Original Article / Özgün Araştırma

Retrospective Evaluation of the Effect of Tenoxicam and Paracetamol Applied as Intraoperative Analgesics During Orthognathic Surgery on Postoperative Pain

Ortognatik Cerrahi Sırasında İntraoperatif Analjezik Olarak Uygulanan Tenoksikam ve Parasetamolün Postoperatif Ağrı Üzerine Etkisinin Retrospektif Değerlendirilmesi

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Abstract

Objective: Postoperative pain caused by orthognathic surgery significantly affects patient comfort. Non-steroidal anti-inflammatory drugs, corticosteroids and opioid analgesics can be used to relieve postoperative pain. The aim of this study was to retrospectively evaluate the effect of tenoxicam and paracetamol administered intraoperatively during orthognathic surgery on postoperative pain.

Materials and Methods: The study was conducted with 63 files in accordance with the determined criteria. For postoperative pain control, patients were divided into two groups according to the types of analgesics administered. Patients who were administered tenoxicam 20 mg (35 patients) or paracetamol 10 mg/kg (28 patients) IV without extubating were included in the study. In the follow-ups in the postoperative period, the values at 0, 1, 3, 6, 12, 24, 36, and 48 h from the visual analogue scale (VAS) data, the presence of nausea and vomiting and the need for opioid analgesics were evaluated in the files recorded.

Results: There was no statistically significant difference in VAS values between the tenoxicam group and the paracetamol group in the postoperative follow-up. Nausea and vomiting were higher in the tenoxicam group than in the paracetamol group, but no statistically significant difference was observed. Also found no significant difference in rescue opioid requirements.

Conclusion: When intraoperative tenoxicam administration and paracetamol administration were compared in patients undergoing orthognathic surgery, lower VAS scores were observed and analgesic efficacy was found to be sufficient in patients in the tenoxicam group, but no statistically significant difference was found. Similarly, statistically close results were found between the presence of nausea and vomiting and the need for rescue opioids.

Keywords
Pain, orthognathic surgery, analgesia

Anahtar Kelimeler
Ağrı, ortognatik cerrahi, analjezi

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Öz

Amaç: Ortognatik cerrahi ile oluşan postoperatif ağrı hasta konforunu önemli ölçüde etkilemektedir. Postoperatif ağrının giderilmesi amacıyla non-steroid antienflamatuvar ilaçlar, kortikosteroidler ve opioid analjezikler kullanılabilmektedir. Bu çalışmanın amacı, ortognatik cerrahi sırasında intraoperatif olarak uygulanan tenoksikam ve parasetamolün ağrı üzerine etkisini retrospektif olarak değerlendirmektir.

Gereç ve Yöntemler: Belirlenen kriterlere uygun 63 dosya verisi ile çalışma gerçekleştirildi. Postoperatif ağrı kontrolü için, uygulanan analjezik türlerine göre hastalar iki gruba ayrıldı. Ekstübe edilmeden IV olarak tenoksikam 20 mg (35 hasta) veya parasetamol 10 mg/kg (28 hasta) uygulanan hastalar çalışmaya dahil edildi. Postoperatif dönemdeki saatlik takiplerde vizüel analog skalası (VAS) verilerinden 0, 1, 3, 6, 12, 24, 36 ve 48. saatteki değerler ile bulantı kusma varlığı ve opioid analjezik ihtiyacı kaydedilen dosyalardaki veriler değerlendirildi.

Bulgular: Tenoksikam grubu ve parasetamol grubu arasında postoperatif saatlik takiplerde VAS değerleri arasında istatistiksel olarak anlamlı fark bulunmadı. Tenoksikam grubunda bulantı ve kusma parasetamol grubundan daha yüksek görülürken istatistiksel olarak anlamlı bir fark gözlenmedi. Ek opioid gereksinimlerinde de tenoksikam grubu ile parasetamol grubu arasında anlamlı bir fark bulunamadı.

Sonuç: Ortognatik cerrahi geçiren hastalarda intraoperatif tenoksikam uygulaması ile parasetamol uygulaması karşılaştırıldığında, tenoksikam grubu hastalarında daha düşük VAS skorlarının gözlendiği ve analjezik etkinliğin yeterli olduğu tespit edilmiş, ancak istatiksel olarak anlamlı bir fark bulunamamıştır. Benzer şekilde bulantı kusma varlığı ile ek opioid gereksinimi arasında da istatiksel olarak yakın sonuçlar edildi.

