

Comparison of the Effectiveness of Ketorolac Injection into the Masseter and Medial Pterygoid Muscles in Preventing the Post-Operative Complications after Mandibular Third Molar Surgery

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Abstract

Objective: One of the problems we face in the field of oral health is the extraction of the third molars. The aim of this study was to evaluate the effect of preoperative ketorolac injection on reducing or eliminating postoperative complications in order to find the best site for injection. Thus, the amount of annoyance and dissatisfaction of the patient is reduced so that the patient can move toward surgery with facing less problems and complications after treatment.

Material and Methods: In this study, patients were divided into 2 groups of 42 individuals. After injection of IANB anesthesia, 30 mgs of ketorolac was injected into the masseter muscle for the first group and 30 mgs of ketorolac was injected into the medial pterygoid muscle for the second group. Pain, edema, trismus, mouth opening rate and patients' general satisfaction was assessed on the second and seventh days after surgery. Data were analyzed by Stata v 14.2 software and statistical tests.

Results: In the present study, although in the group receiving ketorolac in medial pterygoid muscle, the outcomes of pain on both the second and seventh days and swelling on the second day, less and maximum mouth opening and general satisfaction of the patient on the second day, were higher, but these differences were not statistically significant and the only significant difference was in the satisfaction parameter of patients after surgery on the seventh day, so that the patients receiving the ketorolac in the medial pterygoid muscle reported higher satisfaction ($p=0.021$).

Conclusion: The results of this study showed that there was no significant difference in the outcomes of pain, swelling, trismus, and maximum mouth opening between the two groups of injection of ketorolac into the masseter muscle and medial pterygoid muscle, and only a significant difference was in the general satisfaction parameter of patients after surgery on the seventh day, so that patients receiving the ketorolac into the medial pterygoid muscle reported more satisfaction than the masseter muscle. In general, the results about the difference in the injection site are very close to each other.



Introduction

With human progress and dietary changes, the human evolutionary process has progressed towards the reduction of the jaw arch and, as a result, the removal of the fourth molar teeth and, in recent centuries, the removal of the third molar. In the last century, due to the change in diet, the third molar tooth has often become embedded, and this embedment has caused problems such as caries, pericoronitis, pressure on the second molar and its root erosion, periodontal problems, etc. in people [1-3]. Therefore, one of the recommended treatments and individual preferences is surgery and removal of the impacted third molar tooth. But this surgery causes trauma to the hard and soft tissue due to the variations of the impaction of the third molar. In addition to the difficulty of work for the dentist and mental pressure and stress for the patient, there are a series of complications after surgery, which can be referred to lower alveolar nerve paresthesia, pain, swelling, trismus, etc.; These complications themselves have changed the living conditions and created limitations in the person's social activities, and this causes the person's reluctance towards third molar surgery [4-8].

The purpose of this study was to investigate the effect of ketorolac injection before surgery on reducing or eliminating complications after treatment in order to find the best position for intramuscular injection of the drug near the surgical site. In this way, the level of annoyance and dissatisfaction of the person is reduced so that the person can go to surgery without facing problems and complications after the treatment.

One of the problems we face in the oral and dental field is the removal of the third molar. The third molar tooth of the mandible grows at the age of 17 to 23 years and its impact is very common (1). A hidden tooth is a tooth that has not fully erupted and is surrounded by other teeth, bone or soft tissue [2]. Due to pericoronitis, infection, root resorption of the second molar, pain, cyst, tumor and to facilitate orthodontic and prosthetic treatments, removal surgery of the mandibular third molar is performed [3], which is the most common intervention in oral surgery [4]. It is the most common model for evaluating analgesic effects for an acute dental pain [5]. Pain is one of the most common complaints of humans. The intensity of pain after third molar surgery is different. Moderate to severe pain starts during the first 12 hours after the operation and reaches its maximum level in the first 8

hours after the local anesthesia wears off [6, 7]. It is said that the pain caused by third molar surgery is one of the most painful surgeries [8]. In fact, this surgery causes trauma to hard and soft tissue, which is the physiological response of the body to this trauma, inflammation and pain [9]. Although this inflammation is useful and necessary for the healing process, excessive inflammation itself causes complications such as pain, swelling and trismus [10]. Although these side effects are transient, they can make the patient anxious and uncooperative [11], which also affects the patient's quality of life in the post-surgery period [12].

