

Comparison of the Effect of Ketorolac and Betamethasone Injection on Post Complications of Third Molar Surgery (A Clinical Trial)

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Abstract

BACKGROUND: The aim of this study was to evaluate the effect of preoperative ketorolac and betamethasone injections on reducing postoperative complications mandibular third molar surgery.

MATERIALS AND METHODS: In this randomized clinical trial, 134 patients at the age group of 18-40 years who required mandibular molars surgery were studied. Patients were randomly divided into two groups. In A group, 1 mL of betamethasone LA was injected into the master muscle before surgery, and in the A group, 30 mg of ketorolac per 1 mL was injected before surgery. On the second and seventh days after surgery, patients were evaluated for the variables of maximum mouth opening, pain, swelling, and general satisfaction with the surgery through telephone calls on the second and seventh days. Independent t-test and Mann-Whitney test were used to evaluate the variables.

RESULTS: The mean of pain intensity and the swelling variables in the betamethasone group were lower than the ketorolac group in second and seventh days ($P < 0.05$). The mean of maximum mouth opening and the patient satisfaction variables in the betamethasone group were higher than the ketorolac group in second day ($P < 0.05$). There was no statistically significant difference in the patient satisfaction and maximum mouth opening variables on the seventh day ($P > 0.05$).

CONCLUSION: This study concluded that betamethasone performed significantly better in reducing swelling, pain, maximum mouth opening limitation, and general satisfaction.

KEYWORDS: Ketorolac; Injection; Masseter Muscle; Betamethasone LA; Third molar surgery

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Introduction

Impacted mandibular third molar surgery is one of the most common interventions and that is a traumatic process in the field of oral and maxillofacial surgery, which has many

complications such as pain, swelling, and trismus. These phenomena are caused by excessive inflammatory processes [1,2]. Pain is an unpleasant sensory experience that is connected to real or potential tissue damage and is originated from inflammatory

mediators such as bradykinin, histamine, and prostaglandin. Prostaglandins and leukotrienes play a role in the inflammatory process and pain production. These substances are produced from arachidonic acid, which is caused by

the cell membrane destruction and damage due to surgery [3,4]. Edema or swelling is the body's expected physiological response to injury, which is due to the accumulation of fluids at the injury site. Accumulation of fluids and extensive inflammation in the masticatory muscles after surgery can lead to mouth opening restriction or trismus [5,6]. Third molar extraction can reduce the life quality in patients who experience pain and swelling up to 3 times [7]. It seems that factors such as age, sex, medical history, oral contraceptives, pericoronitis, inappropriate oral hygiene, smoking, type of impaction, the third molar relationship with inferior alveolar nerve, surgical time, surgical technique, surgeon's experience, using Postoperative antibiotics, local antiseptics, intraoral drugs, anesthetic techniques [8], individual physiological inflammatory response, tissue trauma degree and bone manipulation [9] effect on the third molar extraction post complications.

Different medical treatment methods have been proposed to control the impacted third molar surgery post complications- which are caused by inflammation- to reduce the complications by inhibiting the inflammatory pathway, including non-steroidal anti-inflammatory drugs and corticosteroids [4,10].

Corticosteroids inhibit the phospholipase A2 enzyme, which plays a role in the inflammatory pathway and the conversion of cell

membrane phospholipids into arachidonic acid. This inhibitory effect reduces the release of arachidonic acid and ultimately leads to a reduction in inflammatory mediators (bradykinin, prostaglandin, etc.) production [4]. Long-acting betamethasone is a combination of short-acting (betamethasone diphosphate) and long-acting (betamethasone acetate), two forms of corticosteroids, and its acting duration is more than 36 hours, and its anti-inflammatory power is 25 times of body's natural cortisol, and it is similar to the dexamethasone power [11,12].

Using corticosteroids in dentistry in low doses and for a short period does not cause significant side effects [4,13].

NSAIDs inhibit the inflammatory mediators' productions by inhibiting cyclooxygenases 1 and 2. Ketorolac from the NSAID category has a moderate to strong analgesic effect and has been useful for acute and chronic pain and it has anti-inflammatory effects and has shown a good analgesic effect on tooth extraction [14].

Ketorolac is more potent among different anti-inflammatory drugs under similar experimental conditions [15].

