

## Investigating the effect of topical vancomycin on the rate of recovery and complications after mandibular third molar surgery

### Abstract

Third molar surgery is one of the most common surgeries performed to treat problems caused by impacted teeth. The use of vancomycin along with tobramycin polymethyl methacrylate topically has been successful in the treatment of chronic osteomyelitis and reducing the recurrence of osteomyelitis, and reducing pus drainage in maxillofacial. The present study investigates the effect of vancomycin on oral function and complications after mandibular impacted and partially-impacted third molar surgery. This study was a double-blind clinical trial (Surgeons, nurses, and patients were unaware of the type of medicine) conducted on patients who were candidates for mandibular impacted tooth surgery and were referred to the Kerman Faculty of Dentistry in 2022. In this regard, 40 patients with the same demographic characteristics and ASA conditions were randomly assigned to two groups of 20 people. One group did not receive any topical antibiotics (normal saline-impregnated Gelfoam) in the bone in the surgical site of the third molar of the mandible before closing the wound. The second group received 1 mg of vancomycin topically (Antibiotic-impregnated Gelfoam) in the existing bone defect. Then, the patients were compared in terms of pain severity and improvement of function and other complications one day after and the first week after surgery through a developed questionnaire. Based on the analysis and the results, the topical use of vancomycin antibiotic in the mandibular molar surgery improves the opening of the mouth one day after the procedure and the ability to return to a normal diet one day after surgery (mouth function) (two patients from the control group versus 5 patients from the control group). An improvement in the soft tissue was observed one week after surgery (6 patients had relatively complete recovery in the control group) and the need for debridement and drainage and systemic antibiotics (2 patients from the control group and none of the patients from the control group) during the first week. It was also effective in reducing pain within one day to one week after surgery. Accordingly, all patients have no pain or little pain for one day to one week after surgery in the control group. The effect of topical vancomycin on improving the ability to pronounce letters and improving mouth opening one week after surgery and the occurrence of dry socket, and debridement at the surgical site was not significant and effective in this project.

**Keywords:** *Vancomycin, Molar surgery, Trismus*

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### Introduction

Impacted tooth surgery is effective in improving pericoronitis, second-molar periodontal problems, second and third-molar caries, neurological pain, odontogenic cysts, and prosthetic and orthodontic procedures (1). It is one of the common surgeries with few complications among referring patients (26). The majority of these complications regarding the swelling of the area are pain, swelling, infection, trismus, and alveolar osteitis. They finally lead to discomfort and an increase in morbidity. Thus, clinicians are very interested in finding ways to reduce these problems (28). Based on a study by Sisk et al., the prevalence of alveolar osteitis was reported between 0.4% and 17% (2). Based on a study by Cochran Maria et al., dry socket is one of the most common complications after tooth extraction. All articles have made efforts to relieve the patients' pain and activate the mucus as much as possible in the healing of the area. A number of these articles have reported the use of topical antibiotics can be effective in improving it (29).

Based on a study by Phillips et al., alveolar osteitis and site infection were mentioned as the causes of delayed recovery after mandibular third molar surgery (5). Based on a

retrospective study by Piecuch et al., the rate of wound infection after surgery was reported from 3.5% in the erupted wisdom tooth to 26.5% in the impacted tooth (covered by bone) (3,4). Also, the purposeful use of antibiotics along with third molar surgery has been recommended for patients with a high risk of delayed recovery (6). A delayed recovery means the patient's re-visit along with therapeutic measures such as antibiotic therapy or the use of analgesics, reopening the wound for debridement, or covering the wound site (8). Vancomycin is an actinobacteria-produced glycopeptide, which is effective against gram-positive bacteria (31). The studies conducted on the effectiveness of topical antibiotics have yielded conflicting results. In this regard, Alexander considered its use to be ineffective. However, Piecuch et al. stated that its effectiveness is equal to that of systemic antibiotics (6,7). Based on the study by Mary et al., the topical use of minocycline in third molar surgery reduced the incidence of complications and delayed recovery in risk patients (9).