Introduction

Orthognathic surgery is a treatment method that includes invasive, major operations that are frequently applied to repair maxillofacial deformities. Pain, edema, and loss of function, which are symptoms of widespread inflammation, may occur in the postoperative period as a result of tissue damage in orthognathic surgery (1). Postoperative pain after orthognathic surgery significantly affects patient comfort. Therefore, good management of the inflammatory process is very important.

Intraoperative analgesia, one of the preventive analgesia methods, is a comprehensive analgesia method aiming to control the development of central sensitization in the postoperative period. It is a practice that adopts the conventional perioperative strategy for anticipated physiological pain.

Tenoxicam, an oxicam derivative among non-steroidal anti-inflammatory drugs (NSAIDs), can be used once a day with its 100% bioavailability, approximately 99% blood protein binding, adequate penetration into synovial fluid, low systemic clearance, and long elimination half-life. Therefore, it can be used as an intraoperative analgesic and as the preferred analgesic in the treatment of postoperative pain (2).

Paracetamol (acetaminophen) is a para-aminophenol derivative drug with antipyretic analgesic properties. Unlike tenoxicam, it has no antithrombotic activity and its anti-inflammatory activity is negligible. The therapeutic effect of acetaminophen begins quickly, is short-lived, and does not prolong bleeding time, as it does not affect platelet function. It has no potential toxic effects on the cardiovascular, respiratory, and gastrointestinal systems (3).

The main purpose of this study is to evaluate the efficacy of tenoxicam and paracetamol intraoperatively in orthognathic surgery for postoperative pain control. Also, secondarily, it is aimed to evaluate the effect of these drugs on nausea and vomiting, as well as the need for additional analgesia during the postoperative period.

Materials and Methods

In this study; The aim was to retrospectively evaluate the patients who underwent orthognathic surgery. Our study was analysed by the Aydın Adnan Menderes University Faculty of Dentistry Clinical Research Ethics Committee with protocol number 2020/11 (date: 13.01.2021).

Inclusion criteria for the study:

- Le Fort 1, patients undergoing bilateral sagittal split osteotomy (BSSO) and bimaxillary surgery,
- Patients undergoing routine anesthesia protocol,
- Patients with The American Society of Anesthesiology (ASA) I-II group were included in the study.

The exclusion criteria for the study were as follows:

- Patients with ASA III and above, hepatic or renal dysfunction
- Patients who use long-term NSAIDs or opioid-derived drugs and have a history of allergic reactions to drugs,
- Patients with symptoms of pain, swelling, inflammation in the head and neck region before the operation,
- Pregnant and lactating patients,
- Patients with missing file data were not included in the study.

Data Recording

Demographic Data and Surgical Characteristics

Age, gender, weight, and ASA data of the patients were noted. Surgery time, type of surgery (single or double chin surgery), and demographic data were recorded as surgical characteristics.

Type of Analgesic Used

Patients using tenoxicam in the intraoperative period were enrolled in the tenoxicam group, and patients using paracetamol were enrolled in the paracetamol group.

Evaluation of Opioid Requirement and Presence of Nausea and Vomiting

The presence or absence of need for opioid analgesia in the postoperative period and the presence or absence of nausea and vomiting in addition to the amount of opioids used were recorded.

Measuring the Level of Pain

Visual analogue scale (VAS), a visual technique, was used for pain level measurement. The VAS score was accepted as 0 in the preoperative period. All individuals whose post-surgical pain levels were included in the study were told that on the pain scale arranged in the form of a 10 cm horizontal marker on the prepared forms, they stated that there was no pain at the "zero" level and the most severe pain at the "10" level. The values recorded at the 0^{th}, 1^{st}, 3^{rd}, 6^{th}, 12^{th}, 24^{th}, 36^{th}, and 48^{th} hours of the postoperative routine measurements for each individual were used in our study.

Anesthesia Protocol and Surgical Method

Our routine general anesthesia protocol was applied to all included patients. After the patients were taken to the operating room, an vascular access was opened and anesthesia induction was performed with 1 µg/kg fentanyl, 2 mg/kg propofol, and 0.8 mg/kg-1 rocuronium. During the maintenance of anesthesia, all patients were administered sevoflurane in a volume of 1-2% in 50% O_2 and 50% N_2O. Electrocardiography, non-invasive blood pressure, oxygen saturation, and end-tidal carbon dioxide monitoring were performed for each patient. Nasal intubation was performed with an endotracheal tube in all patients. The patients were taken to the recovery room after extubation following the end of the surgery. All hemodynamic parameters, vital signs, and early postoperative complications of each patient were recorded.

