ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/dentalsci.2021-86763

Effects of Single-Dose Preemptive Intravenous Dexketoprofen Trometamol and Ibuprofen on Pain and Edema Control Following Third Molar Surgery: A Prospective, Randomized, Double-Blind and Clinical Study

Tek Doz Preemptif İntravenöz Deksketoprofen Trometamol ve İbuprofen'in Üçüncü Molar Cerrahisi Sonrası Ağrı ve Ödem Kontrolü Üzerine Etkileri: Prospektif, Randomize, Çift Kör ve Klinik Bir Çalışma

Suheyb BİLGE[a], Mustafa KARAKAYA[b], Ebru BAYDAN[a], Ahmet Emin DEMİRBAŞ[a]

[a]Department of Oral and Maxillofacial Surgery, Erciyes University Faculty of Dentistry, Kayseri, Türkiye
[b]Clinic of Oral and Maxillofacial Surgery, Sultanbeyli Oral and Dental Health Hospital, İstanbul, Türkiye

ABSTRACT Objective: This comparative study aims to investigate the single-dose preemptive effects of intravenous (IV) dexketoprofen trometamol, ibuprofen for pain and edema control in mandibular wisdom teeth surgery. **Material and Methods:** In this study, 75 patients were randomly divided into 3 groups. Group 1 received IV ibuprofen 60 min before surgery; Group 2 received IV dexketoprofen trometamol 60 min before surgery; Group 3 received IV placebo (100 cc saline) 60 min before surgery. The pain and facial swelling were evaluated. Postoperative pain was recorded with a Visual Analog Scale (VAS) during 24 h. The total recovery acetaminophen intake dose was recorded in the first 24 h. Also, a 3D surface imaging device was used in the evaluation of swelling. **Results:** There was no statistically significant difference in the pain between the ibuprofen and dexketoprofen groups. There was a statistically significant difference in the edema on the 2nd day (T1) between the ibuprofen and dexketoprofen group (p=0.010). On the 2nd day edema, the amount of edema observed in the ibuprofen group was recorded as the least. Postoperative edema and pain were higher in the placebo group than in the other groups (p<0.05). **Conclusion:** The findings obtained in this study suggest that the preemptive application of IV ibuprofen and dexketoprofen is effective in the control of edema and pain compared to the placebo group after third molar surgery.

Keywords: Pain management; facial pain; analgesic; preemptive analgesia; oral surgery

ÖZET Amaç: Bu karşılaştırmalı çalışma, mandibular gömülü yirmi yaş dişlerin cerrahi çekimlerinde intravenöz (IV) deksketoprofen trometamol ile IV ibuprofenin ağrı ve ödem kontrolünde preemptif kullanımlarının etkilerini araştırmayı amaçlamaktadır. **Gereç ve Yöntemler:** Bu çalışmada, 75 hasta rastgele olacak şekilde 3 gruba ayrıldı. Grup 1 ameliyattan 60 dakika önce IV ibuprofen aldı; Grup 2 ameliyattan 60 dakika önce IV deksketoprofen trometamol aldı; Grup 3, ameliyattan 60 dakika önce IV plasebo (100 cc salin) aldı. Ağrı ve yüzdeki şişlik değerlendirildi. Postoperatif ağrı 24 saat boyunca Vizüel Analog Skala (VAS) ile kaydedildi. İlk 24 saatlik dönemde toplam asetaminofen alım dozu kaydedildi. Ayrıca ödemin değerlendirilmesinde 3 boyutlu yüzey görüntüleme cihazı kullanıldı. **Bulgular:** İbuprofen ve deksketoprofen grupları arasında ağrı kontrolü açısından istatistiksel olarak anlamlı fark bulunamadı. Ödem kontrolünde ise operasyon sonrası 2. günde (T1) ibuprofen ve deksketoprofen grupları arasında istatistiksel olarak anlamlı fark tespit edildi (p=0,010). İkinci gün ödem kontrolünde ibuprofen grubunda gözlenen ödem miktarı en az olarak kaydedildi. Plasebo grubunda ise postoperatif ödem ve ağrı değerlerinin diğer gruplara göre daha yüksek olduğu tespit edildi (p<0,05). **Sonuç:** Bu çalışmada elde edilen bulgular, 3. molar cerrahisi sonrası plasebo grubuna kıyasla IV ibuprofen ve deksketoprofenin preemptif uygulanmasının ödem ve ağrı kontrolünde etkili olduğunu düşündürmektedir.

Anahtar Kelimeler: Ağrı yönetimi; yüz ağrısı; analjezi; önleyici analjezi; oral cerrahi

Correspondence: Suheyb BİLGE
Department of Oral and Maxillofacial Surgery, Erciyes University Faculty of Dentistry, Kayseri, Türkiye
E-mail: suheybbilge@erciyes.edu.tr

Peer review under responsibility of Turkiye Klinikleri Journal of Dental Sciences.