Treatment and planning for pain, before the onset and spread of pain, is a wise approach because a lot of pain makes the patient uncooperative and the work more difficult for the surgeon [13]. Therefore, dentists are looking for a way to reduce pain and inflammation after surgery. In past clinical studies, they used various treatments to reduce post-operative complaints, including the use of antiseptic mouthwashes, different flap designs, antibiotic prophylaxis [14], wound closure with various sutures, muscle relaxation, corticosteroid drugs and non-steroidal anti-inflammatory drugs (NSAID) [15,16]. Although the mechanism of action of all NSAIDs is the inhibition of prostaglandin synthesis, the effect of one drug may be different from another. Ketorolac tromethamine is a member of the pyrrolo-pyrrole group, which is equivalent to meperidine in terms of analgesic power. This substance has an analgesic and anti-inflammatory effect, which is very effective for toothache after surgery, while it has no effect on opioid receptors and sedative and anti-anxiety properties. It seems that its main action is the inhibition of the COX enzyme, which metabolizes arachidonic acid through endoperoxide and prostaglandins, which increase pain [3]. On the other hand, the injection site has a significant effect on the effectiveness of surgical procedures in patients with pain, swelling and trismus. The injection site (ie, proximal or distal to the surgical site) can also determine the effectiveness of the injection [17]. In the study of Selvaraj and Shirani, the effectiveness of injection in the mesenteric muscle and internal pterygoid in relation to the reduction of pain and swelling after surgery of the third molar of the mandible has been observed [12, 17]. A comparative study of the analgesic effect of muscle pain relievers for the third molar is rare [18]. A study on the topic of intramuscular injection of Ketorolac in two different muscle areas has not been done in the past to

check absorption and better effectiveness. Therefore, it is important to compare the analgesic effect of Ketorolac intramuscular injection before surgery in order to find the best injection muscle position for postoperative pain control.

Materials and Methods

In this double-blind randomized clinical trial study, 84 patients who referred to Dr. Hamed Nazari's private office for impacted wisdom tooth surgery were studied. The patients in the study were unaware of the procedure of the injection site. Patients were evaluated by the outcome evaluation doctor on the second and seventh days, who was also unaware of the injection site. The study was conducted after the approval of the implementation method by the ethical committee of Kermanshah University of Medical Sciences. Patients aged 18 to 40 were included in the study. Data on latency were collected before the start of the study. Randomization was performed for similarity between the 2 groups. Also, the difficulty and duration of surgery were considered as confounding and effective variables, and the effect of these variables was applied in data analysis.

Randomization and allocation of patients

In this study, a statistician generated a random number using Excel software. For this, three-digit codes were generated, which determined the last digit on the right side of the patient group. If the obtained number was odd (1, 3, 5, 7, 9), the patient was in the ketorolac injection group in the internal pterygoid muscle, and if the obtained number was even (2, 0, 4, 6, 8), the patient was in the injection group. It was placed in the master muscle. Finally, the data was collected and analyzed using a checklist [12].

Blinding (Double blind)

The patient and the physician were blinded to the outcome. Since Ketorolac injection was done after anesthetic injection, the patient did not notice the exact injection site (muscle or internal pterygoid). The doctor evaluating the outcome was not informed which site was injected, so the evaluating doctor was also blinded and was unaware of the injection site.

Ethical considerations

Before starting the study, it was explained to the patients that their participation in the study is optional and they can withdraw from the study at any time if they do not want to cooperate. They were assured that their information will be collected for statistical studies and that their personal information will not be shared with other people, and only the information obtained from the entire study may be shared with scientific publications for the use of others. Then, after identifying the patients interested in participating in the study, the method of implementing the goals and how to implement the plan were explained to the patients.

