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A comparison of the effects of methylprednisolone and tenoxicam on pain, edema, and trismus after impacted lower third molar extraction

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Background: The aim of the present study was to compare the effects of preemptive intravenous tenoxicam and methylprednisolone administrations on extraction of impacted third molars.





Material/Methods: This was a placebo-controlled, randomized, double-blind, clinical trial. A total of 60 adult patients ages 18–40 years with the complaints of impacted third molar teeth were included in the study.

Results: The postoperative swelling ratios ($p < 0.05$) and pain scores ($p < 0.05$) were significantly better in both study groups than in the control group and there was no statistically significant difference between methylprednisolone and tenoxicam groups with regards to the edema and pain relief.

Conclusions: Preoperative administration of 80 mg methylprednisolone achieves better control of trismus than tenoxicam without any significant differences in edema and pain control in impacted third molar teeth extraction.

MeSH Keywords: **Tenoxicam • Anti-Inflammatory Agents, Non-Steroidal • Methylprednisolone – therapeutic use • Trismus • Tooth, Impacted**

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Background

During the surgical removal of impacted lower third molar teeth, since the region is constricted and the visibility is insufficient and the position and bony structure of the teeth may be rigid, the patient is affected by trauma causing postoperative problems such as pain, edema, decreased function, and trismus. These challenges cause problems for surgeons and patients since they disturb the aesthetics and function. Moreover, they may affect the activities of daily living and may result in a severe labor force loss [1,2]. To prevent all these complications, studies have been investigated use of various drugs and surgical methods [3,4].

Nowadays, the most commonly used drugs for the prevention of inflammation after extraction of impacted lower third molar teeth are non-steroidal anti-inflammatory drugs (NSAIDs). These drugs prevent or at least diminish postoperative edema [5,6]. Tenoxicam is an enolic acid derivative in the oxamic group of NSAIDs. It inhibits cyclooxygenase and the lipoxygenase enzyme, thus preventing the formation of prostaglandins and leukotrienes that play an essential role in inflammation by diminishing active oxygen radicals and inhibiting migration and phagocytosis of leucocytes. In addition to its anti-inflammatory effects by these mechanisms, it also has analgesic and antipyretic effects. Similar to many other NSAIDs, it also inhibits thrombocyte aggregation [7,8]. There are various dosages, timings, and routes of administration of NSAIDs [9].

Corticosteroids are another group of drugs that also suppress the production of prostaglandins and leukotrienes at initial phases and thereby inhibit inflammation [10]. Methylprednisolone, a type of corticosteroid, inhibits the development of macrophages in the inflammation zone, diminishing the number and proliferation of fibroblasts in connective tissue, and suppressing the immune system. Methylprednisolone, by stabilizing cellular and organelle membranes, reduces kinin and bradykinin formation and blocks histamine and histamine-like substances intracellularly [10]. Various routes and times of administration (e.g., oral, intravenous, and intramuscular; preoperative and perioperative) have recently been proposed because of limited benefits when the therapy was applied postoperatively [11,12].

Although there are many studies in the literature about the effectiveness of corticosteroids and NSAIDs on reducing complications after the surgical extraction of impacted third molar teeth, there is still no consensus on the type of drug administration [13,14]. In light of these data, the aim of the present study was to compare the effects of administration of pre-emptive intravenous (IV) Tenoxicam (Tilcotil® Roche-İstanbul, Turkey) (an NSAID) and IV methylprednisolone (Prednol L® Mustafa Nevzat – İstanbul, Turkey) (a corticosteroid) in postoperative control of pain, edema, and trismus of patients following the extraction of impacted third molars.

Material and Methods

This study was a placebo-controlled, randomized, double-blind, clinical trial. A total of 60 adult patients admitted to our oral and maxillofacial surgery clinic due to impacted third molar teeth, without any known systemic diseases, were included in the study. Informed consent was obtained from all patients. To standardize the 60 teeth with an orthodontic indication of surgical extraction in the study, their mesio-angular or vertical positions were recorded. Patients who are exposed to severe trauma due to bony retention during surgery were excluded, as were patients who used an anti-inflammatory or analgesic agent during the study or within 15 days prior to the beginning of the study. The ethics committee at Dicle University Faculty of Medicine approved the study, which has been performed in accordance with the ethics standards of the 2008 Declaration of Helsinki.

The patients were randomized into 3 groups according to the drug administered before the operation; IV 20 mg tenoxicam was administered to group A (n=20), IV 80 mg methylprednisolone sodium succinate was injected in group B (n=20), and IV isotonic sodium chloride was administered to group C patients (n=20) 1 hour before the operation.