Received: 24 Oct 2021 ***Received in revised form:*** 06 Feb 2022 ***Accepted:*** 14 Feb 2022 ***Available online:*** 18 Feb 2022

Surgical extraction of wisdom teeth is a traumatic procedure that is frequently used in oral surgery. Some complications may be observed after surgery. Postoperative complications are pain, localized swelling and trismus.[1] Third molar surgical procedures may result in many inflammatory reactions.[2] This inflammatory process can be the source of pain and edema.[3]

Some pharmaceutical agents are preferred in pain control and generally include local anesthetics, opioids, and anti-inflammatory drugs with peripheral analgesic action are divided into steroidal and non-steroidal anti-inflammatory drugs (NSAIDs).[4] Steroids and NSAIDs act by inhibiting the same chain reactions and cyclooxygenase activity that degrade phospholipids released by cell membranes injured by surgical trauma and leading pro-inflammatory mediators production.[5] One of the accepted methods for postoperative pain and edema control is the preoperative administration of NSAIDs. Dexketoprofen trometamol and ibuprofen are among the commonly preferred drugs in preemptive pain control.[3,6] Preemptive analgesia provides pain control by preventing afferent stimulation in the area to be incised during the surgical procedure.[6,7]

The hypothesis of this study was to address the following question: Is the use of preemptive intravenous (IV) ibuprofen as effective as preemptive IV dexketoprofen trometamol in the control of pain and edema in surgical extractions of impacted wisdom teeth? In this sense, the hypothesis for this study was that individuals who receive preemptive analgesia with the use of ibuprofen (800 mg, IV) 60 min before the surgery present lower postoperative pain and edema in relation to individuals receiving IV dexketoprofen trometamol and placebo medication.

MATERIAL AND METHODS

Seventy-five patients, both male and female, attending the Department of Maxillofacial Surgery at Erciyes University for removal of impacted third molars, were enrolled in this study. This controlled clinical study was planned as a prospective, double-blind, single-center and randomized study. This study was planned as preemptive medication without any changes in the wisdom tooth extraction procedure and its follow-up. This study was approved by the Clinical Research Ethics Committee of the Erciyes University Faculty of Medicine of and all participants signed an informed consent agreement (date: November 21, 2018, no: 2018/601).

Before the surgery, all patients gave written and signed informed consent form for the surgical procedures and to participate in this research. The protocol was in compliance with the Helsinki Declaration.

A sample size of 20 patients per group was calculated to be necessary to detect a strong effect using Cohen's approach; an error of 0.05 and power 80% was defined to calculate the sample size.

This study included 75 voluntary patients who met the study criteria. They were divided randomly into equal groups using a random number generated by a computer (25 patients in each) with symptomatic, impacted lower third molars. The surgery for each study group was determined as Group 1 patients received 800 mg IV ibuprofen 60 min before surgery; Group 2 patients received an IV dexketoprofen trometamol; Group 3 patients received an IV placebo (100 cc saline) 60 min before surgery. The inclusion criteria in this study were being between 18-35 years old, having no systemic disease (American Society of Anesthesiologists 1 status), not having regular medication use, not having an allergy to the drugs used in this study. Pregnant or breastfeeding patients, patients allergic to NSAIDs, patients with systemic diseases such as diabetes and uncontrolled hypertension; and patients with extreme cowardice and anxiety, were excluded. According to the Winter Classification, fully bony impacted mandibular third molars were included in the study in a horizontal position.

After the surgical procedures, all patients recorded the intensity of pain felt over 24 hours on a 100 graduated Visual Analog Scale (VAS). Postoperative pain in the VAS was recorded at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 16, 20 and 24 hours after the surgical procedure. In addition, patients recorded their total acetaminophen intake in the first 24 hours.[8-10]

Many methods are used in the evaluation of postoperative edema. Among these methods, 3D imaging technique was preferred in this study. The amount of postoperative edema was measured using the 3dMD imaging system and 3dMD Vultus software (3dMD Face System; 3dMD, Atlanta, GA). Three-dimensional images were taken before the operation and on the 2nd and 7th days after surgery. The images of the patients were taken at maximum intercuspation when the lips were free and the eyes were open. To obtain standardization on 3-dimensional images, the bilaterally anatomic landmarks; tragion, cheilion, gonion and on the midline landmarks; stomion, menton and neck-throat point were determined, and the area between these points were calculated (Figure 1). The postoperative edema were measured three times by one blinded researcher (E.B.). For analysis, image recordings were taken before (T0), 2 days after (T1) (48 h) and 7 days after (T2) (168 h) surgery. In this program, linear and volumetric measurements can be made by aligning two different images on selected surfaces.[11]

All surgical procedures were performed by the same surgeon (S.B.) and assistant throughout the study. Neither the oral surgeon nor the patient was informed of the group assignment throughout the entire study process.