Intramuscular Corticosteroid injection is very effective for reducing pain, and while it is injected into the masseter muscle, there is no need for

additional anesthesia injection to the patient and it is easily available for the dentist [16-18]. *Grossi et al.* showed that injection in the anesthetized area of the mouth is comfortable for the patient and the surgeon, While the injection in the gluteal muscle requires special facilities and equipment [19]. In addition, a study by *Selvaraj et al.* showed that there is no statistically significant difference between methylprednisolone injection into the masseter muscle and gluteal muscle injection in terms of pain after impacted third molar surgery [20].

Skjelbred et al. showed in their study that betamethasone can be effective in reducing pain after mandibular third molar surgery [21]. *RAO et al.* have shown in their study that ketorolac provides better analgesia than acetaminophen in tooth extraction [14]. Ketorolac has a similar effect to morphine [22] and is even better than opioids in pain relief [23].

In a study, *Majid et al.* showed that the use of corticosteroids can be useful in improving the complications and quality of life after mandibular third molar surgery [6]. More studies are necessary to compare the effect of corticosteroids with NSAIDs on the wisdom teeth surgery post complications. The purpose of this study is to compare the effect of betamethasone long acting (LA) or ketorolac injection on the masseter muscle immediately after mandibular block anesthesia injection, on pain,

swelling, overall patient satisfaction, and maximum mouth opening after mandibular impacted third molar surgery.

Material and Methods

Ethics approval of the study

This randomized, single blind, clinical trial study included 134 patients, Aged 18-40 years with impacted lower third molar. The study methods were approved by the Ethics Committee of Kermanshah University of Medical Sciences with the registry ID of IR.KUMS.REC.1400.801 .

Witnessed written consent was obtained from of all participants before enrolment in the study. .This study was registered at WWW.IRCT.IR with IRCT Registration Code: IRCT20191127045516N6.

The inclusion criteria were:

Age of 18 -40 years, healthy medical assessment (ASA I or II), diagnosis of bony impacted mandibular third molars requiring surgery with panoramic radiography , free of pericoronitis or infection at the time of operation.

Exclusion criteria included:

concurrent lactating or pregnancy, systemic disease, allergy to the drugs , history of smoking or drinking alcohol, impaction according to Pell & Gregory [24] and Winter [25] classifications with severe complexity and those who use the antibiotic and anti-inflammatory medication in the

one week before surgery and surgery lasting more than 1 hour.

Participants, study design, and setting

According to Paiva-Oliveira J, et al [15] the sample size was calculated using a standard deviation and mean of $s_1=1.29$, $\bar{X}_1 = 1.05$ for Dexamethasone group and $s_2=2.24$, $\bar{X}_2 = 2.35$ for Ketorolac Tromethamine group, With considering $\alpha = 0.05$ (power) $1-\beta=90\%$, minimum sample size in each group was 62 persons. The sample volume was calculated with the following formula:

$$N = \frac{1}{1-f} \times \left(\frac{(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2 (S_1^2 + S_2^2)}{(\bar{X}_1 - \bar{X}_2)^2} \right)$$

$$N = \frac{1}{1-0.30} \times \left(\frac{(1.96 + 1.28)^2 (1.29^2 + 2.24^2)}{(1.05 - 2.35)^2} \right) = 62$$

Total of 134 patient using a Sequentially Numbered, Opaque Sealed Envelopes (SNOSE) divided into two groups (A, B) with a 1:1 allocation ratio. Each patient allocated to the groups was based on systematic random numbering; letter "A" was allocated to the first group, letter "B" was allocated to the second group . Group "A" received 6 mg/1ml ampoule betamethasone LA (Alborz Iran Company) in masseter muscle and the group B received 30 mg/ml of ketorolac (Alborz Iran Company) into the masseter muscle immediately after anesthesia.

Neither the surgeons nor the participants were blinded to use of the receiving drugs .Postoperative amoxicillin 500 mg , metronidazole 250 and acetaminophen 325mg were prescribed for All patients in the study. The operations were performed by one surgeon in private office.

Two surgeries in both sides were carried out in each patient with a minimum interval of 15 days.