Additionally, some studies conducted in Europe have introduced new and favorable methods of receiving antibiotics (instead of using old parenteral methods such as antibiotic-

impregnated beads containing vancomycin and tobramycin) for better management of chronic osteomyelitis (10). Patients' experience of health and disease after wisdom tooth surgery can be measured by a questionnaire that assesses health-related quality of life (HRQOL) (11). The use of systemic and local antibiotics in third molar surgery in high-risk patients to improve clinical quality and increase HRQOL has reduced the delay in recovery (12). HRQOL has been developed to evaluate recovery, pain severity, lifestyle, oral function (including the maximum opening of the mouth and chewing and ability to speak and return to normal diet), and other symptoms after molar surgery. Based on a study by Federico Solla et al. on SSI (surgical site infection) in pediatric orthopedic surgery, the use of topical vancomycin along with increased washing of the surgical site with two liters of normal saline improved this index (15). Moreover, the study by Kalil et al. revealed that the topical use of vancomycin powder was effective in reducing SSI in cranial and spine surgeries (30). Based on a study by Harold, the effect of topical antibiotics (tetracycline and metronidazole) and chlorhexidine in improving periodontitis in dogs was examined. Results showed that tetracycline was effective in reducing bone resorption if used for a long time. It was also found that metronidazole was more effective than tetracycline in improving swelling and reducing spirochetes (16). Based on a study by Mallet et al. on the impact of the simultaneous use of vancomycin powder and PVP-irrigation, an improvement was observed in the SSI in patients with scoliosis after spine surgery (17). Based on a cohort study by Martin et al. (2014) on the effect of topical vancomycin powder in spinal deformity surgeries on 306 patients with skeletal deformity, no significant differences were observed between the use and non-use of this antibiotic regarding the occurrence of SSI. Using other treatment modalities along with it is necessary to make it effective (18). In the studies conducted by Chohfi et al. on the use of vancomycin-loaded bone cement, 3 g of vancomycin was mixed in every 60 g of cement. The results showed the bone surface in an animal study receiving this compound during the first trimester was tripled. Also, the blood level of vancomycin was 30 times lower than the toxic level in patients who underwent hip arthroplasty and received vancomycin-loaded bone cement as a prophylactic antibiotic. After ten days, no level of vancomycin was found in the blood (19). In a study by Kalil et al., the topical use of vancomycin caused systemic complications in only two patients out of more than 2000 patients (30).

Given what was stated, the present study investigated the effect of topical vancomycin on the recovery and complications after mandibular third molar surgery in patients referred to the Kerman Faculty of Dentistry in 2022-2023. The implementation of this project to improve function and return

to normal life, and quality of life of patients undergoing mandibular molar surgery can be effective in reducing pain and complications after surgery.

### **Materials and Methods**

The present study was a double-blind clinical trial. The statistical population of the study included the patients who are candidates for surgery on the impacted and partially-impacted mandibular teeth and were referred to the Faculty of Dentistry in Kerman in 2022. The inclusion criteria of the study were being male, being in an age range of 20 to 30 years, ASA I without systemic disease or controlled systemic disease, having mesioangular impacted third molar, and having surgery time of less than one hour. The exclusion criteria of the study also included having a history of allergy to vancomycin and local anesthetics, chronic use of narcotics, pregnancy, breastfeeding, history of heart failure, and liver and kidney CHF, users of ACEI, either controlled or uncontrolled hypertension, uncontrolled hypertension, and heart rate less than 50. Data were collected by questionnaire.