Following the protocol of preoperative antisepsis, local anesthesia was performed by blocking the inferior alveolar and lingual buccal nerves with a maximum of two doses of 2 mL articaine hydrochloride (40 mg) with epinephrine (1:200.000) using a dental injector. The surgery was performed following the classic technique; 10 min after anesthesia, a horizontal and sulcular incision was performed, and a mucoperiosteal flap was elevated. The bone covering the impacted third molar tooth was removed with the use of a surgical hand-piece and rotary instrument. During the operation, saline water was applied on a surgical drill with a second hand. After extraction of the teeth, the cavity was treated with curet-

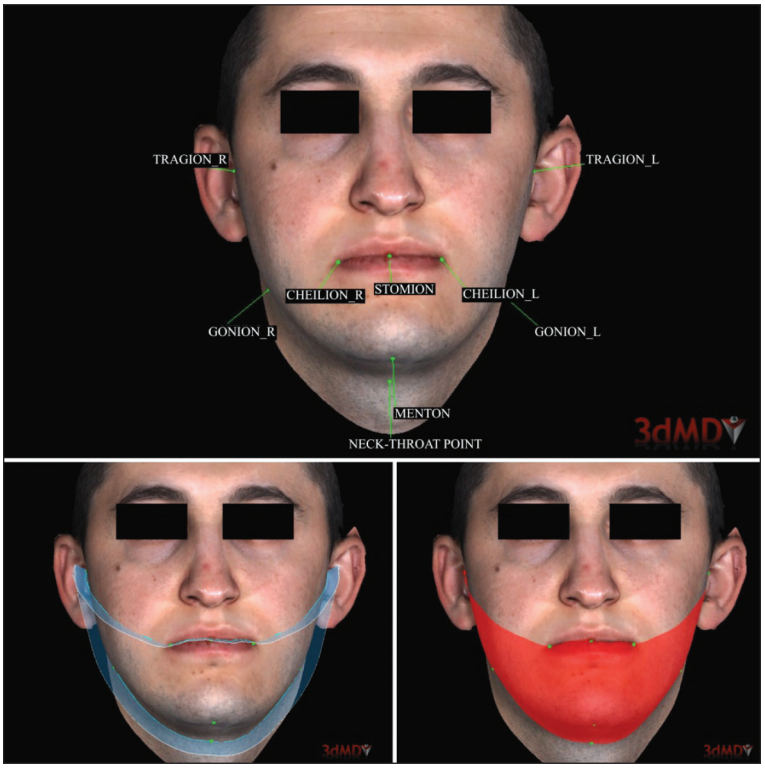

FIGURE 1: 3dMD device and selected area for swelling.

tage, irrigate with saline and sutured. The patient received the post-surgical assigned drug after sixty minutes. In addition, acetaminophen 500 mg was prescribed as a rescue medication for each patient, in case the study medication did not provide sufficient pain relief.

STATISTICAL ANALYSIS

A sample size of 20 patients per group was calculated to be necessary to detect a strong effect using Cohen's approach; an error of 0.05 and power 80% was defined to calculate the sample size.[6] The data normality was assessed using higtogram, q-q plots and Shapiro-Wilk's test. The variance homogeneity was examined using Levene test. To compare the differences among groups, either two-way analysis of variance (ANOVA) or Kruskal-Wallis tests were applied for quantitative data. Tukey, Siegel-Castellan and Bonferroni-adjusted z tests were used for multiple comparisons. Data values were expressed using mean±standard deviation, median (1^{st}-3^{rd} quartiles) or frequencies (percentages). Analyses were conducted using TURCOSA (Turcosa Analytics Ltd. Co., Türkiye, www.turcosa.com.tr). A p value less than 5% was considered as statistically significant.

RESULTS

This controlled clinical trial was performed between January 2019 and March 2020. A total of 72 patients, 41 female (56.9%), 31 male (43.1%) were included in this study. Parameters, such as the length of the surgical procedure and body-mass index were evaluated and considered to be homogeneous between three groups. Demographic data are presented in Table 1. No complications were observed during or after the operation; one patient was excluded from the study due to anxiety and excessive fear, and 2 patients were excluded because of not attending the follow-up appointments and the study protocol could not be completed (Figure 2).

TABLE 1: Demographic variables.

Demographic data	
Age (Mean±SD)	25.1±8.32
Sex distribution (Male/Female)	31/41
Winter position (Horizontal)	72
Number of adverse events	0
Complicated surgical procedures	0

SD: Standard deviation.

