Effect of Ozone Gel on Postoperative Sequelae after Surgical Removal of Impacted Lower Third Molars.

Sherwan Faisal Hamadamin [(1)], Ahmad Abdulla Haider [(1)]

Background and objectives: the study aims to evaluate the efficacy of ozone gel in reducing pain, swelling, trismus and also to evaluate soft tissue healing and dry socket after surgical removal of impacted lower third molars.

Methods: the current study enrolled 50 patients divided randomly in to two equal groups, Group I (study group) received ozone gel intra-socket and oral placebo postoperatively and Group II (control group) received a systemic antibiotic . Clinical examination includes assessment of maximal mouth opening on the day of surgery, panoramic x-ray was used for evaluation of the location and configuration of impacted lower third molars, surrounding bone, mandibular canal and adjacent tooth. Pain and swelling were assessed by visual analogue scale (VAS) and recorded daily for one week by the patients, dry socket was checked at 3rd day postoperatively, maximal mouth opening also was checked at 3rd and 7th day postoperatively and soft tissue healing was checked at 7th day postoperatively.

Results: Results showed statistical significance difference regarding pain and swelling and there was no statistically significant difference regarding maximal mouth opening (trismus), dry socket and soft tissue healing in Group I (study group).

Conclusion: This study concluded that the use of ozone gel was effective in the reduction of postoperative pain and swelling but it was not effective in reducing trismus, dry socket and soft
tissue healing after surgical removal of impacted lower third molars.

Key words: ozone gel, impaction, third molar surgery, pain, swelling, trismus, dry socket, soft tissue healing.

[(1)] Department of Oral and Maxillofacial Surgery, College of Dentistry, Hawler Medical University, Erbil, Iraq.
Corresponding author: Sherwan Faisal Hamadamin
email: sherwandentist86@gmail.com

INTRODUCTION

Surgical removal of impacted lower third molars is one of the most common procedures performed in the field of oral surgery. This procedure needs accurate planning and surgical skills.[1] The reported frequencies of complications after lower third molars removals are between 2.6% -30.9%, the spectrum of complications ranges from the minor expected squeal of postoperative pain and swelling to permanent nerve damage, mandibular fractures, tooth displacement and life-threatening infections.[2] The most common complications of third molar surgery are pain, swelling, dry socket and trismus. Morbidity increases with the age of the patient, position, location of the tooth and duration of the surgical procedure.[3]

Patient discomfort and postoperative swelling limitation may decrease by preoperative use of systemic corticosteroids and ice application extra orally postoperatively for the first day. Some

studies showed that preoperative administration of corticosteroids produces a mild to moderate reduction in edema and improvement in range of motion after third molar surgery. [4]

Recently ozone therapy has been used in medical and dental practice. [5] Ozone therapy is a modern, non-medicated alternative to control post-operative complications.[6] The antibacterial properties of ozone, as well as its efficacy in the treatment of infection, and hemodynamic and anti-inflammatory properties have been demonstrated. [7] The advantages of this treatment are: simplicity of execution, good tolerance of patients, absence of side effects or adverse reactions and high medical-social efficiency. [8] Medications for treating any diseases and complications have some side effects and some patients have resistance to them because of these nowadays scientist making a substitution for this problem. [9]

Ozone gel is oil infused with active oxygen, the oxygen in this substance can inhibit bacteria, fungi and pathogens proliferation and can stimulate tissue regeneration and repair.[10] It is effective against gram-positive and Gram-negative bacteria by creating cell membrane damage, Ozone gel is highly effective against antibiotic-resistant species.[11] this study aimed to evaluate the efficacy of ozone gel in reducing-pain, swelling, dry socket; trismus and to evaluate soft tissue healing after impacted lower third molar surgical extraction.

METHODS:

The presented study was designed as a single-blind comparative prospective clinical study. The study is conducted at the department of oral surgery, College of Dentistry, Hawler Medical University and the department of oral and maxillofacial surgery in Rzgary teaching hospital. Fifty patients of both genders were enrolled in the study from October 2021 to August 2022. All patients had impacted lower third molars indicated for surgical extraction. This study has received approval from the institutional ethics committee of the College of Dentistry/Hawler Medical University.

