treatment (1). Today, despite the use of effective local anesthetic and analgesic drugs, many patients still have anxiety problems related to dental treatments (2,3). In the treatment of dental anxiety, general anesthesia procedures are used when psychological approaches are not sufficient (4). General anesthesia is described as a situation in which a patient is rendered unconscious, completely or partially loses his protective reflexes, no responses to physical and verbal stimuli, airway patency cannot be achieved, and is connected to a respiratory support unit (1). Pain is the most common complication observed after operations performed under general anesthesia (5). Pharmacological, surgical and non-pharmacological methods are used in the management of postoperative pain (6). In pharmacological applications, drugs are prescribed upon the request of a doctor and administered using different methods. The purpose of this method is the maximum relieve of pain with no or minimal side effects. Pain control with pharmacological methods aims to reduce the patient's pain in the postoperative period with narcotic and non-narcotic analgesics applied in the preoperative period. These protocols are determined by considering the type of surgery and individual characteristics and according to the expected pain intensity (6). In addition, it has been reported that effective management of postoperative

pain after surgery ensures shortened recovery time and decreased duration of hospital stay (7). At the same time, effective analgesia provided to patients can prevent many complications that may develop (8,9).

Restorations, endodontic treatments, periodontal and surgical procedures are performed under general anesthesia for children and adults with mental illness, anxiety problems, psychological disorders and severe nauseareflexes(10-12). Although root canal treatments (RCTs) under general anesthesia is technically difficult and time consuming, it is indicated for teeth that can remain functional (10). Postoperative pain after RCT is one of the most common complications (13,14) and its incidence has been reported between 3 to 58% (14). Although the main purpose of endodontic treatment is to produce appropriate biological results, it should be ensured that the patient does not feel pain during and after the treatment (14). Postoperative pain is as a result of many factors and its causes are divided into preoperative and procedural factors. Several factors such as the gender and age of the patient, the presence of systemic disease, the presence of preoperative pain, the condition of the pulp, the number of visits, and the use of intra-canal medication can affect postoperative pain (15). The management of postoperative pain after RCT is multifactorial and includes the combination of a good endodontic procedure and appropriate use of analgesics. Most of the drugs used to manage postendodontic pain consist of non-narcotic analgesics including paracetamol,

non-steroidal anti-inflammatory drugs (NSAIDs) and narcotic analgesics (16).

Paracetamol is an analgesic agent that is thought to have an effect on the central nervous system through central cyclooxygenase (COX) inhibition and is thought to have a significant effect on platelet aggregation (17). On the other hand, tenoxicam is a NSAID that can be used reliably with minimal hematological side effects, has a long half-life and sufficient analgesic effect. Due to the low incidence of side effects, these two analgesic drugs are agents used in outpatient surgical procedures (18).

RCTs completed under general anesthesia are performed in single visit. There are few studies evaluating postoperative pain in dental procedures completed under general anesthesia (19,20). However, management of early postoperative pain in endodontic treatments performed under general anesthesia has never previously been investigated in the literature. Therefore, the aim of this study was to investigate the effects of parenterally administered paracetamol and tenoxicam on early postoperative pain in healthy adults under standard general anesthesia protocols for analgesia. The null hypotheses of the present study are as follows;

1. There was no difference between the paracetamol and tenoxicam groups in healthy adults undergoing RCTs under general anesthesia on early postoperative pain.

2. There was no difference between the groups in terms of the need for rescue analgesia after the administration of paracetamol and tenoxicam.

Materials and Methods

This study was conducted with an approval from the Non-Invasive Clinical Research Ethics Committee (protocol no: 2020/75, date: 02.07.2020) of the Faculty of Medicine Aydın Adnan Menderes University. This retrospective study was carried out by scanning the files of 83 adult patients between the ages of 18-60 who were referred to Faculty of Dentistry, Aydın Adnan Menderes University, during a three-year period between January 2016 and December 2018. Patients were only limited to have performed endodontic and restorative treatments under general anesthesia. Inclusion and exclusion criteria are presented in Table 1. Before the general anesthesia consents forms stating that the patients data can be

used in the scientific research were signed by the patients.

Preoperative Evaluation

Routine hemogram, blood glucose, liver enzymes, kidney function tests, blood electrolyte values, coagulation markers were evaluated for all patients to be treated in the operating room. Patients who had no issues in physical examination and blood tests were approved for procedures under general anesthesia. Each patient was made to observe at least an 8 hours fasting period prior to the operation. IV vascular access was established for patients on the day of operation. Routine vital signs of the patients and preoperative period anxiety levels were recorded according to Beck Anxiety scale. Beck Anxiety scale is an index with questions scaling up to 63 points. Patients' anxiety levels were determined as; 0-7 points: no anxiety, 8-15 points: mild anxiety, 16-25 points: moderate anxiety, 26-63 points: severe anxiety.