Collecting data

Using a checklist, information related to gender, age, OCP use, smoking, allergies, history of systemic disease, history of antibiotic or anti-inflammatory use, dental impaction and radiographic information of tooth position were collected. In all patients, tooth extraction was performed in the personal office of oral and maxillofacial surgeon Dr. Hamed Nazari using the standard surgical method. Alveolar and lingual nerve block anesthesia was injected with prazocaine, each milliliter of this injection solution contains 20 mg of lidocaine hydrochloride and 12.5 micrograms of epinephrine (as bitartrate).

Procedure

The principles and steps of extracting impacted teeth are similar to surgical extraction of other teeth:

First step: Creating adequate access to the impacted tooth by placing a flap. The soft tissue flap should be of sufficient length.

The second step: removing bone from the tooth as much as needed.

Third step: sectioning the tooth if needed or creating a catch point.

Fourth step: extracting the tooth from the alveolus.

The fifth step: smoothing the bone sharps, abundant washing and suturing the wound, the flap was closed by 0.3 silk thread, and finally a gauze was placed in the surgical site as a compress for 30-45 minutes (94).

Intervention

Ketorolac 30 mg (Alborz Company, Iran) was injected into the mesenteric or internal pterygoid muscle immediately after anesthesia injection. The surgery was performed by the same surgeon. Anesthesia procedures were performed for all patients with the same protocol. After work, the patients were given painkillers (acetaminophen 325 mg) and the same antibiotic (amoxicillin 500 mg and metronidazole 250 mg, one every 8 hours for 7 days). Patients who had bilateral surgery were considered at least 15 days apart between each surgery and were included in the study for only one of the surgeries.

Outcome evaluation

Outcome evaluation was done in 2 specific time periods. The first time was two days after the surgery and the second time was 7 days after the day of surgery. The evaluation was based on the severity of pain, trismus, edema, patient satisfaction with the surgery and questions about the changes in the patient's daily life in the days after the implanted tooth surgery [12]. Patient evaluation after surgery was self-

reported by the patient. On the specified days, the doctor who determined the outcome called the patient and asked the patient for a clinical evaluation report. Before the surgery, the patient was given a brochure in which all the investigated outcomes were described in detail.

Results and Discussion

Descriptive information

84 people participated in this study. The mean (SD) age of the participants was 25.26 ± 5.28 years and most of the participants (58.3%) were women. In Table 1, the demographic and basic characteristics of the participants of the two groups are compared. According to Table 1, as can be seen, there was no significant difference between the two groups under study in terms of the basic variables affecting the outcome, including the average duration of surgery and the average score of work difficulty, with randomization in the allocation of samples. Although there was a significant difference in terms of age, this difference was about 3 years and can be ignored

Table 1. Demographic characteristics of the groups under study

Variable	Masseter muscle	Pterygoid muscles	p-value
Mean (SD) age	26.55 (5.26)	23.97 (5.04)	0.025
Mean (SD) duration of surgery	7.74 (2.1)	9.90 (2.85)	0.132*
Mean (SD) difficulty of surgery	1.7 (0.45)	1.6 (0.48)	0.489
Gender, abundance (percentage)			
Man	16 (38.1)	19 (45.2)	0.507
Woman	26 (61.9)	23 (54.8)	0.507

Examining the average pain intensity

The average pain intensity after surgery in the ketorolac injection group in the pterygoid muscles and the ketorolac injection group in the master muscles are different. According to Table 2, as can be seen, although the average pain score on the second day in the pterygoid injection group

was slightly lower than the master group, but this difference was not statistically significant ($p=0.876$). According to Table 3, as can be seen, although the average pain score on the seventh day in the pterygoid injection group was slightly lower than the master group, but this difference was not statistically significant ($p=0.156$).

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Table 2. Examination of average pain intensity on the second day between 2 groups.