Prior to surgery, the patients received extra-oral antisepsis with a solution of 10% povidone-iodine. Local anesthesia was performed with lidocaine 2% and epinephrine 1:100 000. Using standard methods, the teeth were extracted by removing retentive bony structures by the same surgical team. After the surgery, all patients were informed about the local hemostatic measures, feeding, and cleaning. During the postoperative period, prophylaxis amoxicillin 3×500 mg, paracetamol 3×500 mg as pain-killer, and chlorhexidine gluconate 2x1 times as oral antiseptic were prescribed to all patients.

Edema evaluation

Postoperative swelling was assessed by an ultrasound (Toshiba SSH 1401) and a 7.5 MHz transducer. In the evaluation of edema, the soft-tissue measurements were performed in Dicle University Hospital, Radiology Department, Division of Ultrasound. The preoperative and postoperative 48th hour ultrasound imaging of all patients were performed from the same point while the teeth were on centric occlusion. To assure that the ultrasound images were taken from the same point, the preoperative measured point was marked with a pen. To achieve maximum standardization, all measurements were performed on the same machine by the same doctor, with minimum pressure on the skin (Figure 1).

Mouth opening evaluation

After the radiological evaluation of all patients, they were asked to open the mouth as much as possible and limited mouth



Figure 1. Sample imaging of ultrasound evaluation for subcutaneous + masseter muscle edema.

opening (trismus) was assessed by determining maximal unassisted mouth opening, measured with a simple calliper between the upper and lower central incisors. This distance was measured in the preoperative period and at the 48th postoperative hour. The measurement process was repeated 3 times and the mean of these 3 measurements was assessed each time. Trismus was determined by the difference between the preoperative and postoperative period.

Visual analogue scale

In the evaluation of postoperative pain, visual analogue scale (VAS) forms were given to the patients. To indicate the intensity of pain, the following categorization was used: 0 = no pain; 2 = mild pain; 4 = moderate pain; 6 = severe pain; 8 = very severe pain; and 10 = unbearable pain. The patients were asked

to mark the pain level hourly during waking hours starting from the first hour of the operation. By use of these forms, the severities of pain were evaluated for the first 24 hours (Figure 2).

Statistical analysis

Data analysis was performed using the Statistical Package for Social Sciences (SPSS for Windows, version 18.0; SPSS Inc., Chicago, IL, USA). In the determination of differences between the groups, one-way ANOVA (variance analysis) test was used. For the multiple comparisons among groups in variance analysis, Tukey and Tamhane tests were used. Dunnett test was used to evaluate the comparison of significant differences between study groups and the control group. Significance was accepted at $p < 0.05$.

Results

The study included a total of 60 patients (41 females and 19 males) aged 18–40 years (Table 1). The duration of surgery of groups A, B, and C were 26.10 ± 0.95 , 25.70 ± 0.98 , and 23.80 ± 0.79 minutes, respectively. No significant difference was found between the groups regarding the duration of surgery ($F = 1.798$, $P > 0.05$) (Table 2).

In evaluation of edema, postoperative edema (subcutaneous + masseter muscle) ratios of groups were 38%, 57%, and 150% in group A, group B, and control groups, respectively ($p < 0.05$). Swelling ratios were significantly better in both study groups than in the control group. There was no statistically significant difference between methyl prednisolone and tenoxicam groups regarding the edema (Table 3).

A reduction occurred in mouth opening of all groups of patients. The postoperative trismus ratios of groups were 5.25%, 2.95%, and 13.90% in group A, group B, and the control group, respectively. Although the trismus ratios were significantly better in

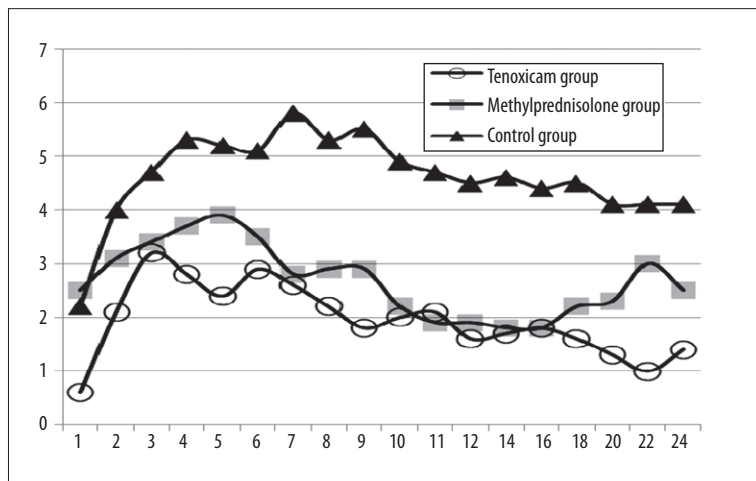


Figure 2. Evaluation of the pain severities of patients in group A, B, and C within the first 24 hours.