After determining the anxiety levels of the patients, midazolam at a dose 0.04-0.05 mg/kg (maximum dose not exceeding 4 mg) was administered as IV 15 minutes before the surgery for premedication, All preoperative practices are routine clinical procedures specified in the files.

General Anesthesia Procedure

A routine general anesthesia protocol was applied to all patients who came to the General Anesthesia Unit. All patients were preoxygenated with a face mask after their monitorization. The same anesthesiologist (Ö.Ö.) with 10 years of clinical experience performed all of the procedures. Fentanyl 1-2 $\mu\text{g}\cdot\text{kg}^{-1}$ IV, propofol 2-2.5 $\text{mg}\cdot\text{kg}^{-1}$ IV and rocuronium 0.5-0.6 $\mu\text{g}\cdot\text{kg}^{-1}$ IV were administered for induction. One minute after unconsciousness and respiratory suppression, nasal intubation was performed with a flexible spiral tube. In the maintenance of anesthesia, 1.5-2% sevoflurane was used in a mixture of N_2O 1.0 L/min, O_2 1.0 L/min. Rocuronium 0.15-0.2 $\text{mg}\cdot\text{kg}^{-1}$ IV bolus was administered as an additional muscle relaxant. Metoclopramide 0.2 $\text{mg}\cdot\text{kg}^{-1}$ IV was administered to each patient as an antiemetic before the end of general anesthesia. All intraoperative practices are routine procedures specified in the files.

Endodontic Treatment Procedure

All endodontic treatment procedures in this study were performed in a single session under general

anesthesia by endodontists with at least 5 years of experience. Root canal lengths were determined with the help of an endodontic apex finder (VDW, München, Germany) after opening the entrance cavity under rubberdam isolation. All canals were preformed with K-type hand files (DiaDent, Cheongju, Korea). The root canals were then shaped by applying the recommended file sequence with the Protaper Next rotary file system (ProTaper Next; Dentsply Sirona, Ballaigues, Switzerland) at the torque and speeds recommended by the manufacturer. Between each file, 2 mL of irrigation with 2.5% NaOCl was made, and in total, each channel was irrigated with at least 12 mL of NaOCl. For final irrigation, 2 mL of 17% EDTA, 2 mL of 2.5% NaOCl and 2 mL of distilled water was applied to each root canal, respectively. The root canals were then dried with sterile paper cones and filled with epoxy resin-containing root canal sealer (AH Plus; Dentsply DeTrey, Konstanz, Germany) and Gutta-percha cones (Dentsply Sirona) using a single cone technique. Teeth whose RCTs were completed were permanently restored using a single-stage self-adhesive (Tokuyama Bond Force, Tokuyama Dental, Tokyo, Japan) and light-cured composite restoration material (Clearfil Majesty, Kuraray, Tokyo, Japan).

Analgesia Dose

As a routine analgesia protocol, 15 mg/kg paracetamol or tenoxicam 0.5 mg/kg was administered intravenously 30 minutes before the end of general anesthesia to patients who underwent dental treatments under general anesthesia in our operating

room. The choice of tenoxicam or paracetamol was made according to the availability of the drugs in the hospital pharmacy during the study period. In the recovery unit, the postoperative pain levels of the patients were routinely assessed using a 10 cm visual analog scale (VAS) (beginning from -0- "no pain", to the other end -10- "unbearable pain"). In addition, the patients were followed in terms of other expected side effects and their data were recorded in the patient files (nausea, vomiting, gastric burning and/or pain, rash, allergic reaction, bleeding). Patients with VAS > 4 are given 0.5 mg/kg tramadol as rescue analgesia as mentioned in the studies of Niemi-Murolo et al. (21) and Gupta et al. (22). These informations were recorded in the patient files.

Patients treated with paracetamol were sorted into group P and patients given tenoxicam in group T. Early postoperative VAS measurements were recorded at the 5th minute and subsequently at 2nd hour after the patients in both groups were taken to the recovery room. The patients' initial anxiety levels, demographic data, number of teeth treated with RCT, duration of general anesthesia, postoperative pain VAS values and rescue analgesia requirements were statistically evaluated.