PAIN (VAS SCORE ANALYSIS)

The average 24-hour VAS values of the ibuprofen group and dexketoprofen group were 20.3% and 23.9%, respectively. The mean VAS values in both groups were statistically significantly lower than the placebo group ($p<0.05$). The mean VAS values of the placebo group (34.05%) were the highest. The analysis of the data is shown in Table 2 (Figure 3, Figure 4).

RESCUE ANALGESIC INTAKE DOSE

The average dose of acetaminophen intake for 24 hours in the ibuprofen group was 740 mg, while the average dose was 1,640 mg in the placebo group and 920 mg in the dexketoprofen group (Figure 5). The use of acetaminophen for 24 hours was significantly higher in the placebo group. It was observed that there was no statistically significant difference between the 24-hour average acetaminophen use in the ibuprofen and dexketoprofen groups ($p=0.58$). The recovery analgesic dose analysis is presented in Table 2.

POSTOPERATIVE EDEMA

When the in-group edema control was examined, it was observed that there was an increase in all groups on the 2^{nd} day and that on the 7^{th} day, the edema decreased. On the 2^{nd} day, it was observed that the highest increase was in the placebo group, while the least increase was observed in the ibuprofen group (Table 3). When in-group analysis was conducted, it was observed that the edema increase up to day 2 (T1) in the ibuprofen group was not statistically significant compared to day 0 (T0), and the increase in edema up to day 2 in the placebo and dexketoprofen group was statistically significant compared to day 0 (T0). It was observed that there was no statistically significant difference in all groups between the 7^{th} day (T2) and the 0^{th} day (T0) (Table 3).

In the analysis conducted between the groups, when the increase in edema on the 2^{nd} day was evaluated, it was seen that there was a statistically significant difference between the ibuprofen group and

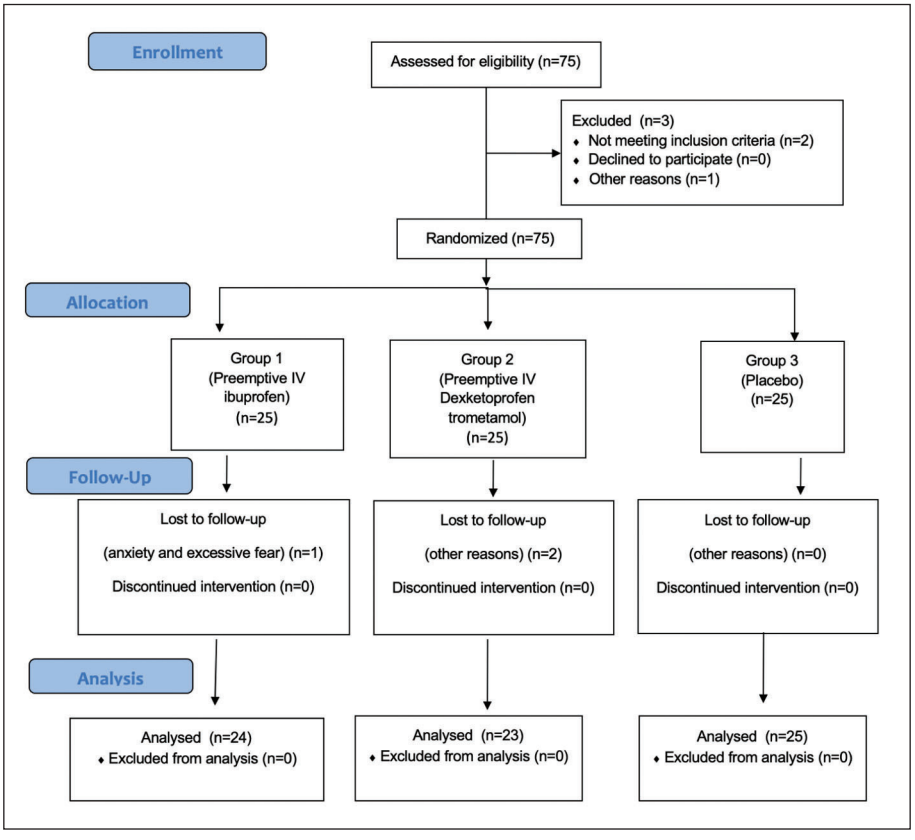

FIGURE 2: Consolidated standards of reporting trials flow chart of each stage of randomized controlled trial. IV: Intravenous.