Group	The number of samples	The average pain on the second day	Standard deviation	The difference between the two groups	p-value*
Masseter muscle	42	4.14	2.74	0.09 (0.61)	0.876
Pterygoid muscles	42	4.05	2.84	0.09 (0.61)	0.876

Table 3. Examination of average pain intensity on the seventh day between 2 groups

Group	The number of samples	The average pain on the seventh day	Standard deviation	The difference between the two groups	p-value*
Masseter muscle	42	1.28	2.14	0.55 (0.38)	0.156
Pterygoid muscles	42	0.74	1.25	0.55 (0.38)	0.156

Examining the average intensity of edema

The average severity of edema after surgery in the ketorolac injection group in the pterygoid muscles and the ketorolac injection group in the master muscles are different. According to Table 4, as can be seen, although the average

score of edema on the second day in the pterygoid injection group was slightly lower than the master group, but this difference was not statistically significant ($p=0.436$). According to Table 5, as can be seen, although the average score of edema on the seventh day in the injection group was slightly lower than in the pterygoid group, this difference was not statistically significant ($p=0.250$).

Table 4. Examination of the average intensity of edema on the second day between the 2 groups

Group	The number of samples	The average edema on the second day	Standard deviation	The difference between the two groups	p-value*
Masseter muscle	42	3.57	1.33	0.26 (0.33)	0.436
Pterygoid muscles	42	3.31	1.72	0.26 (0.33)	0.436

Table 5. Examination of the average intensity of edema on the seventh day between the 2 groups

Group	The number of samples	The average edema on the seventh day	Standard deviation	The difference between the two groups	p-value*
Masseter muscle	42	0.90	1.26	0.40 (0.35)	0.25
Pterygoid muscles	42	1.31	1.88	0.40 (0.35)	0.25

Examining the level of satisfaction of patients after surgery

The average score of patient satisfaction after surgery in the ketorolac injection group in the pterygoid muscles and the ketorolac injection group in the master muscles is different. According to Table 6, as can be seen, although the

average satisfaction score on the second day in the pterygoid injection group was slightly higher than the master group, this difference was not statistically significant ($p=0.341$). According to Table 7, as can be seen, the average satisfaction score on the seventh day in the pterygoid injection group was slightly higher than the master group, which was statistically significant ($p=0.021$).

Table 6. Examining the average satisfaction score of patients in two groups on the second day

Group	The number of samples	The average satisfaction score of patients on the second day	Standard deviation	The difference between the two groups	p-value*
Masseter muscle	42	7.71	1.86	0.38 (0.39)	0.341
Pterygoid muscles	42	8.09	1.78	0.38 (0.39)	0.341

Table 7. Examining the average satisfaction score of patients in two groups on the seventh day

Group	The number of samples	The average satisfaction score of patients on the seventh day	Standard deviation	The difference between the two groups	p-value*
Masseter muscle	42	9.17	1.75	0.67 (0.28)	0.021
Pterygoid muscles	42	9.83	0.54	0.67 (0.28)	0.021

Investigating the incidence of trismus after surgery

The incidence of trismus after surgery is different in the ketorolac injection group in the pterygoid muscles and the ketorolac injection group in the master muscles. According to Table 8, as can be seen, on the second day after surgery, almost 5% of patients in the injection group experienced

trismus in the Master muscle. While the incidence of trismus in the pterygoid muscle injection group was about 7%, this difference was not statistically significant ($p=0.5$). According to table 9, as can be seen, on the seventh day, almost 19% of patients in the injection group experienced trismus in the master muscle. While the incidence of trismus in the pterygoid muscle injection group was about 33%, this difference was not statistically significant ($p=0.136$).