Table 1. Distribution of age groups and sex of total 60 patients.

Age groups	Male	Female	Total
18–25	11	35	46
26–33	3	4	7
34–40	5	2	7
Total	19	41	60

Table 2. The mean duration of surgery of groups were as follows; 26.10±0.956, 25.70±0.981 and 23.80±0.799 for group A, group B and control groups respectively (F=1.798, p<0.05).

	Duration of surgery
Group A	26.10±0.956
Group B	25.70±0.981
Group C	23.80±0.799

both study groups than in the control group, the methyl prednisolone patients had statistically significantly superior results as regards the trismus compared with the tenoxicam patients (F=110.3, P<0.001) (Table 4).

Mean pain scores of groups A, B, and C were 35.30±5.64, 48.20±7.22, and 81.40±4.79, respectively. In the evaluation of pain scores, the tenoxicam and methylprednisolone groups had similar mean pain scores, which were statistically significantly lower than in the control group (F=15.89, p<0.001) (Table 4).

In the follow-up period after single-dose administrations of IV tenoxicam or methylprednisolone, no postoperative complications, including gastrointestinal problems, hemorrhage or delay in wound healing, were observed in any of the patients.

Discussion

Although there are many reports in the literature about use of drugs in prevention of postoperative pain, edema, and trismus after impacted third molar teeth extraction, to the best of our knowledge this is the first study comparing the effects of 2 very commonly used drugs – methylprednisolone and tenoxicam – for this purpose. Moreover, even though this procedure is a very common oral surgical procedure, there is still no consensus about the optimal type, time, method of administration, and dose of drugs to use in prevention of complications. In this respect the results of this study gain more importance.

A gradual facial swelling occurs in response to tissue trauma in the third molar region, with peak swelling 48 h after surgery.

Table 3. In evaluation of oedema; postoperative oedema of subcutaneous and masseter muscle ratios of groups were as follows; 23.40%; 32.60%, 14.45%; 27.25% and 62.75%; 101.3% (p<0.05).

	Postoperative oedema	
	Masseter muscle	Subcutaneous
Group A	23.40±3.872	32.60±6.503
Group B	14.45±3.411	27.25±5.906
Group C	62.75±7.668	101.3±19.97

Table 4. The postoperative trismus ratios of groups were as follows; 5.25%, 2.95% and 13.90% in group A, group B and control groups respectively (p<0.001). Mean pain scores of groups A, B and C were; 35.30±5.64, 48.20±7.22 and 81.40±4.79 respectively (p<0.05).

	Postoperative trismus	Postoperative pain
Group A	5.250±0.565	35.30±5.648
Group B	2.950±0.431	48.20±7.227
Group C	13.90±0.631	81.40±4.790

There are various methods used in the evaluation of edema after oral surgeries, including visual analogue scale, measuring with silk suture, or by the aid of plethysmography [3]. Many studies have reported that postoperative edema may be precisely evaluated by ultrasound [10,15]. Methyl prednisolone and tenoxicam were both effective in controlling swelling in the present study. This effect may be explained by the long duration of action and high anti-inflammatory potencies of both drugs. Each drug may be preferred for the purpose of reducing edema after impacted third molar teeth extraction.

Limited mouth opening is another unwanted effect commonly reported after oral surgeries. In investigations, inter-insisal distance measurements before and after the operation is commonly used for the evaluation of trismus, as in our study [14,16]. Lesser trismus was observed with methylprednisolone administration in this study than with tenoxicam. Trismus impedes eating and talking and reduces the quality of daily life of patients; in this sense, decreased trismus means decreased discomfort as well as increased life-quality for the patients. Therefore, methyl prednisolone may be preferred to tenoxicam for patients with a lesser trismus.

In evaluation of postoperative pain, visual analogue scale or number of analgesic tablets consumed after surgery are the methods commonly used [6]. In this study, since patients were prescribed paracetamol 3×500 mg routinely after surgery, number of analgesics consumed was not recorded. In pain control,

tenoxicam and methylprednisolone had similar efficiencies in this study. In fact, this is an interesting finding because the exact contribution of corticosteroids in the control of pain is not yet fully clarified, but NSAIDs are very potent pain-killers. This finding may also be associated with or affected by the use of paracetamol 3×500 mg routinely. However, it gives us important data only for more potent pain killer effects. There is no need to combine corticosteroids (with their adverse effects) with NSAIDs, since combining corticosteroids with a relatively safe drug (e.g., paracetamol) is enough to achieve the same pain-relief. Supporting this data, Joshi et al. compared the effect of preoperative ibuprofen, diclofenac, paracetamol with codeine, and placebo tablets on postoperative dental pain and found no significant difference between the different therapeutic groups [14].