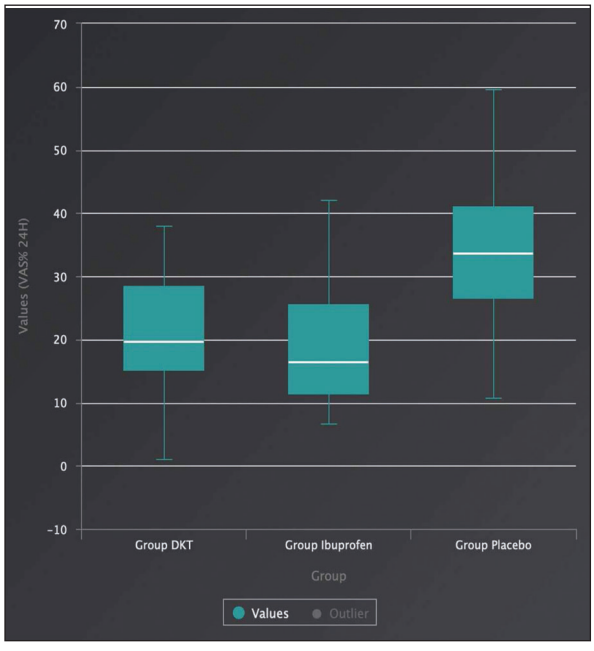

FIGURE 3: Analysis of the average VAS scores for the entire 24-hour period of obsertion. VAS: Visual Analog Scale; DKT: Dexketoprofen trometamol.

dexketoprofen group, the placebo group and the ibuprofen group and between the placebo group and the dexketoprofen group (Table 3).

DISCUSSION

As of today, the use of NSAIDs and corticosteroids in the control of postoperative pain and edema has become quite common.[6,12,13] Pre-operative application of these medications provides a reduction in pain, pain medication dosage and edema in the postoperative period.[6,14] Many studies have been conducted on the effects of preemptive use of NSAIDs on pain and edema control in surgical extraction of third molar teeth.[3,6,15] Studies have suggested that surgical trauma leads to an increase in nociceptive afferent conduction and stimulation threshold changes in both peripheral and central neurons. It is considered that postoperative pain can be controlled by pre-operative blocking of this mechanism.

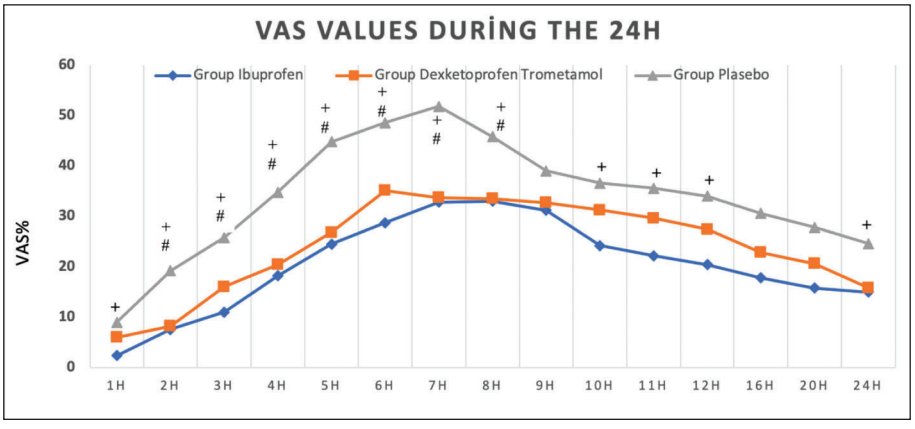

FIGURE 4: Pain intensity (mean VAS scores) during first 24 hours after surgery. +p<0.05 (Group Ibuprofen vs Group Placebo); #p<0.05 (Group Dexketoprofen Trometamol vs Group Placebo). VAS: Visual Analog Scale.

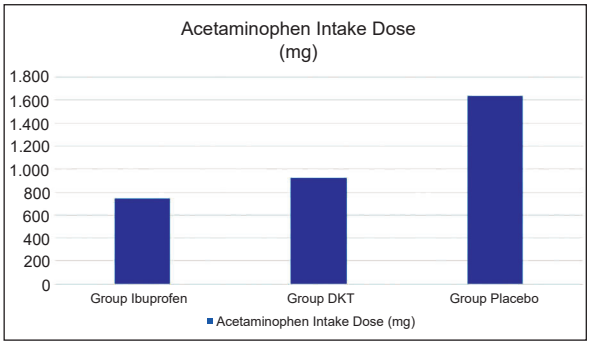

FIGURE 5: The mean of acetaminophen dose intake during the 24 h. DKT: Dexketoprofen trometamol.