Bilateral buccal, inferior alveolar, and lingual nerve block anesthesia in the mandible, bilateral buccal local infiltrative and posterior superior alveolar block anesthesia in the maxilla were performed in all patients with 2% articaine 80 mg+1/200,000 epinephrine.

Le fort 1 osteotomy was performed with the Bell (4) method. BSSO was performed according to the Hunsuck (5) modification. For postoperative pain control, patients were administered intraoperative tenoxicam and paracetamol.

In the hourly follow-ups in the postoperative period, the values at 0^{th}, 1^{st}, 3^{rd}, 6^{th}, 12^{th}, 24^{th}, 36^{th}, and 48^{th} hours from the VAS data in the patient file, the presence of nausea and vomiting and the need for opioid analgesics were recorded.

Statistical Analysis

Data analysis was performed using SPSS (version 18.0, SPSS Inc., Chicago, Illinois, USA). The assumption of normal distribution for quantitative variables was tested with the Kolmogorov-Smirnov test. Correlations between categorical variables were analysed by the chi-square test. Comparisons between groups were analysed by independent sample t-test or Mann-Whitney U test. Descriptive statistics were presented as mean with standard deviation, number and percentage, quantitative and categorical variables, respectively. A p-value below 0.05 was considered significant for all comparisons.

Results

A total of 63 patients, 36 female, and 27 male, were included in the study. The patients were divided into two main groups according to the analgesia used in the file data. The group in which tenoxicam was used as intraoperative analgesia in the orthognathic surgery was called the "tenoxicam group" and the group in which paracetamol was used was called the "paracetamol group".

In Table 1, the demographic data and the mean and p-values of the surgical characteristics in our study are summarized. There was no statistically significant difference between the tenoxicam group and the paracetamol group in terms of age, gender, body weight, and ASA classification ($p>0.05$).

The VAS values of the tenoxicam and paracetamol groups in the hourly follow-up postoperatively are shown in Figure 1. Very close values were recorded in

Table 1. Demographic data and clinical characteristics of the tenoxicam group and paracetamol group

	Tenoxicam group n=35	Paracetamol group n=28	p-value
Age (years)	23.60±9.72	21.53±2.88	0.552
Body weight (kg)	68.97±17.93	64.67±11.15	0.663
Gender Female Male	 16 (45.7%) 19 (54.3%)	 20 (71.4%) 8 (28.6%)	0.073
Duration of anesthesia (min.)	316.42±96.01	325.35±82.61	0.819
Type of surgery			0.112
Single chin	11 (85.7%)	4 (14.29%)	
Double chin	24 (14.3%)	24 (85.71%)	
ASA			0.819
I	30	24	
II	5	4	
Total	35	28	

P<0.05 value was considered statistically significant. ASA: The American Society of Anesthesiology, Min: Minute

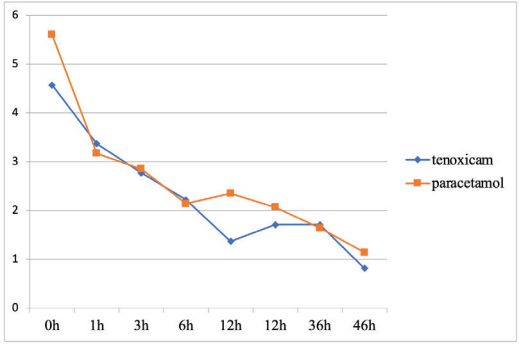

Figure 1. Mean VAS values of the groups in the postoperative period
VAS: Visual analog scale

the tenoxicam group and paracetamol group on average at the 6th hour postoperatively. However, the VAS value at the 12th hour followed in the paracetamol group was higher than in the tenoxicam group. The lower VAS score in the tenoxicam group at the postoperative 12th hour made us think that tenoxicam may be a longer-acting analgesic than paracetamol.

The variation of VAS values according to gender is summarized in Table 2. Except for the 3rd hour, mean VAS values were higher in females at every hour. In the 48 hours follow-up, the female gender gave statistically significant higher scores than the male gender (p<0.05).