Using a solution of 2% lidocaine with 1:2 00,000 adrenaline (persocaine-E ; Darou Pakhsh, Tehran, Iran). inferior alveolar nerve block and long buccal nerve block were carried out.

Standard impacted third molar surgery were carried out with bone removal and irrigation with sodium chloride 0.9%. Sutures were performed with 3.0 silk (Braided silk; Supa, Tehran, Iran).

A gauze pack was held in the surgical site for 30 -45 minutes.

The effect of the surgery on Postoperative pain, swelling, general patient satisfaction and maximum mouth opening were measured on days 2 and 7 after operation by telephonic interview.

Postoperative pain scores were estimated using a visual analog scale(VAS), 10 mm in length, ranging from 0 for "no pain" to 10 for "the worse unbearable pain" [1,15].

Swelling scores was assessed by asking the patient to rate it on a visual analog scale of 0 to 5 [1,26-28]. General patient satisfaction of the surgery was recorded from 0 to 10 by telephonic interview at 2 and 7 days after surgery [1]. The patients were asked to score their satisfaction from 0 to 10, where 0 represents no satisfaction and 10 representing complete satisfaction of the surgery. Patients measured maximum distance inter upper central and lower central incisal with ruler for 2 and 7 days after operation [15,29]. Before enrollment the study, these variables were explained to all patients by leaflet and how to report them to the operator, who called them through a phone at 2 and 7 days after operation.

Statistical analysis

Data analysis was carried out using SPSS version 18 Statistical software (SPSS, Inc, Chicago, IL). Subject

demographic data were analyzed by Chi-Square or Independent Samples T-Test, as appropriate. To compare the paired results among groups and across time were used Mann Whitney test and Wilcoxon, respectively. P value of less than 0.05 was considered significant.

Results

134 participants of both genders, between 18 and 39 years (mean 25.03±5.47 years) with impacted lower third molars were present in this study. 57of the participants (42.5%) were male and the rest (77 individuals (57.5 %)) were female. 68 of which (50.7%) were allocated to the group A (betamethasone) and 66 individuals (49.3) to the group B (ketorolac). There were no statistically significant differences in the distribution of the mean age (P=0.788) and gender (P=0.979) between the two groups. There wasn't a significant difference in

Difficulty level of impacted teeth between the two groups (Table 1).

The betamethasone group had significantly less pain and swelling scores on the second and seventh days after the surgery compared with the ketorolac group (p<0.001) (Table 2). General patient satisfaction and maximum mouth opening on the second day were significantly higher in the betamethasone group than the ketorolac group. However, no significant difference was showed between the groups on 7th day (Table 2).

Pain and swelling scores on the seventh day after the surgery were lower than the second day after surgery in both groups (p < 0.0001). General patient satisfaction and maximum mouth opening on the seventh day after the surgery were higher than the second day after surgery in both groups (p < 0.0001) (Table 2).

Table 1: Demographic and Difficulty level of impacted teeth data

		Medication group		P-value
		Betamethasone	Ketorolac	
Sex	Male	29(42.6%)	28(42.4)	0.979 [†]
	Female	39(57.4%)	38(57.6)	
Difficulty level of impacted teeth	Minimally difficult	27(39.7%)	26(39.4%)	0.971 [†]
	Moderate	41(60.3%)	40(60.6%)	
Age		25.16±5.83	24.89±5.11	0.778 [‡]

Mean±standard deviation and percentage (%) are presented for parametric and categorical data, respectively.

[†]Chi-Square test was used.

[‡]Independent Samples T-Test was used.

Table 2: P values in comparing the pain, swelling, general patient satisfaction scores between each 3 groups

Items	Medication group		P value
	Betamethasone	Ketorolac	
	Mean ±SD	Mean±SD	
Pain Vas day 2nd	2.75± 2.43	4.37±3.04	0.001 [†]
Pain Vas day 7th	0.44±1.04	1.50±2.06	<0.001 [†]
	<0.001 [‡]	<0.001 [‡]	
Swelling Vas day 2nd	2.16±1.50	3.36±1.39	<0.001 [†]
Swelling Vas day7th	0.29±0.52	0.67±0.93	0.005 [†]
	<0.001 [‡]	<0.001 [‡]	
General patient satisfaction day 2nd	8.91 ±1.05	8.20±2.01	.012 [†]
General patient satisfaction day 7th	9.43±0.97	9.09±1.77	.178 [†]
	<0.001 [‡]	<0.001 [‡]	
maximum mouth opening day 2nd	29.12±7.72	25.94±8.73	.027 [†]
maximum mouth opening day 7th	38.37±5.05	38.85 ±8.73	.698 [†]
	<0.001 [‡]	<0.001 [‡]	