Neuropeptides (histamine, bradykinin, prostaglandins, leukotrienes) released from damaged tissue after surgical trauma are effective in the development of pain.[9]

NSAIDs is alleged that preemptive analgesia has a role in preventing the formation of central hypersensitization by painful stimuli originating from the periphery.[6,13] There are many studies in the literature reporting that the preemptive use of NSAIDs in third molar surgery reduces pain from the postoperative 24-hour to the 7-day.[6,9,15,16] In this study, it was shown that the pre-operative use of IV dexketoprofen and

TABLE 2: Comparison of 24-hour follow up VAS averages and 24-hour rescue analgesic intake dose averages between groups.

	Differences VAS (%)	p value
Group DKT-Group Ibuprofen	3.65	0.36ϕ
Group Placebo-Group Ibuprofen	13.7	<0.001*ϕ
Group Placebo-Group DKT	10.1	0.013*ϕ
24-hour rescue analgesic intake dose averages between groups.		
	Differences dose average (mg)	**p value**
Group Placebo-Group Ibuprofen	900	<0.001*ϕ
Group Placebo-Group DKT	720	<0.001*ϕ
Group DKT-Group Ibuprofen	180	0.58ϕ
24-hour rescue analgesic intake dose averages (mg) and 24-hour VAS (%) averages values.		
	Dose (mg) Mean±SD	VAS (%) Mean±SD
Group Ibuprofen	740±104.5	20.3±2.3
Group DKT	920±128.06	23.9±3.5
Group Placebo	1,640±148.6	34.05±2.3

ϕOne-Way ANOVA; *p<0.05; Values are expressed as, mean±SD or median (1st-3rd quartiles); VAS: Visual Analogue Scale; DKT: Dexketoprofen trometamol; SD: Standard deviation.

TABLE 3: Comparison of post-op edema of between the groups.

	Groups			Test statistics†	
	Ibuprofen Mean±SD	DKT Mean±SD	Placebo Mean±SD	F value	p value
Day 0 (T0)	44.4±3.4^{X}	44.1±3.1^{X}	46.4±5.4^{X}	1.932	0.152
Day 2 (T1) (48 h)	46.2±3.1^{aY}	49.4±4.2^{abY}	51.9±6.1^{bY}	9.401	<0.001
Day 7 (T2) (168 h)	44.7±3.3^{X}	44.8±3.4^{Z}	46.8±5.4^{Z}	1.907	0.156
Test statistics¥	F=4.812; p=0.011	F=41.275; p<0.001	F=50.136; p<0.001		
Model summary&					
Group effect: F=3.940; p=0.024 **Day effect:** F=81.085; p<0.001 **Group*Day Interaction effect:** F=6.441; p<0.001					

&General linear mixed model (One of the factors in factorial order is repeated analysis of variance) with interaction; †General linear mixed model (multiple comparisons by group) Bonferroni-Dunn test; ¥General linear mixed model (multiple comparisons on time basis) Bonferroni-Dunn test; ^{a} and ^{b}Different superscripts indicate that the groups were significantly different in day 2; $^{X, Y}$ and ^{Z} Different superscripts indicate that the days were significantly different in each groups; DKT: Dexketoprofen trometamol; SD: Standard deviation.

ibuprofen after third molar tooth extraction had positive contributions to analgesia in the postoperative 24-hour and reduced the amount of rescuer-analgesic intake and edema in the postoperative 24-hour.

In the literature, there are studies showing that ibuprofen and dexketoprofen are effective in preemptive analgesia and edema control.[3,6,17-19] Esparza-Villalpando et al. reported in their study that the preemptive use of dexketoprofen in the impacted third molar surgery was effective in pain control in the postoperative 8-hour.[19] They stated that the use of pre-operative dexketoprofen in surgical extraction of wisdom teeth was effective in pain control in the postoperative 12-hour. In this study, it was concluded that the use of preemptive dexketoprofen was effective compared to the placebo group in the control of pain and swelling after surgical extraction of the third molar teeth in the postoperative 24-hour ($p<0.05$). Aznar-Arasa et al. reported that the study on the effects of ibuprofen on edema in embedded third molar surgery when administered preemptively or postoperatively, and they stated that there was no difference in pain and edema control between pre- and post-procedure use.[20] However, they did not create a placebo group in their study. Morse et al. stated in their study that ibuprofen is effective in pain control after the extraction of wisdom teeth.[21] Viswanath et al. also reported in their study on ibuprofen that IV ibuprofen was effective in the postoperative 24-hour.[10] In this study, IV ibuprofen was effective compared to the placebo group in the control of pain and edema after the third molar surgery ($p<0.05$) (Figure 4). Furthermore, the intake dose of painkillers after the procedure was significantly lower than the placebo group in both groups ($p<0.05$). In addition, a positive, moderate and statistically significant correlation was found between the average of the 24-hour painkiller intake dose and the mean values of the VAS percentages ($r=0.4336$, $p<0.001$).