According to the intraoperative analgesia preference, the VAS pain values recorded at the 0th hour did not show a statistically significant difference between the tenoxicam and paracetamol groups (p>0.05) (Table 3). However, statistical findings suggest that the results may be more significant in favor of tenoxicam when the sample size is larger. There was no statistically significant difference in postoperative VAS values between the tenoxicam group and the paracetamol group in the other hours followed.

The statistical data of nausea and vomiting and additional opioid requirements of the tenoxicam group and paracetamol group are shown in Table 4. Nausea and vomiting were more common in the

Table 2. Postoperative VAS values by gender

	Female	Male	p-value
VAS0	5.16±2.24	4.85±2.19	0.774
VAS1	3.38±1.94	3.14±1.61	0.927
VAS3	2.74±1.97	2.88±1.73	0.649
VAS6	2.27±1.70	2.07±1.49	0.690
VAS12	2.20±2.24	1.29±1.85	0.082
VAS24	2.23±1.81	1.40±1.75	0.093
VAS36	2.00±1.96	1.46±1.72	0.281
VAS48	1.31±1.22	0.53±0.94	0.013

P<0.05 value was considered statistically significant. VAS: Visual analogue scale

Table 3. Comparison of VAS means over time and between groups

	Tenoxicam group	Paracetamol group	p-value
VAS0	4.57±2.40	5.60±1.83	0.069
VAS1	3.37±1.97	3.17±1.58	0.955
VAS3	2.77±1.92	2.85±1.77	0.800
VAS6	2.22±1.62	2.14±1.60	0.843
VAS12	1.37±1.62	2.35±2.49	0.119
VAS24	1.71±1.74	2.07±1.86	0.422
VAS36	1.71±1.84	1.64±1.74	0.891
VAS48	0.82±0.98	1.14±1.26	0.388
P	0.023	0.001	

P-value <0.05 was considered statistically significant. VAS: Visual analog scale

Table 4. Nausea, vomiting, and need for additional opioids in the tenoxicam group and paracetamol group

	Tenoxicam group	Paracetamol group	p-value
PONV (n, %) Existent Non-existent	 23 (65.7%) 12 (34.3)	 14 (50%) 14(50%)	0.303
Additional opioid needs (n, %) Existent Non-existent	30 (85.7%) 5 (14.3%)	19 (64.3%) 9 (35.7%)	0.129
PONV: Postoperative nausea and vomiting			

tenoxicam group than in the paracetamol group, but no statistically significant difference was observed. No statistically significant difference was found in additional opioid requirements (p>0.05).

Discussion

Bimaxillary surgery is a well-executed orthognathic surgical procedure that includes BSSO and Le Fort I osteotomy. It has been reported in the literature that young adult women undergoing double chin surgery have higher pain scores following surgery. Mobini et al. (6) reported in their study conducted in 2018 that women felt more pain after bimaxillary orthognathic surgery compared to men. In our study, similar to these literatures, regardless of the groups, it was found that women felt more pain than men.

Although various accepted or approved analgesia protocols are used to keep pain under control after orthognathic surgery; Researchers could not reach a consensus regarding the ideal method of administering analgesia. Many drugs and methods such as steroids, patient-controlled analgesia method, opioids, NSAIDs, combination of NSAIDs and local anesthetics, antiemetics, antiepileptics, nerve blocks are used in order to provide postoperative analgesia in double maxillofacial surgery (7-10).

Tenoxicam is an effective agent that has an intravenous (IV) form of NSAIDs and has a longer duration of action than lornoxicam, and is frequently used in mild to moderate pain. The recommended daily dosing regimen for tenoxicam is 20-40 mg. Akca et al. (11) reported in their study that administration of IV 20 mg tenoxicam in 80 patients undergoing inguinal hernia repair and laparoscopic cholecystectomy is a simple, safe, and highly effective method for postoperative pain control. Vandermeulen et al., (12) in a multicenter, placebo-controlled study on 258 patients undergoing abdominal or orthopedic surgery, showed that IV administration of 40 mg tenoxicam was effective in postoperative pain control and reduced the use of postoperative morphine. In the light of similar studies, IV 20 mg tenoxicam was administered as a single dose in our study, and this application was found to be sufficient to provide effective analgesia in the early postoperative period.