Statistical Analysis

IBM SPSS version 25.0 (IBM, New York, NY, USA) package program was used for the analysis of the data obtained in this study. Shapiro-Wilk test, kurtosis-skewness values and histogram graphics were used to test the compliance of the data of the study to normal

Table 1. Inclusion and/or exclusion criteria of patients

| Inclusion criteria | Exclusion criteria |
|---|---|
| Patients between the ages of 18-60 and who were physically and/or mentally healthy Patients who consented to the use of their data in research | Patients who did not consent to and/or from whom consent was not obtain for the use of their data in research |
| Patient in the I-II group of the ASA (American Society of Anesthesiologists) | Mentally unhealthy and ASA III-IV group patients |
| Patients undergoing a routine general anesthetic procedure | Patients undergoing treatments other than routine general anesthesia procedures |
| Patients who have completed at least one root canal treatment in a single visit during general anesthesia | Patients who have undergone surgical, periodontal and/or prosthetic procedures together with endodontic procedures during general anesthesia. |
| | Patients allergic to paracetamol Patients allergic to non-steroidal anti-inflammatory agents and/or have a history of asthma |
| | Patients who had pain in the preoperative period and/or used painkillers at least 3 days before the operation |

distribution. Descriptive statistics were used to analyze demographic data. Repeated measures ANOVA test was used to evaluate VAS scores according to groups and measurement times. At the end of the 2nd hour, whether there was a difference between NSAIDs in terms of the number of patients with a VAS score of 4 and above was examined by Fisher's Exact chi-square test.

Results

In the specified time range, 11 out of 83 adult patients who underwent RCT under general anesthesia were excluded from the study because they did not meet the inclusion criteria. Of the

remaining 72 patients, 32 were sorted into group P, 40 patients in group T. Three patients from group P and 1 patient from group T were excluded from the study due to missing data in their files. As a result, the data of 29 patients in group P and 39 patients in group T (68 patients in total) were analyzed (Figure 1). Demographic variables and clinical characteristics of the patients are as shown in Table 2. The number and the types of the treated teeth in the groups are as shown in Table 3.

No statistically significant difference was found between group T and group P in terms of demographic data, American Society of Anesthesiologists scores, duration of intraoperative anesthesia, and the number of teeth treated during RCT ($p>0.05$) (Table 2).

There was no difference between the averages of Beck Anxiety scores in the preoperative period in both groups, and both groups were found to have mild-moderate preoperative anxiety scores (Table 4).

In terms of postoperative pain values at 5th minute (VAS 1), statistically significant lower VAS scores were observed in group T compared to group P ($p=0.010$) (Table 4). Similarly, in the postoperative pain values at the 2nd hour (VAS 2), statistically significantly lower VAS score averages were observed in group T compared to group P ($p=0.019$) (Table 4). Considering the differences in change over time, the effect of drugs on the mean of VAS score over time in both group P and group T was not statistically significant ($p=0.452$). Both drugs decreased the VAS score to the same extent over time (Figure 2). However, there was no significant difference between group T and group P in terms of rescue analgesia need ($p=0.571$) (Table 4).

Postoperative side effects were observed in 2 patients in group T (nausea-vomiting), in 1 patient in group P (mild epistaxis due to nasotracheal