Table 8. Examination of the amount of trismus on the second day in two groups

Group	Having trismus		p-value*
	No	Yes	
Masseter muscle	2 (4.76)	40 (95.24)	0.5
Pterygoid muscles	3 (7.14)	39 (92.86)	0.5
Total	5 (5.95)	79 (94.05)	0.5

Table 9. Examination of the amount of trismus on the seventh day in two groups

Group	Having trismus		p-value*
	No	Yes	
Masseter muscle	8 (19.05)	34 (80.95)	0.136
Pterygoid muscles	14 (33.33)	28 (66.67)	0.136
Total	22 (26.19)	62 (73.81)	0.136

Examining the average opening of the mouth after surgery

The average maximum opening of the mouth after surgery is different in the ketorolac injection group in the pterygoid muscles and the ketorolac injection group in the master muscles. According to Table 10, as can be seen, the average maximum mouth opening on the second day in the

pterygoid injection group was slightly higher than the master group, which difference was not statistically significant ($p=0.125$). According to Table 11, as can be seen, the average maximum mouth opening on the seventh day in the pterygoid injection group was slightly higher than the master group, which difference was not statistically significant ($p=0.361$).

Table 10. Average mouth opening on the second day in two groups

Group	The number of samples	The average mouth opening on the second day	Standard deviation	The difference between the two groups	p-value*
Masseter muscle	42	25.64	9.31	2.97 (1.92)	0.125
Pterygoid muscles	42	28.62	1.27	2.97 (1.92)	0.125

Table 11. Average mouth opening on the seventh day in two groups

Group	The number of samples	The average mouth opening on the seventh day	Standard deviation	The difference between the two groups	p-value*
Masseter muscle	42	31.14	9.65	1.71 (1.86)	0.361
Pterygoid muscles	42	32.85	7.28	1.71 (1.86)	0.361

In the last century, due to the change in diet, the third molar tooth has often become embedded, and this embedment has caused problems such as caries, pericoronitis, pressure on the second molar and its root erosion, periodontal problems, etc. in people. Therefore, it is one of the proposed treatments and individual preferences in surgery and removal of the impacted tooth of the third molar [4-7]. But this surgery causes trauma to the hard and soft tissue due to the variations of the impaction of the third molar, which, apart from the difficulty of work for the dentist

and psychological pressure and stress for the patient, has a series of complications after surgery, which can be referred to lower alveolar nerve paresthesias, pain, swelling, trismus, etc.; these complications themselves have changed the living conditions and created limitations in the social activities of the person, and this causes the person's reluctance towards third molar surgery [7-9].

Implanted third molar surgery is one of the most common dentoalveolar surgeries, which brings a degree of post-operative discomfort, which affects the patient's quality of life

in the days after the operation [14]. This surgery causes trauma to the soft and hard tissue, and against the trauma, the body gives a physiological response, which is manifested in the form of inflammation and pain [19]. Pain is one of the most common complaints of humans. It is said that the pain caused by third molar surgery is one of the most painful surgeries [8]. This pain is mainly caused by the inflammatory response [11]. Although our body needs inflammatory processes to heal, excessive inflammation can cause complications such as pain, trismus, and swelling. Although these side effects are transient, they can make the patient anxious and uncooperative [20-22]. Treatment and planning for pain before the onset of pain and its spread is a wise approach because a lot of pain makes the patient uncooperative and also makes the work more difficult for the surgeon [13].

There are countless ways to manage pain and discomfort caused by third molar surgery [23-25]. One of the methods is to prescribe non-steroidal anti-inflammatory drugs and some narcotics before surgery to reduce postoperative pain [26-29]. It has been suggested that the administration of analgesia before the onset of the painful stimulus can replace the treatment for pain after third molar surgery. Ketorolac is an NSAID, which oral or injectable use of this drug creates a strong analgesic effect by inhibiting postaglandins, fat and pain-enhancing acids, which is used to treat moderate to severe pain [30]. Ketorolac has moderate anti-inflammatory activity [31]. Also, Ketorolac, with its long-lasting analgesic activity, can replace opioids in some conditions, including mild to moderate postoperative pain [31].