Consent had been obtained from all the patients.

Inclusion Criteria

Mandibular 3rd molars as assessed by Pell & Gregory scale class II position B

adult patients their ages between 18 – 30 years old

The patients who meet the inclusion criteria were randomly divided in to two groups:

group I (study group): Patients received ozone gel 2 ml inside the socket after the surgery and placebo glucose capsules (Dabur-India) three times daily for one week.

group II (control group): Patients received systemic antibiotics amoxiclav tablets 625mg (HIKMA-Jordanian) three times daily for one week, mouthwash (Wisdom-British) (chlorhexidine gluconate 0.12% two times daily for one week after 24 hours postoperatively) and analgesics ibuprofen (JPM-Jordanian) 400mg two times daily for one week on need after surgery.

Preoperative Evaluation

1. A complete clinical history had been taken at the first visit, with collection of the patients' personal data (name, age, sex, address).
2. Panoramic x- ray is used for the evaluation of the impacted 3rd molar, surrounding bone, mandibular canal and adjacent tooth.
3. Evaluation of the maximal mouth opening preoperatively (day of surgery) by using a Vernia to measure the distance between the incisal edges of upper and lower anterior teeth.

Materials

1. Using Ozone gel (SAFOZ) from URETICI FIRMA TURKISH medical company in the dose of 30 ml in one jar presented in Figure 1.
2. Surgical instruments: presented in Figure 2.

Figure 1: ozone gel

Surgical Procedure

For both groups, a standardized surgical procedure was adopted, a single surgeon performed all surgical procedures to avoid inter-personal differences, which could influence the result, surgery was performed under local anesthesia with lidocaine 2% hydrochloride with epinephrine 1:200.000 (lignospan septodent ,French) using inferior alveolar, lingual nerves block and buccal nerve infiltration-, a three-sided mucoperiosteal flap was utilized. Using blade number 15(Swann Morton - UK), Osteotomy was performed to expose the crown using a low-speed handpiece(NSK-Japanese) with a round head bur(IndiaMart – Indian) and abundant irrigation(Pioneer-Iraq). Tooth sectioning when needed was performed using a highspeed handpiece(Vigor – Chinese) with fissure bur(Crocomed – Chinese). Tooth was delivered and the bone edges were refined, the socket was inspected for any remaining piece of fractured tooth and bone, then irrigated copiously with normal saline. Placing the Ozone gel

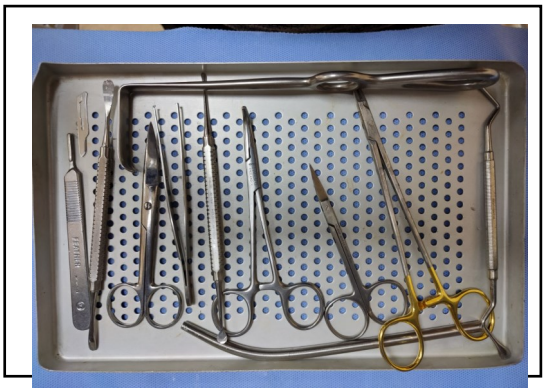
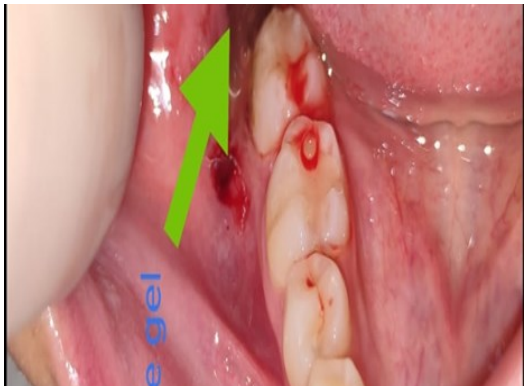


Figure 2: instruments

2ml. inside the socket in group I and secured by suturing as presented in figures 3 and 4 and in group II the socket remains empty and sutured. The flap was sutured back by a silk suture 4-0(Dolphin-India), Placing a gauze (DUKAL-China) over the socket and bite on it for 30 minutes to control of bleeding. Instruct the patients to have a soft and cold diet and not to eat on the site of suturing at least 24 hours post operatively. prescribing a medicine for the patients of group II (control group), antibiotic (amoxiclav 625 mg three times daily for one week), mouthwash (chlorhexidine gluconate 0.12% two times daily for one week after 24 hours post operatively) and analgesic (ibuprofen 400mg two times daily for one week on need) and for the patients of group I (study group) we were used placebo capsules three times daily for seven days and follow up.