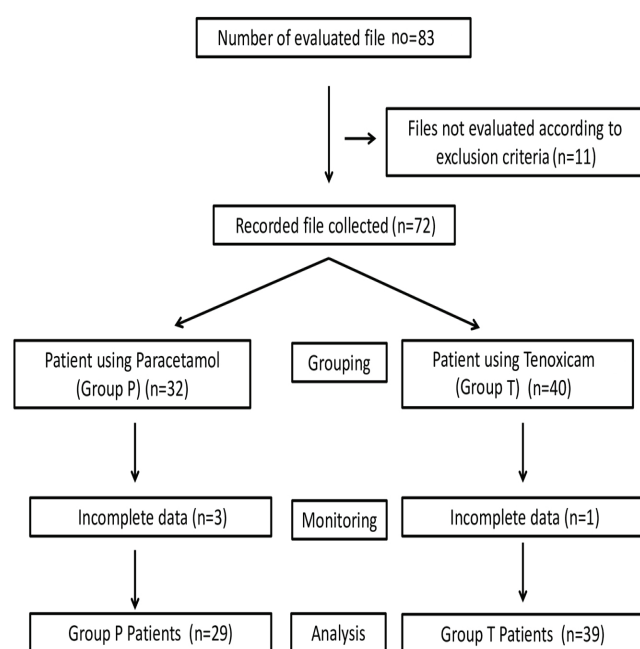


Figure 1. Flow chart of the participants

Table 2. Demographic data and intraoperative characteristics

| | Tenoxicam | Paracetamol | p |
|-------------------------|--------------|--------------|-------|
| Age | 31.10±10.87 | 30.17±11.91 | 0.665 |
| Gender (f/m) (n) | 21/18 | 14/15 | 0.808 |
| Weight (kg) | 72.07±10.25 | 73.00±10.40 | 0.691 |
| Anesthesia duration | 234.74±51.70 | 238.10±52.54 | 0.960 |
| Number of treated teeth | 1.79±0.97 | 1.75±0.83 | 0.925 |
| ASA I/II (n) | 32/7 | 24/5 | 0.940 |

*Mean ± standard deviation. F: Female, m: Male, ASA: American Society of Anesthesiologists

intubation), and in 2 patients in group P (headache). No side effects were observed in other patients.

Discussion

According to the findings of the present study, it was observed that significantly lower postoperative pain values were observed in both early period measurements (5 minutes and 2 hours after) in patients who received tenoxicam in endodontic treatments performed under general anesthesia compared to those who received paracetamol. Therefore, the first null hypothesis was rejected. Since, there was no statistically significant difference between the two groups in terms of the need for rescue analgesia, the second null hypothesis should be accepted.

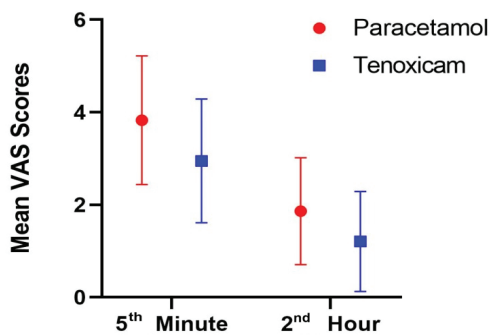


Figure 2. The distribution of mean VAS scores between groups for checked time periods

VAS: Visual analog score

Pain is a condition that is oftentimes more important than the disease itself and often needs to be treated quickly (23). Since the most common clinical complication after RCT is pain (14), there are many studies in the literature on the management of pain after RCT (24,25); however, there is no study in the literature regarding the management of early pain after RCT under general anesthesia. Therefore, the results of the present study may highlight major issues in the literature. While intra-operative pain is prevented in endodontic treatments with effective local anesthesia methods and operative techniques, paracetamol, non-narcotic analgesics containing NSAIDs and narcotic analgesics are being used in postoperative pain management (16,24,25). An IV analgesic may be the preferred choice for patients who are unable to take drugs administered orally in the early postoperative period after general anesthesia and need rapid onset of analgesia (26). Tenoxicam is a NSAID with high potential in terms of its analgesic and anti-inflammatory effects, and due to its possible use in IV form, it is frequently preferred after surgical procedures under general anesthesia where oral administration is not possible. Due to its long half-life and the sufficiency of a single dose tenoxicam has moved to the forefront in postoperative pain control for outpatient surgeries compared to other NSAID groups (27). Regarding these reasons, tenoxicam was chosen as an NSAID in the present study. However,

Table 3. The number and types of the treated teeth in the groups

| | Paracetamol | | Tenoxicam | |
|-----------|-------------|--------------|-------------|--------------|
| | Maxilla (n) | Mandible (n) | Maxilla (n) | Mandible (n) |
| Incisors | 9 | 5 | 11 | 8 |
| Canine | 8 | 3 | 9 | 9 |
| Premolars | 7 | 6 | 10 | 7 |
| Molars | 6 | 8 | 9 | 10 |
| Sum | 52 | | 73 | |

Table 4. Visual analog scores and anxiety levels

| | Tenoxicam | Paracetamol | p |
|--------------------------------|--------------|--------------|--------|
| VAS 1 (5 th minute) | 2.94±0.21 | 3.82±0.25 | 0.010* |
| VAS 2 (2 nd hour) | 1.20±0.75 | 1.86±0.20 | 0.019* |
| Rescue analgesia need | 1 | 2 | 0.571 |
| Anxiety level ^b | 14.69 ± 0.17 | 16.24 ± 6.60 | 0.452 |

Mean ± standard deviation. *p<0.05, ^bTotal anxiety score according to the Beck Anxiety scale. VAS: Visual analog score

NSAIDs have some undesirable side effects on many body systems, especially the gastrointestinal system, as well as their proven analgesic effects, reducing platelet aggregation and prolonging the bleeding time (28).