In this regard, 40 patients were selected using a convenience sampling method and they were randomly assigned to two groups of 20 people using random table numbers. The pain severity was evaluated using the visual analog scale (on a scale of 0 to 10). Other factors were examined as (0) = absence of symptoms and (1) = presence of symptoms. After the approval of the ethics committee and obtaining informed consent from the patients and providing complete explanations about the study, the patients were classified into two groups (patients without topical antibiotics at the third molar surgery site of the mandible and patients with topical vancomycin at the third molar surgery site). In both groups, absorbable gel foam was placed in the surgical site. In the control group, the gel with dimensions of 8 x 5 x 8 cubic millimeters (soaked with 0.9% normal saline (washing serum), and in the intervention group, sterile gel foam impregnated with the solution obtained by mixing 20 ccs of distilled water with a sterile vancomycin 1 mg vial (all gel foam 8 x 8 x 10 cubic millimeters was impregnated with powder were placed topically in the exposed bone. The surgery was performed under local anesthesia by the same operator. After the surgery, the subjects consumed 15 antibiotic amoxicillin capsule 500 mg every eight hours for five days and chlorhexidine mouthwash 0.20% three times a day (washing mouth once every eight hours), acetaminophen tablet 500 mg, and ibuprofen 200 mg orally every eight hours up to 3 days (9 tablets). Then, the patients were compared regarding pain severity and improvement of function and other complications the next day (24 hours after surgery) and the first week after surgery.

To analyze the data, the frequency, relative frequency, and the central index of the mean were used for descriptive statistics and the chi-square test, independent t-test, relative risk, and

repeated data test were used for analytical statistics. SPSS 20 software was used to analyze the results. In the present study, the oral function is defined as the pronunciation of letters, trismus (limitation in the maximum opening of the mouth), and the ability to chew with a normal diet. Among the 40 participating patients, none of them had problems pronouncing the words. Pronunciation ability in the two groups shows that there is no significant difference between the antibiotic-treated group and the antibiotic-free group regarding pronunciation ability on the day of surgery and one week later (P-value = 0.14)

Among the 40 patients, 7 patients (17.5%) had mild trismus one day after surgery that 5 patients (12.5%) were in the antibiotic-free group and 2 patients (5%) were in the antibiotic-treated group. Only one patient from the antibiotic-free group had mild trismus after the first week (2.5%). Comparing the level of trismus in two groups showed that there was a significant difference between the antibiotic-treated group and the antibiotic-free group on the day of surgery in terms of improving mouth opening (p-value = 0.033) and the study groups did not show a significant difference regarding improving mouth opening in the first week after surgery (p-value=0.14). Table 1 shows the results of dental flexion.

Table 1- Dental flexion results

Group	Dental flexion		
	Ability to pronounce letters	Restriction in opening the mouth	Restriction in chewing
Antibiotic-free	20 (100%)	5 (12.5)	5 (12.5)
Typical antibiotic	20 (100%)	2 (5%)	2 (5%)

Table 2 shows the symptoms of each group.

Table 2- Results of other symptoms

Group	Other symptoms			
	Debridement on the site	Pus drainage	Dry socket	Recovery of soft tissue
Antibiotic-free	0%	2 (5%)	0%	0%
Typical antibiotic	0%	0%	0%	6 (15%)

Based on Table 2, no patient had any debridement in the surgical site and dry socket. There was no significant difference between the two groups regarding the surgical site and dry socket (p-value=0.11). Out of the 40 patients, 2 patients (5%) from the antibiotic-treated group had pus drainage in the first week after surgery, and they underwent systemic antibiotic therapy and debridement and drainage. Comparing the amounts of pus drainage in two antibiotic-free and antibiotic-treated groups showed a significant relationship

(p-value=0.043). No patients in antibiotic-free and antibiotic-treated groups had pus drainage on the day after the surgery (p-value=0.11). Among the 40 patients, 6 patients in the antibiotic-treated group within the first week of soft tissue recovery had no bone exposure. The comparison of the healing rate of soft tissue in the two groups shows a significant difference between the study groups regarding the healing rate of soft tissue in the first week (p-value=0.038). Table 3 shows the treatments performed.