Corticosteroids and NSAIDs are 2 large groups of drugs that are widely studied for the prevention of postoperative inflammatory complications and to diminish unwanted effects such as pain or trismus [13–16]. NSAIDs have been reported to be effective in pain relief, while corticosteroids are effective in diminishing edema. This being the case, some investigators preferred to combine these 2 groups of drugs [10,14]. Schultze-Mosgau et al. [10] studied the combined usage of ibuprofen and methylprednisolone in the prevention of pain and edema after third molar teeth extraction and revealed that combined usage of these 2 drugs decreased the edema by 56% and pain by 67% compared with the control group. However, in the present study we did not observe any significant difference between tenoxicam and methylprednisolone groups regarding pain relief.

Corticosteroids have been used widely in diminishing complications after third molar teeth extraction, but with different dosages and types. Milles and Desjardins et al. [18] gave 18 mg oral methylprednisolone 1 night before and 20 mg IV methylprednisolone during surgery and reported that this combination decreased the postoperative edema by 42% within the first 24 h and there was no trismus observed in these patients and no need for other analgesic preparations. Baxendale et al. [19] investigated the effects of pre-emptive 8-mg oral dexamethasone on pain, trismus and edema of impacted third molar surgery patients and reported that this drug significantly decreased postoperative pain and edema but did not have any effects on trismus. More recently, in a study comparing dexamethasone 8 mg and methylprednisolone 40 mg in control of pain, swelling, and trismus following the impacted third molar teeth extraction, 8-mg dexamethasone has been determined to be better in control of swelling and trismus, with no difference in pain control between drugs [20]. Another study comparing the effects of weight-dependent methylprednisolone (40–80 mg) or a placebo orally 1 h prior to surgery, determined that a single preoperative

weight-dependent administration of methylprednisolone is a safe and effective method for diminishing postoperative discomfort, pain intensity, and total intake of analgesics after wisdom tooth extractions [21].

There are also some studies in the literature comparing the effects of corticosteroids and NSAIDs on postoperative complications. Sisk and Bonnington [14] compared the effects of methylprednisolone and flurbiprofen on postoperative pain, edema, and trismus after impacted third molar teeth surgery on 60 patients aged 16–35 years. They determined that flurbiprofen was more effective in pain control while methylprednisolone was more effective in control of edema. Hyrkas et al. [16] compared 50-mg diclofenac with 50-mg diclofenac and 40-mg methylprednisolone combination and reported that the pain scores were diminished in the combined group but there was no significant difference between the groups in terms of trismus. Bamgbose et al. compared the administration of diclofenac potassium alone and in combination with dexamethasone and found that the combination therapy was more effective in controlling pain, swelling, and trismus following third molar surgery [22].

The doses of drugs examined in this study were based on previous reports of the maximum effective dosages without any adverse effects. Kumara and Zacharias [23] gave 40 mg tenoxicam to impacted third molar teeth surgery patients – orally to the first group 1 night before the operation and IV to the second group during the operation – and reported that the methods were equally effective in healthy young patients. It has been reported that there was no significant difference between 20 mg or 40 mg IV tenoxicam after oral surgery in terms of pain relief [20]. In light of these data, tenoxicam 20 mg was preferred. On the other hand, there is not a consensus about the optimal dosage of methylprednisolone in the literature. The recommended dosages range from 40 mg to 125 mg; however, 80 mg was chosen as it was one of the most commonly used dosages [21,24].

In a recent study, short-term outcomes of third molar operations (swelling, trismus, and pain) has been determined to differ depending on patient characteristics, including age, sex, and body mass index [25]. Moreover, in that study surgery characteristics such as operating time and tooth sectioning were also associated with postoperative variables. Patient characteristics may be the main limitation of this study [25]. Although the ages were similar, we did not calculate the body mass indices of patients. However, the duration of surgery was recorded and evaluated for each group to determine possible confounding factors that could influence our results. There was no statistically significant difference between groups in the duration of surgery, showing that the procedures, performed by the same surgical team, were as standardized as possible.

Conclusions

In conclusion, the results of this study indicate that although methylprednisolone and tenoxicam are both effective in diminishing complications of impacted third molar teeth extraction, preoperative administration of 80 mg methylprednisolone achieves better control of trismus than tenoxicam, without any differences in edema and pain control. In light of these data,

we conclude that methylprednisolone may be a better alternative than tenoxicam in the prevention of complications associated with impacted third molar teeth extraction.

Ethics approval

Human Research Ethics Committee of the Dicle University Medicine Faculty, Diyarbakır-Turkey.

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