It has been observed that studies in the literature regarding the comparison of the 2 drugs are limited. In this study, the effectiveness of the two drugs in reducing pain and swelling in the postoperative period was compared, and the amount of VAS and swelling was lower in the ibuprofen group compared to the dexketoprofen group, also swelling difference was statistically significant ($p=0.010$).

Edema is a very common condition after the surgery of wisdom teeth. Many methods, such as thermography method, three-dimensional optical scanners, magnetic resonance imaging, ultrasonography, photographic methods, facial arch, measurement of determined topographic points and VAS, are used to evaluate postoperative edema increase. With the developing technology, the swelling level that occurs after surgical interventions can be determined numerically using computer systems. Alan et al. evaluated the effects of low-dose laser therapy on edema and pain after the embedded third molar tooth and measured the amount of edema volumetrically using computer-aided 3D imaging (3dMD).[11] In this study, a similar method was used to evaluate the level of edema and the photographic method was used.

CONCLUSION

In consequence, the results of this study suggest that the preemptive application of IV ibuprofen and dexketoprofen after surgical extraction of third molar teeth is effective in the control of edema and pain compared to the placebo group and reduced the need for painkillers in the 24-hour. In addition, the results of this study showed that IV ibuprofen is more effective than IV dexketoprofen in edema control. IV ibuprofen and dexketoprofen applied before the procedure may contribute to reducing pain and edema in the surgery of the third molar teeth.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Suheyb Bilge, Mustafa Karakaya, Ahmet Emin Demirbaş;* ***Design:*** *Suheyb Bilge, Mustafa Karakaya, Ahmet Emin Demirbaş;* ***Control/Supervision:*** *Suheyb Bilge, Mustafa Karakaya, Ahmet Emin Demirbaş, Ebru Baydan;* ***Data Collection and/or Processing:*** *Suheyb Bilge, Mustafa Karakaya, Ahmet Emin Demirbaş, Ebru Baydan;* ***Analysis and/or Interpretation:*** *Suheyb Bilge, Mustafa Karakaya, Ahmet Emin Demirbaş, Ebru Baydan;* ***Literature Review:*** *Suheyb Bilge, Mustafa Karakaya, Ahmet Emin Demirbaş, Ebru Baydan;* ***Writing the Article:*** *Suheyb Bilge, Mustafa Karakaya, Ahmet Emin Demirbaş, Ebru Baydan;* ***Critical Review:*** *Suheyb Bilge, Mustafa Karakaya, Ahmet Emin Demirbaş, Ebru Baydan;* ***References and Fundings:*** *Suheyb Bilge, Ahmet Emin Demirbaş, Ebru Baydan;* ***Materials:*** *Suheyb Bilge, Mustafa Karakaya, Ahmet Emin Demirbaş, Ebru Baydan.*