Table 3- Treatments performed

Group	Treatments performed		
	Wound debridement	Systematic antibiotic	Drainage

Antibiotic-free	2 (5%)	2 (5%)	2 (5%)
Typical antibiotic	0%	0%	0%

Table 4- Results of pain severity

Group	Pain severity		
	Low pain (no pain)	Moderate pain	Severe pain
Antibiotic-free	16 (40%)	3 (7.5%)	1 (2.5%)
Typical antibiotic	20 (100%)	0%	0 %

As seen in Table 4, out of 40 patients, all patients receiving vancomycin mentioned no pain and low pain. Among the antibiotic-free patients, 3 patients reported moderate pain and one patient reported severe pain one day after surgery. Only two patients from the antibiotic-free group had low pain in the first week after surgery. Comparing the two groups regarding the pain severity showed a significant difference between the antibiotic-free and antibiotic-treated groups regarding the pain severity one day after the surgery ( $p$ -value= 0.047). There was a significant difference between the two groups regarding pain severity in the first week after surgery ( $p$ -value=0.043).

#### Discussion and Conclusion

Since mandibular third molar surgery is one of the most common procedures performed by oral and maxillofacial surgeons, identifying the risk factors and complications after surgery and medical methods to reduce these complications have always been discussed (20). In this regard, in the study by Gary et al., one-third of 480 patients who were candidates for maxillary molar surgery suffered from pain and swelling after the surgery (21). However, in our study, all patients who were treated with topical antibiotics at the surgical site had mild pain and 10% of patients had moderate to severe pain, all of whom were treated with gel foam impregnated with normal saline without topical antibiotics.

Based on the study by Sanchis et al. regarding the effect of topical tetracycline in the socket extraction of the third molar of the mandible, local application of tetracycline does not affect the occurrence of dry sockets. However, it has a positive effect in reducing swelling and pain after the procedure (22). In the conducted study, topical application of vancomycin showed no significant positive or negative effect on the occurrence of dry sockets. Reekie et al. conducted a double-blind randomized clinical trial on 302 patients undergoing mandibular molar surgery. Among them, 23 patients had alveolar osteitis, eight of whom had metronidazole gel in the

socket and 15 received a placebo. Consistent with our study, the results showed that topical antibiotics are not very effective in improving dry sockets (27).

In the study conducted by Indranil et al. to examine the effect of topical tetracycline on pain relief and increasing the speed of wound healing after mandibular molar extraction on 72 patients, results showed that tetracycline, thanks to its anti-inflammatory properties, reduced pain and the need for analgesics and increased healing speed in patients receiving topical antibiotics. In this regard, the antibiotic-free group of patients needed Zeroldol tablets twice a day for three days. However, the antibiotic-treated group used analgesics in the SOS form (23). This result is consistent with the result of our study. Based on the data analysis, the topical application of vancomycin in the socket along with gel foam reduced the pain and increased the healing speed of the tissue in the surgical site. Elitsa et al. examined the complications after mandibular third molar surgery, trismus was a normal and expected finding after this procedure, and to facilitate its evaluation, the authors found a 5 mm difference in mouth opening before and after surgery to be reliable (24). There is a strong relationship between postoperative pain and trismus. Moreover, edema of the surgical site is considered to be the cause of trismus (25). Hence, it can be concluded that topical antibiotics are effective in reducing the occurrence of trismus by reducing postoperative swelling and pain. This result is in line with that of our study. The study conducted by Srinivas et al. examined the effect of antibiotics (systemic or topical) on the occurrence of infection after mandibular molar surgery. The results showed that the use of antibiotics is effective in reducing the occurrence of infection and thus the need for debridement and drainage (26).

The study by Mary et al. used minocycline topically in the surgery of 63 patients and showed that only ten patients had pain for one session and no patients in the intervention group

had the second visit. However, the patients in the control group had one re-visit session and 13% of them had a second visit ( $p=0.01$ ). Based on the mentioned study, chewing improved, and maximum mouth opening (9) was observed in the antibiotic-treated group patients ( $p<0.05$ ), which is consistent with the results of the present study on the effect of topical vancomycin in improving the chewing ability and the degree of mouth opening. Based on the results, it is recommended that similar studies be conducted in the future on a larger statistical population and in several centers to clarify the role of environmental conditions on the rate of infection. Moreover, it is recommended to examine the effect of other antibiotics to reduce complications after surgery. Finally, it is recommended to conduct separate studies on the conditions, manner, and duration of the operation and its relationship with the rate of infection and post-operative complications.

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