Figure 3: Ozone Gel Inside the Socket



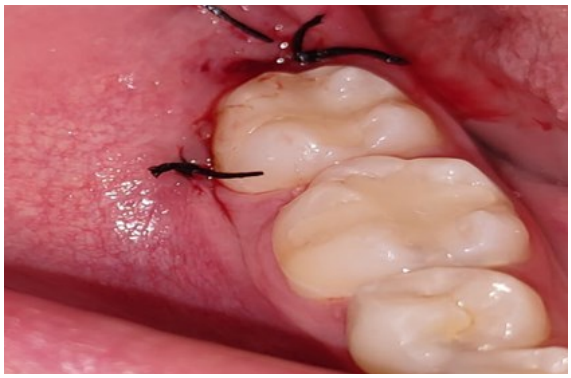


Figure 2: instruments

Post-Operative Observation:

The patients were recalled on 3rd and 7th days postoperatively for checking of dry socket (on 3rd day) and maximal mouth opening (trismus) with a daily recording of (pain and swelling) by the patient for one week postoperatively on the case sheet by visual analog scale VAS. as presented in table 1 and 2, and (soft tissue healing) after 7th day postoperatively.

Table 1: Swelling will be measured by visual analog scale VAS as the following. (Samad et al., 2018) [12]

N	Degree of swelling	Explanation of swelling
0	No swelling	The patient does not detect any swelling
1	Slight swelling	The patient detects a slight swelling but it is not very noticeable
2	Mild swelling	The swelling is noticeable but does not interfere with normal mastication and swelling
3	Severe swelling	The swelling is evident and hinders normal mastication
4	Very severe swelling	The swelling is marked. Mastication is hindered but there is no reduction in mouth opening
5	Extremely severe swelling	The swelling is very evident and mouth opening is reduced

Table 2: Pain will be assessed by using a visual analog scale VAS.(Samad et al., 2018) [12]

N	Degree of pain	Explanation of pain feeling
0	No pain	The patients feel well
1	Slight pain	If the patient is distracted, he or she does not feel pain
2	Mild pain	The patient feels pain even if concentrating on some activity
3	Severe pain	The patient is very disturbed but can continue with normal activities
4	Very severe pain	The patient is forced to abandon normal activities
5	Extremely severe pain	The patient must abandon every type of activity and feels he needs to lie down

- For soft tissue healing index (Gonshor 2002) [13] was used when patients were recalled on 7th days postoperatively to evaluate soft tissue healing.

- Diagnosis of Dry socket will be established by the clinical symptoms at 3rd day postoperatively as given by (Blum IR2002) [14] :
  - denuded socket
  - food accumulation
  - foul taste (halitosis)
  - Severe pain

  No, dry socket when the above symptoms are not present
  Yes, dry socket (when the above symptoms present)
  - Maximal mouth opening was also measured and recorded on 3rd and 7th days postoperatively.

Statistical Analysis:
Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 26). The Chi square test of association was used to compare the proportions of two or more groups. Fisher's exact test was used when the expected frequency (value) was less than 5 of more than 20% of the cells of the table. Student's t-test for two independent samples was used to compare the means of two groups. Friedman test was used to assess the significance between the readings of the different days of the study. Wilcoxon signed ranks test was used to compare the medians of the same sample but at two different periods. The Mann-Whitney test was used to compare the mean ranks of the two groups. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS
Age and Gender Distribution of the Sample
fifty patients were enrolled in the study, their mean age (SD) was 24.7 (3.5) years, the median was 25 years, and the age range was 18-30 years. They were divided into two equal groups, 25 in each group. Ozone gel was used for the first group, and antibiotic was used for the second group. More than half (52%) of the patients were aged 25-30 years.