[†]Independent Samples T-Test was used

[‡]Paired T-Test was used

Discussion

The main findings of this study were that there was a statistically significant difference in variables of pain intensity and swelling on the second and seventh day between the two study groups, as the average of these variables was lower in the betamethasone group than in the ketorolac group, and there was a statistically significant difference in the maximum mouth opening rate

variable. There was a difference in the patient's maximum mouth opening on the second day between the two study groups, as the mean of this variable in the betamethasone group was higher than in the ketorolac group. Also, the average of the maximum mouth opening on the second day in both groups was less than 35 mm.

This study shows that betamethasone performed significantly better in

reducing swelling, pain, and maximum mouth opening and general satisfaction. Moghadasi et al [30], Messer et al. [31], and Mahmoud et al.[16] reported a significant reduction in pain, swelling, and trismus by administering dexamethasone intramuscularly, which was according to the results of our study. In the clinical trial study by Jose Marques et al. ,[29] a dose of 12 mg long-acting betamethasone was administered submucosally after

surgery, and no significant difference was observed between the two study groups in terms of postoperative pain, facial swelling, and trismus, which was contrary to the results of our study. The clinical trial study by Bertossi et al. [32] showed that the use of a 4 mg submucosal injection of betamethasone after surgery leads to a reduction in edema, trismus, and pain in the patients undergoing extraction of impacted third molar which was according to the results of our study. In a clinical trial study, Chopra et al. [33] showed that ibuprofen is more effective than betamethasone in reducing pain and swelling, which was contrary to the results of our study.

In Paiva-Oliveira [15] clinical trial study in 2016, compared 10 mg of oral ketorolac (1 hour before third molar surgery and then every 8 hours for two days) with 8 mg of oral dexamethasone (1 capsule 1 hour before Third molar surgery) and concluded that there was no statistically significant difference between the two groups in terms of pain and edema variables. However, for mouth opening limitation, 24 hours and 7 days after surgery, the dexamethasone group had less limitation in mouth opening, and it behaved better than Ketorolac for this variable in these periods, which was contrary to the results of our study.

In Martin's 2021 [34] clinical trial study, 8 mg single dose of oral dexamethasone was compared with 20 mg single dose of sublingual ketorolac tromethamine 1 hour before surgery. Compared to ketorolac tromethamine, dexamethasone showed a significant reduction in pain level up to 72 hours, in swelling, and trismus up to 72 hours and 7 days later, and the clinical performance of dexamethasone in controlling pain, swelling, and trismus following mandibular third molar removal was superior to ketorolac tromethamine. It seems that the superiority of dexamethasone compared to ketorolac in this study is related to the characteristics of its broad anti-inflammatory effect mechanism and its long half-life.

Therefore, it is a more accessible and more suitable option for preventive prescription in oral surgery. In a clinical trial study by *Meta et al.*, [35] postoperative pain and swelling after dental implants were compared in patients treated with nonsteroidal anti-inflammatory drugs (NSAIDs) versus NSAIDs and corticosteroids. This RCT did not show a difference between patients treated with ketorolac-betamethasone versus ketorolac alone in terms of postoperative pain and swelling, which was against the results of our study. These controversies among the results of the studies may be related to various factors, including drugs, dosage, administration method,

administration time, and method of measuring postoperative complications including swelling and pain, and the follow-up period of patients after surgery. One of the limitations of this study is the measurement of swelling and maximum mouth by using a telephone report from the patients. It would be better to evaluate the intensity of pain on the first day after surgery, which is most intense in the first 6 hours after surgery.

Conclusion

Long-acting corticosteroids can be more effective in reducing swelling, pain, and maximum mouth opening, and in increasing general satisfaction than NSAIDs. Briefly, the present study shows that betamethasone has acted significantly better in reducing swelling, pain, limitation of maximum mouth opening, and general satisfaction.

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