

Effect of 1% Metronidazole Rinsing Solution on the Occurrence of Complications after Tooth Extraction: A Clinical Trial Study

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ABSTRACT

Introduction: Extraction of impacted third molar is a very common operation performed by dentists and oral and maxillofacial surgeons. This surgery is usually done without complications occurring; however, some complications arise from time to time. The aim of this study was to evaluate the effect of 1% metronidazole rinsing solution on the occurrence of complications after extraction of impacted third molars.

Materials and methods: In this clinical trial study 120 males and females aged 20 to 35 took part, randomly divided into two groups, each including 60 participants. In the case group, mandibular third molar socket was rinsed with 1% metronidazole rinsing solution in duration of the surgery extraction, while normal saline was used for the control group. Afterwards, four common complications—dry socket syndrome, swelling, pain and trismus - were evaluated at 24 hours, 3, 7 and 14 days following the operation. Data were analyzed with Mann-Whitney and t-test using SPSS software version 16.

Results: Except for pain 24 hours after the operation, none of the differences between the two groups were statistically significant ($p \leq 0.05$).

Discussion: The results of this study show that using 1% metronidazole rinsing solution is not helpful in decreasing the occurrence of complications after extraction of an impacted third molar. It is therefore not recommended to use this solution until advantages are proved to prevent bacterial tolerance.

Keywords: Complications of extraction, Metronidazole, Third molar.

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INTRODUCTION

Extraction of an impacted third molar is one of the most common surgery procedures; it is done daily by many general dentists and maxillofacial surgeons. Each year about \$150 to 400 million is spent on extraction of impacted third molars in the United States and this amount reaches to about £50 million in the United Kingdom.^{1,2}

Extraction of impacted teeth, especially third molars, is considered the most common procedure in the field of

maxillofacial surgery.³⁻⁵ Usually, some interventions are required prior to extracting these impacted teeth due to some difficulties in their eruption.⁶ Extraction of impacted third molars can sometimes cause unwanted complications, such as pain, bleeding, infection, paresthesia, temporomandibular disorders, abscess formation, trismus and dry socket syndrome.⁶⁻¹⁰ The incidence rate of surgery related complications have been reported to range from 4.6 to 30.9%.^{3,11} Surgeons should inform all patients about possible complications, allowing patients to accept complications more easily and to seek for appropriate treatment.³

Some factors like age, gender, drugs such as antibiotics, corticosteroids and oral contraceptive pills, smoking, previous infections, periodontitis, poor oral hygiene, previous surgery, duration of surgery, inadequate irrigation, number of extracted teeth and anesthesia technique can affect the severity and rate of complications, such as dry socket syndrome.^{12,13} Some researchers have emphasized the role of anaerobic bacteria in wound infections; therefore antibiotics, such as metronidazole (5-nitroimidazole) have attracted the attention of researchers.⁸ These can be prescribed in many different fields of surgery. Due to the high capacity to suppress anaerobic bacteria, parasites and nonspecific infections, this drug can be used to prevent and treat oral infections.^{14,15} Some researchers also know this drug as an appropriate antibiotic after oral surgeries and declare this drug to be effective in the prevention of complications after extraction of impacted teeth.^{15,16} Also, this drug is effective to prevent and treat dry socket syndrome. However, the efficacy of this drug has not been assessed with local use of the antibiotic for the prevention of dry socket. Therefore, this study has been conducted in order to investigate the effect of metronidazole 1% rinsing solution on the occurrence of complications after extraction of impacted third molars.

MATERIALS AND METHODS

In this is clinical trial study, 120 male and female patients aged between 20 and 35, who had been referred to the Maxillofacial Department of Dentistry School of Isfahan University of Medical Sciences were selected. At first all of the patients were examined and evaluated based on panoramic radiographs (if required) and they were included,

if having a mesioangular mandibular impacted third molar with B form and Pell and Gregoty class 1, acceptable oral hygiene and normal mouth opening. Patients with abscesses, cellulitis, pericoronitis, xerostomia, antibiotic consumption, previous history of radiotherapy, pregnancy, allergy to metronidazole, systemic disease, cancers or smoking history were excluded from the study. Finally, all of the patients were randomly divided into two groups with 40 females and 20 males in each group.

In the case group, 1% metronidazole solution was used for irrigation during the extraction procedure of the impacted tooth, while in the control group normal saline was used for irrigation. The most common complications after surgery were assessed after 24 hours, 3 days, 1 and 2 weeks' time. These complications were dry socket syndrome, pain, trismus and swelling.