Descriptive Statistics of Swelling:
It is evident in table 3 that the mean ranks (and means) of the swelling scores of the ozone gel group were significantly higher than the mean ranks (and means) of the other group on each day of the study ($p = 0.001$ on day 1, and $p < 0.001$ for the other days) as presented in Table 3.

Table 3. Swelling scores of the two groups on each of the days of the study.

	Ozone gel			Antibiotic			
Swelling	Mean	SD	mean	Mean	SD	mean	P*
Day 1	2.68	0.48	31.50	2.20	0.41	19.50	0.001
Day 2	3.80	0.41	34.20	2.88	0.67	16.80	< 0.001
Day 3	4.72	0.46	34.12	3.80	0.65	16.88	< 0.001
Day 4	4.60	0.65	36.44	2.96	0.68	14.56	< 0.001
Day 5	3.64	0.57	36.60	2.12	0.60	14.40	< 0.001
Day 6	2.76	0.72	36.24	1.28	0.54	14.76	< 0.001
Day 7	1.68	0.63	34.64	0.64	0.57	16.36	< 0.001

*By Mann-Whitney test

Descriptive Statistics of Pain:
On each day of the study, the mean and mean ranks of pain score of the ozone gel group were significantly higher than those of the other group ($p = 0.001$ on day 1, $p = 0.002$ on day 2, and $p < 0.001$ on days 3 -7 (Table.4)

Descriptive Statistics of Maximal Mouth Opening (Trismus):
Before surgery, no significant ($p = 0.148$) difference in mouth opening was found between the two groups as presented in Table 5. But on the third post-operative day, the mean mouth opening of the antibiotic group (38.76 mm) was significantly ($p < 0.001$) higher than that of the ozone gel group (35.72 mm). On the seventh post-operative day, the mean mouth opening of the antibiotic group (42.16 mm) was significantly ($p < 0.001$) higher than that of the *ozone gel group* (39.64 mm).

Descriptive Statistics of Soft Tissue Healing:
The mean and mean rank of the soft tissue healing index was significantly ($p < 0.001$) higher in the antibiotic group than the ozone gel group Table 6.

Table 4. Pain scores of the two groups on each of the days of the study.

	Ozone gel			Antibiotic			
Pain	**Mean**	**SD**	**mean rank**	**Mean**	**SD**	**mean rank**	**P***
Day 1	2.68	0.69	31.42	2.12	0.44	19.58	0.001
Day 2	3.64	0.57	31.42	3.04	0.68	19.58	0.002
Day 3	4.68	0.48	35.58	3.52	0.59	15.42	< 0.001
Day 4	4.20	0.71	35.74	2.72	0.74	15.26	< 0.001
Day 5	3.52	0.77	36.28	1.72	0.74	14.72	< 0.001
Day 6	2.64	0.70	36.68	0.68	0.75	14.32	< 0.001
Day 7	1.48	0.77	34.60	0.32	0.63	16.40	< 0.001

*By Mann-Whitney test.

Table 5. Means of mouth opening(trismus) of the two groups at different periods

	Ozone gel			Antibiotic			
	Mean	**SD**	**Mean rank**	**Mean**	**SD**	**Mean rank**	**P***
Soft tissue healing index	**2.56**	**0.65**	**16.46**	**3.76**	**0.78**	**34.54**	**< 0.001**

*By unpaired t-test

Table 6: Soft tissue healing index of the two study groups.

	Ozone gel			Antibiotic			
	Mean	**SD**	**Mean rank**	**Mean**	**SD**	**Mean rank**	**P***
Soft tissue healing index	**2.56**	**0.65**	**16.46**	**3.76**	**0.78**	**34.54**	**< 0.001**

*By Mann-Whitney test.

Descriptive Statistics of Dry Socket:
The incidence of dry socket was 12% in the ozone group, compared with 4% in the antibiotic group, but the difference was not statistically significant (p = 0.609) as presented in Table 7.