Paracetamol is also another agent which can be administered intravenously, has a proven analgesic efficacy and less side effects compared to NSAIDs (26,29), hence it is another agent of choice in pain control after endodontic treatment. Cheung and Rodrigo (30) used a single oral dose of 40 mg tenoxicam and 1,000 mg paracetamol in 30 dental surgery cases and reported that both drugs provided similar postoperative analgesia. Similar to our results, it has been reported that when administered as IV, tenoxicam provides an effective analgesia at doses of 20 mg and 40 mg especially after oral surgeries (29). Likewise, Gunusen et al. (31) reported that IV tenoxicam reduced both postoperative pain and additional need of morphine compared to paracetamol in abdominal hysterectomy cases. However, unlike these studies, there are also studies that have found a superior postoperative efficiency with paracetamol (32). Hyllested et al. (32) argued that paracetamol is an appropriate alternative to NSAIDs, especially due to its low incidence of side effects, and that it should be a preferred option in high-risk patients. Khalili et al. (33) reported that there was no difference between paracetamol use alone and combined use of paracetamol with oxycam group NSAIDs especially in orthopedic operations. We are of the opinion that these different findings in analgesic efficacy comparison studies may be due to different surgery types.

In the present study, no significant side effects were observed due to the use of either paracetamol or tenoxicam. In the literature, there are different interpretations about side effects as well as increased analgesia efficacy regarding the use of both groups of drugs separately and in combination. Hyllested et al. (32) stated that combining paracetamol with NSAIDs may be appropriate due to the increased analgesic efficacy, but attention should be paid to the potential increase in side effects resulting from their combined use. The risk increases especially in long-term use without lowering the dose. Ong et al. (34) reported that the combination of long-acting NSAIDs such as paracetamol and tenoxicam theoretically has the disadvantage of pharmacokinetic incompatibility

because tenoxicam has a much longer elimination half-life than paracetamol. On the other hand, Merry et al. (35) stated that the combination of NSAID and paracetamol minimizes the need for rescue analgesia and the side effects caused by opioid use. It is known that there is a relationship between plasma paracetamol concentrations and analgesic efficacy. Attempting to continually maintain paracetamol plasma concentrations may cause the dose to be increased above the required threshold during postoperative follow-up, increasing the risk of hepatotoxicity.

The most important limitation of this study is the small sample size. Surgical, prosthetic and periodontological procedures, which may effect postoperative pain, were also performed in patients who underwent dental procedures under general anesthesia, often with endodontic treatments. As a result, the population of the study was limited due to the exclusion of these processes.

The incidence of post operative pain after RCT has been associated with various factors in the literature such as age, gender, pulpal and periradicular status, tooth type, preoperative pain, sinus tracts, and operational factors (36,37). For his reasons, many factors such as tooth type, pulp and periradicular status of the patient have been tried to be standardized in studies related to postoperative pain after canal treatment in the literature (13,14,36,37). However, as stated above, the most important limitation of this study is its small sample size. Therefore, due to the limited number of patients evaluated in this study, standardization of other factors had to be ignored. Therefore, this issue is another limitation of this study. Consequently, we think that the results of this study should be reconfirmed in larger patient populations with new studies.

Conclusion

As a result, IV tenoxicam provides more effective postoperative analgesia than IV paracetamol in the management of postoperative pain after RCTs performed in single visit under general anesthesia. In addition, since there is no difference between the two drugs in terms of rescue analgesia frequency and paracetamol has less side effects than NSAIDs, it makes IV paracetamol administration preferable in RCT treatments under general anesthesia.

Ethics

Ethics Committee Approval: This study was conducted with an approval from the Non-Invasive Clinical Research Ethics Committee (protocol no: 2020/75, date: 02.07.2020) of the Faculty of Medicine Aydın Adnan Menderes University.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.D.Ö., Ö.K., S.Y.Ö., P.A.O., Design: Ö.K., H.D.Ö., Supervision: Ö.K., H.D.Ö., Fundings: H.D.Ö., Ö.K., S.Y.Ö., P.A.O., Materials: H.D.Ö., P.A.O., Ö.K., Data Collection or Processing: Ö.K., Analysis or Interpretation: Ö.K., Literature Search: Ö.K., H.D.Ö., Writing: Ö.K., H.D.Ö., Critical Review: S.Y.Ö., P.A.O.

Conflict of Interest: No conflict of interest was declared by the authors.

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