Metronidazole Rinsing Solution Preparation

Metronidazole was solved in propylene glycol 10% and then mixed with ethanol 10% and methylparaben 15%. Finally, was increased to 100 cc with ultrapure water.

Ethical Considerations

This study has been ethically approved by Isfahan Dental School (No.390016). Nevertheless, the patients were informed about the process, complications and they all filled out written consent forms. This study has been documented in Iranian Registry of Clinical Trials (IRCT) website.

Surgery Procedure

In this study, the surgery of impacted tooth extraction was performed by one of the residents of maxillofacial surgery. Before surgery, all patients were informed about possible complications of the surgery. Local anesthesia was performed by inferior alveolar nerve block and buccal infiltration technique with 2% lidocain solution and 1/100000 epinephrine (Aria, Tehran, Iran). A mucoperiosteal flap was created and the bone was removed by a round bur. If needed, the tooth was cut to pieces by fissure bur. Bone removal and tooth cutting were done under copious irrigation with normal saline in the control group and with 1% metronidazole in the case group. After removal of the impacted tooth and wound irrigation, the mucoperiosteal flap was repositioned precisely and sutured with 4-0 vicryl. After the surgery, for all patient 400 mg ibuprofen was prescribed three times a day for 5 days to ensure adequate pain control.

Evaluating Dry Socket Syndrome

This complication is defined by a dull and severe pain at the site of surgery 3 to 5 days after surgery. At this time,

most of the pain and swelling due to trauma have faded away and the main reason for pain is alveolar osteitis. The presence of severe pain, halitosis and the lack of blood clot in the socket are known as dry socket syndrome.

Trismus Evaluation

In this study, if 24 hours after surgery patients could not open their mouth more than 25 mm, trismus was considered to be a complication.

Swelling Evaluation

Swelling was measured clinically with the presence of obvious facial asymmetry.

Pain Evaluation

To evaluate patients' pain after surgery, the visual analog scale (VAS) was used. According to this scale, patients scored their pain from 0 to 10, with 0 representing absence of pain and 10 representing maximum and nontolerable pain.

All results were assessed by Mann-Whitney and independent t-statistical indexes using SPSS software version 16.

RESULTS

In this study, 60 people were included in the control group (mouth irrigation during surgery with normal saline) and 60 people in the case group (mouth irrigation with 1% metronidazole during surgery). In each group 40 of the participants were women. The participants' age ranged between 20 and 35 years.

For dry socket syndrome, there was not any significant difference between the two groups' incident frequency was found in any of the time intervals ($p < 0.05$). Table 1 shows the incident frequency of this complication at all-time intervals.

For trismus, the frequency difference between the two groups was not statistically significant either ($p < 0.05$). Table 2 represents the frequency and frequency rate of this complication in each group at all-time intervals.

For swelling, there was no significant difference between two groups in differential times ($p < 0.05$). Table 3 shows the frequency and frequency rate of this complication in both groups.

Difference in pain after extraction of impacted third molar between both groups measured by VAS was statistically meaningful only after 24 hours and did not show significant difference at the other three intervals ($p < 0.05$). Table 4 shows distribution indexes of this complication in all time intervals.

Table 1: Incident frequency rate of dry socket syndrome in both groups

14 days		7 days		3 days		24 hours		Time/groups
Percentage frequency	Frequency							
16.66	10	20	12	16.66	10	—	—	Normal saline
13.33	8	16.66	10	13.33	8	—	—	1% metronidazole
0.611		0.363		0.611		—		p-value

Table 2: Frequency and frequency rate of trismus in both groups

14 days		7 days		3 days		24 hours		Time/groups
Percentage frequency	Frequency							
3.33	2	23.33	14	66.66	40	90	54	Normal saline
0	0	33.33	20	70	42	86.66	52	1% metronidazole
0.156		0.113		0.687		0.611		p-value

Table 3: Frequency and frequency rate of swelling in both groups

14 days		7 days		3 days		24 hours		Time/groups
Percentage frequency	Frequency							
3.33	2	6.66	4	60	36	90	54	Normal saline
3.33	2	13.33	8	60	36	80	48	1% metronidazole
1.000		0.225		1.000		0.159		p-value