Acetaminophen (para-aminophenol derivatives) is evaluated outside of NSAIDs because it does not have anti-inflammatory and antiplatelet activities. Although other central mechanisms of action have a role, it shows analgesic and antipyretic activity by inhibiting prostaglandin synthesis in the central nervous system. However, in peripheral tissues, acetaminophen is a weak inhibitor of cyclooxygenase (10 times less potency than acetylsalicylic acid) and therefore does not significantly affect prostaglandin synthesis, which plays a role in the development of inflammation. The weaker anti-inflammatory activity on peripheral inflammation compared to NSAIDs can be explained in this way (13). In a study by Wininger et al. (14) on 224 patients undergoing abdominal laparoscopic surgery, repeated administration of 2 separate dose regimens of IV paracetamol (1000 mg and 650 mg) was associated with statistically significant analgesic efficacy compared to placebo and after abdominal laparoscopic surgery, it was concluded that this drug is also effective in adults. Tuzuner Oncul et al. (15) in a study on buried third molars; showed that paracetamol provides postoperative analgesic efficacy similar to NSAIDs and is an appropriate analgesic for patient satisfaction. In our study, 10 mg/mL paracetamol was used intraoperatively; It was found to be effective as an analgesic in hourly VAS measurements and additional opioid requirement, consistent with other studies.

No study was found comparing tenoxicam and paracetamol for the control of postoperative pain in orthognathic surgery cases in the database searches. However, there are studies comparing the efficacy of tenoxicam and paracetamol in different applications. In a study conducted by Gunusen et al. (16) in patients with postoperative pain after elective abdominal hysterectomy, 120 patients who received 1 g paracetamol, 20 mg tenoxicam or placebo at the

end of the operation were randomly divided into three groups and all patients were administered postoperative principal component analysis with morphine. As a result of the study, it was found that a single dose of 20 mg tenoxicam after abdominal hysterectomy provided more effective analgesia and reduced total morphine consumption compared to paracetamol and placebo. In addition; side effects except nausea were found to be similar (16). In the study of Cheung and Rodrigo (17) in which they compared the efficacy of tenoxicam for pain relief with paracetamol after third molar surgery, it was observed that both drugs were effective as analgesics after third molar surgery and tenoxicam had comparable efficacy to paracetamol. In our study, the VAS data of the patients at 0^{th}, 1^{st}, 3^{rd}, 6^{th}, 12^{th}, 24^{th}, 36^{th}, and 48^{th} hours postoperatively were compared. It was determined that the VAS measurements of the tenoxicam group at the postoperative 0^{th} hour were less than the VAS measurements of the paracetamol group in the same periods. However, due to the small sample size, no statistically significant difference was found. In other time periods, VAS values were found to be similar in the two groups.

The most important factors affecting patient satisfaction in the postoperative period are nausea, vomiting, and inappropriate postoperative pain management. One of the common causes of high rates of nausea and vomiting is the use of opioid derivatives and opioid-like drugs such as tramadol (18,19). Huang et al. (20) compared intraoperative tenoxicam with placebo for the relief of postoperative pain after cesarean section. In this study, nausea and vomiting of patients were also evaluated compared to the placebo group, and they found that there was no difference. In our study, there was no statistically significant difference between the paracetamol group and the tenoxicam group in terms of postoperative nausea and vomiting, which was consistent with these studies.

One of the most important factors in avoiding the use of NSAIDs for postoperative analgesia is the concern that it will cause bleeding. During our study, we did not detect any side and toxic effects, hypotension, arrhythmia, cyanosis due to the drugs used in the intraoperative and postoperative period.

Conclusion

As a result, in patients undergoing orthognathic surgery; when intraoperative tenoxicam administration and paracetamol administration were compared, lower VAS scores were observed in tenoxicam group patients and analgesic efficacy was found to be sufficient. A single dose of intraoperative tenoxicam and paracetamol administration is an effective and safe method in the treatment of postoperative pain in patients undergoing orthognathic surgery. Various methods have been tried to reduce postoperative pain in these patients, and there is still no agreed-upon analgesia protocol. Future controlled prospective studies are needed to better evaluate the types, doses, and complications of analgesic agents, and to provide a better understanding of the results.

Ethics

Ethics Committee Approval: Our study was analysed by the Aydın Adnan Menderes University Faculty of Dentistry Clinical Research Ethics Committee with protocol number 2020/11 (date: 13.01.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Z.B.D., B.G., Ö.K., Consept: B.G., Design: B.G., Data Collection or Processing: Z.B.D., Analysis or Interpretation: Ö.K., Literature Search: Z.B.D., B.G., Ö.K., Writing: Z.B.D., B.G.

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