Although the oral route of drugs has been investigated as a more comfortable route for patients, its effectiveness is unpredictable compared to other non-oral-gastrointestinal routes such as the injection method [32-34]. Surgical investigations have proven that the intramuscular route is a better route for drug administration compared to the oral route based on plasma drug concentration and the effect of anti-inflammatory activity [35-37]. On the other hand, this method is relatively easier for the surgeon because the injection is performed in the vicinity of the surgical area that is under local anesthesia with lidocaine solution in the mastic area, and the terminal branches of the mastic nerve become numb after the long buccal block [17]. A small number of studies investigated the favorable effect of injection in the mesenteric and internal pterygoid muscles to reduce pain,

swelling and trismus after mandibular impacted third molar surgery. This issue prompted us to evaluate the mesenteric and internal pterygoid muscles as effective sites for ketorolac injection.

The purpose of this study was to investigate the effect of ketorolac injection before surgery on reducing or eliminating complications after treatment in order to find the best position for intramuscular injection of the drug near the surgical site. In this way, the level of annoyance and dissatisfaction of the person is reduced so that the person can go to surgery without facing problems and complications after the treatment. In the present study, both Mister and Pterygoid groups had no significant differences in pain reduction, maximum mouth opening, trismus, and swelling after surgery, and the only significant difference was in the satisfaction parameter of patients after surgery on the seventh day [35-37]. Thus, patients receiving ketorolac reported more satisfaction in the internal pterygoid muscle than in the master muscle. Selvaraj et al. [17] in a study that examined the comparative effect of methylprednisolone injection in the gluteus medius and gluteal muscles in mandibular implanted third molar surgery, reported that there was no significant difference between injections in the gluteus medius muscle in reducing postoperative complications, which was consistent with our study in terms of similar results regarding the difference in the injection site. Mangalgi et al. [3] in a study that examined the analgesic effects of intramuscular injection of ketorolac versus tramadol in minor oral surgeries, showed that the group receiving intramuscular ketorolac experienced less pain compared to the group receiving tramadol, which results were consistent with our study in terms of the effectiveness of intramuscular injection of ketorolac. Shirani et al. [12] investigated the effect of dexamethasone injection in the internal pterygoid and gluteal muscles on reducing complications after third molar surgery. They reported that injection of this substance reduced postoperative complications, but although the internal pterygoid group had less change in mouth opening, but there was no difference between the two injection sites, which was consistent with our study in terms of no significant difference between the two injection sites. Dereci et al. [38] in a study that investigated the effect of immediate intramuscular injection of dexamethasone on swelling after mandibular impacted third molar surgery, they reported that the injection of dexamethasone in the masticator muscle was effective in

reducing the swelling after surgery of the third molar of the mandible, which also shows the suitability of the masticator muscle for injection of anti-inflammatory drugs. Sabhlok et al. [39] in a study that examined the effect of oral dexamethasone versus intramuscular dexamethasone (intramuscular), showed that the group receiving oral dexamethasone had a significant difference in the effective opening of their mouths, which was inconsistent with our study. Nandini [40] in a study that examined the effect of intramural injection of dexamethasone after the extraction of the third molar of the mandible, reported that the injection of dexamethasone in the master muscle is more effective than its systemic use, and the injection in the master muscle is simple, non-invasive, painless and more comfortable for the surgeon and the patient, which was consistent with our study from the point of view of easier injection in the master muscle [35-37]. Chemical and herbal painkillers can also be used in cases of jaw and tooth pain [41-43].

Conclusion

The results of this study proved that there is no significant difference in the results of pain, swelling, trismus and maximum opening of the mouth between the two groups of ketorolac injection in the master muscle and the internal pterygoid muscle. The only significant difference in the parameter of patients' satisfaction after surgery was on the seventh day, so that patients receiving ketorolac reported more satisfaction in the internal pterygoid muscle than in the master muscle. In general, the results regarding the difference in the injection site were very close to each other. Although by randomization between the two nodes, similarity was created in terms of difficulty and duration of surgery, but the sample size was not enough, so it is better to conduct research with a larger sample size to prove our results.

Competing interests:

None.

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