Table 4: Distribution indexes of pain in both groups

2 weeks		1 week		3 days		24 hours		Time Scale
1% metronidazole rinsing solution	Normal saline							
0.83	0.83	1.30	1.90	3.02	3.60	2.20	4.05	Mean
0.5	0	0	0	2.5	3	0	4.5	Median
1.321	1.932	2.403	3.107	2.943	3.026	2.797	3.026	Standard deviation
0.272		0.239		0.287		0.001		p-value

DISCUSSION

Extraction of impacted third molars is one of the most common surgical procedures that is done daily by general dentists and maxillofacial surgeons.¹⁷ Usually, extraction of impacted teeth does not cause serious complications, but some procedures lead to serious complications. The most common complications after surgery are paresthesia, pain, bleeding, dry socket syndrome and infection. Other complications, which are less common, include severe trismus and iatrogenic accidents that may lead to mandibular

fracture and damage to the second molar.^{9,10} The incidence rate of surgery related complications has been reported to range from 4.6 to 30.9% in some studies.^{3,11} The results of this study showed that except for pain reduction in the first 24 hours, 1% metronidazole irrigation solution does not cause any significant reduction for other complications ($p < 0.05$).

In the study by Sekhar C et al, 124 patients between 19 to 36 years were divided in three groups—one placebo group, one group given 1 gm of metronidazole orally 1 hour

before surgery and a third group given 400 mg metronidazole every 8 hours for 5 days. Complications, such as pain, swelling, trismus and wound healing were assessed. No difference between each of the groups was found, leading to the conclusion that the use of metronidazole as antibiotic prophylaxis before surgery does not seem to reduce complications.¹⁸ In another study, conducted by Needleman IG, the use of metronidazole gel in periodontal surgery was assessed. From 38 patients who finished the survey, 12 were not cured from periodontal disease and the rest of the patients showed relative improvement. This study could not prove a therapeutic effect of metronidazole gel in periodontal surgery procedures.¹⁹

In a study by Kaziro G in London aiming at investigating the effect of metronidazole compared to an arnica montana herbal medicine in the prevention of impacted third molar postsurgical complications 118 patients were included. In this study, 41 patients had 400 mg of metronidazole twice a day, 39 used arnica montana and 38 of them had a placebo. This study showed that metronidazole tablets are more effective for the control of pain and swelling than arnica montana and placebo. However, metronidazole did not have any effect on the severity and occurrence of trismus.⁸ In the survey in 1980 by Rood J et al from Newcastle University, it was shown that dry socket syndrome may occur in up to 3% of patients. Furthermore, 200 mg of metronidazole pills could prevent the occurrence of dry socket, if used orally before surgery.¹⁶

In another study done by Lloyd C et al in the maxillofacial surgery ward of Boston University, the efficacy of metronidazole pills in the reduction of postsurgical infection as assessed. It was concluded that use of metronidazole pills 2 to 3 times after surgery can reduce the rate of infection, but that this reduction was not significant between patients who took 3 pills instead of 2.²⁰ In 1992, Stoltze K investigated the systematic absorption of 20% metronidazole and concluded that systematic absorption of metronidazole gel is significantly lower than with use of one pill orally.²¹ Pavicic M showed that unlike surgical method, combination of surgery with amoxicillin and metronidazole can eliminate *Actinobacillus actinomyces comitans*.²² An interesting survey was done by Joyston Bechal S and it showed that even though use of metronidazole in periodontal pockets with less than 4 mm depth does not have significant effect in comparison with conventional treatments, it improved the therapeutic effect of conventional treatments in pockets with more than 4 mm depth.²³ Sterry K in 1985²⁴ and Mahmood M²⁵ in 1987 did not find any significant therapeutic effects after consumption of metronidazole combined with curettage in comparing modified flap surgery with placebo.

In none of the mentioned articles, 1% metronidazole solution was used locally after surgery. The contradictive results might be due to different forms of administration and dosage of metronidazole, such as gels, pills and solutions. Metronidazole concentration has a major role in the extent of its therapeutic effects, so the comparison of therapeutic effects of metronidazole in different studies is meaningful only when the concentration of this medicine is equal in different studies. From another point of view, most of the articles did not present any significant effects of postsurgical consumption of metronidazole in preventing complications and it is therefore good practice to stop consumption of metronidazole during or after surgery until definite positive therapeutic effects are proven. Also, bacterial tolerance is expected with common prescription of antibiotics, which is considered a dilemma for public health. As a result, this study, like previous ones, recommends further investigation, both on the preventive effect of metronidazole and regarding side effects and possible bacterial tolerance, while not recommending the use of this drug after extraction of embedded tooth at present.

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