REFERENCES

1. Salmen FS, Oliveira MR, Gabrielli MAC, Piveta ACG, Pereira-Filho VA, Gabriell MFR. Third molar extractions: a retrospective study of 1178 cases. RGO-Revista Gaúcha Odontol. 2016;64:250-5. [Crossref]
2. Amin MM, Laskin DM. Prophylactic use of indomethacin for prevention of postsurgical complications after removal of impacted third molars. Oral Surg Oral Med Oral Pathol. 1983;55(5):448-51. [Crossref] [PubMed]
3. Sánchez-Pérez A, Mu-oz-Pe-alver J, Moya-Villaescusa MJ, Sánchez-Matás C. Effects of the preoperative administration of dexketoprofen trometamol on pain and swelling after implant surgery: a randomized, double-blind controlled trial. J Oral Implantol. 2018;44(2):122-9. [Crossref] [PubMed]
4. Lima TC, Bagordakis E, Falci SGM, Dos Santos CRR, Pinheiro MLP. Pre-emptive effect of dexamethasone and diclofenac sodium associated with codeine on pain, swelling, and trismus after third molar surgery: a split-mouth, randomized, triple-blind, controlled clinical trial. J Oral Maxillofac Surg. 2018;76(1):60-6. [Crossref] [PubMed]
5. Kadur SN, Ahmed F, Prohit A, Khandelwal M, Mistry T. The effect of intravenous dexamethasone on postoperative pain, nausea and vomiting after intrathecal pethidine and bupivacaine in lower limb orthopedic surgery. Anaesthesia, Pain Intensive Care. 2015;19(3):254-9. [Link]
6. Demirbas AE, Karakaya M, Bilge S, Canpolat DG, Kütük N, Alkan A. Does Single-dose preemptive intravenous ibuprofen reduce postoperative pain after third molar surgery? A prospective, randomized, double-blind clinical study. J Oral Maxillofac Surg. 2019;77(10):1990-7. [Crossref] [PubMed]
7. Naghipour A, Esmaeelinejad M, Dehnad SV, Shahi A, Jarrahi A. Comparison of lidocaine with articaine buccal injection in reducing complications following impacted mandibular third molar surgery: a split-mouth randomized clinical trial. J Dent Anesth Pain Med. 2020;20(4):213-21. [Crossref] [PubMed] [PMC]
8. Yamaguchi A, Sano K. Effectiveness of preemptive analgesia on postoperative pain following third molar surgery: review of literatures. Jpn Dent Sci Rev. 2013;49(4):131-8. [Crossref]
9. Kano K, Kawamura K, Miyake T. Effects of preemptive analgesia with intravenous acetaminophen on postoperative pain relief in patients undergoing third molar surgery: a prospective, single-blind, randomized controlled trial. Med Oral Patol Oral Cir Bucal. 2021;26(1):e64-e70. [Crossref] [PubMed] [PMC]
10. Viswanath A, Oreadi D, Finkelman M, Klein G, Papageorge M. Does preemptive administration of intravenous ibuprofen (caldolor) or intravenous acetaminophen (Ofirmev) Reduce postoperative pain and subsequent narcotic consumption after third molar surgery? J Oral Maxillofac Surg. 2019 ;77(2):262-70. [Crossref] [PubMed]
11. Alan H, Yolcu Ü, Koparal M, Özgür C, Öztürk SA, Malkoç S. Evaluation of the effects of the low-level laser therapy on swelling, pain, and trismus after removal of impacted lower third molar. Head Face Med. 2016;12(1):25. [Crossref] [PubMed] [PMC]
12. Ramires GAD, de Souza Santos AM, Momesso GAC, Polo TOB, Silva WPP, Barbosa S, et al. Combination of etodolac and dexamethasone improves preemptive analgesia in third molar surgery: a randomized study. Clin Oral Investig. 2021;25(4):2297-305. [Crossref] [PubMed]
13. Shah R, Mahajan A, Shah N, Dadhania AP. Preemptive analgesia in third molar impaction surgery. Natl J Maxillofac Surg. 2012;3(2):144-7. [Crossref] [PubMed] [PMC]

14. Srivastava AK, Singh SK, Kumar M, Srivastava A, Pathak PK. Comparative study for effectiveness of preemptive analgesia on postoperative pain and swelling following gingivectomy. IP Int J Periodontol Implantol. 2020;5(1):25-8. [Crossref]
15. Kale SG, Shetty A, Moin A, Archana TS, Kumar P, Bagga V. Comparative evaluation of preemptive analgesia of dextromethorphan and ibuprofen in third molar surgeries. Ann Maxillofac Surg. 2020;10(2):312-9. [Crossref] [PubMed] [PMC]
16. Momesso GAC, Lemos CAA, de Lima VN, Delanora LA, Santiago-Júnior JF, Faverani LP, et al. Is the combination of corticosteroids plus NSAIDs improve the preemptive analgesia after third molars surgery? A systematic review and meta-analysis. Res Soc Dev. 2020;9:e968997979. [Crossref]
17. Küpeli İ, Gülnahar Y. Impact of pre-emptive intravenous ibuprofen on perioperative analgesia in patients undergoing third molar extraction: a randomised controlled study. Turk J Anaesthesiol Reanim. 2019;47(6):480-4. [Crossref] [PubMed] [PMC]
18. Gülnahar Y, Kupeli I. Effect of preemptive intravenous ibuprofen on postoperative edema and trismus in third molar tooth extraction: A randomized controlled study. J Dent Anesth Pain Med. 2018;18(3):161-7. [Crossref] [PubMed] [PMC]
19. Esparza-Villalpando V, Chavarria-Bola-os D, Gordillo-Moscoso A, Masuoka-Ito D, Martinez-Rider R, Isiordia-Espinoza M, et al. Comparison of the analgesic efficacy of preoperative/postoperative oral dexketoprofen trometamol in third molar surgery: a randomized clinical trial. J Craniomaxillofac Surg. 2016;44(9):1350-5. [Crossref] [PubMed]
20. Aznar-Arasa L, Harutunian K, Figueiredo R, Valmaseda-Castellón E, Gay-Escoda C. Effect of preoperative ibuprofen on pain and swelling after lower third molar removal: a randomized controlled trial. Int J Oral Maxillofac Surg. 2012;41(8):1005-9. [Crossref] [PubMed]
21. Morse Z, Tump A, Kevelham E. Ibuprofen as a pre-emptive analgesic is as effective as rofecoxib for mandibular third molar surgery. Odontology. 2006;94(1):59-63. [Crossref] [PubMed]