Table 7. Incidence of dry sockets in the two study groups

	Ozone gel	Antibiotic	Total	
Dry socket	No. (%)	No. (%)	No. (%)	P*
Yes	3 (12.0)	1 (4.0)	4 (8.0)	
No	22 (88.0)	24 (96.0)	46 (92.0)	0.609*
Total	25 (100.0)	25 (100.0)	50 (100.0)	

*By Fisher's exact test.

DISCUSSION

Surgical extraction of impacted lower third molars is widely carried out in dental practice. The surgical procedure causes damage to the tissue which leads to the release of potassium, serotonins and histamines from the damaged cells, and the release of bradykinin from the damaged blood vessels. This causes the activation of nociceptors, change in the tissue coloration and edema as a response of the tissue. Bradykinin causes the release of prostaglandin and the activation of nociceptors. The end result is the development of symptoms like pain, swelling, and restricted mouth opening. [15] The ultimate aim of this study was to evaluate and compare the effect of ozone gel on post-operative sequelae with antibiotics after surgical extraction of impacted lower third molars.

The impacted lower third molar tooth was selected as a model to perform the study. The impacted mandibular third molar is widely used as a model for evaluation of the medicaments, as almost always minor postoperative complications may be expected.[16] Furthermore, the current study presented some limitations. First is the small number of studies, which might lower the statistical power. The second limitation is the heterogeneity of studies from scales of measurement, time interval, and surgical protocol can explain the heterogeneity.

Pain is also one of the most common postoperative complications of extraction[17] and might be caused by the release of pain mediators from the injured tissues.[18] Pain is an important factor in clinical practice and could even discourage patients from seeking dental treatment. [19] It begins after the anesthesia subsides and reaches its peak levels during the first postoperative day. [20] If a dry socket or infection occurs, the onset of inflammation will complicate the alleviation of postoperative pain.[21] In the present study in the study group the pain increases gradually starting from the 2nd day and reach maximum on the 3rd day and then decreases gradually in the 6th and 7th days.

In the present study in the control group the pain increases gradually starting from the 2nd day and reaches a maximum on the 3rd day and then decreases abruptly in the 5th and 6th days. In comparison be-

tween our study with the other study, the results of the present study are in disagreement with Ricardo Pedro da Silva [22] who found in his study that the use of ozone gel as a supportive therapy may be effective in reducing pain and agreement with Alkholy S.S.et al. [5] they found in their study that the patients of ozone gel group had the least pain than the other groups. In my study, the evaluation of pain daily was based on the criteria given by samad et al., [12] the use of ozone gel cause increase in serotonin and endogenous opioids has been shown after Oxygen-Ozone administration and these antioxidant molecules could induce pain relief by stimulating antinociceptive pathways [1].

The swelling is caused by the extravasation of fluid and involves both vascular and cellular events. The surgical wound triggers the release of cascades of mediators that cause transient vasoconstriction of arterioles followed by vasodilatation and increased blood flow and, thereafter, stasis of the blood, increase in the permeability of the postcapillary venules and extravasation of fluid. Mediators are derived from both plasma and cells [23] some investigators have reported that the degree of postoperative swelling is influenced by the surgical trauma to the area and the length of the surgical procedure. [24] The swelling usually reached a maximum level at 2nd to 3rd days postoperatively and should subside by 4 days and resolve by 7 days.[25] In the present study in ozone gel group (study group) the swelling increases gradually starting from the 2nd day and reach maximum on the 3rd day and then decreases gradually on the 5th and 6th days.

In the antibiotic group (control group) the swelling increases gradually starting from the 2nd day and reaches a maximum on the 3rd day then decreases gradually from the 6th and 7th days. In comparison between our study with the other study, the results of our study are in disagreement with Kazancioglu HO et al. [26] and Recardo Pedro da Silva [22] they found in their study the ozone gel had minimal effect on swelling and in agreement with Sivalingman et al. [16] and Shokry et al. [27] they found that swelling had reduced and resolved more rapidly in the ozone gel group than the antibiotic group.

Trismus (Greek - trismos) is defined as a prolonged tetanic spasm of masticatory muscles of the jaw. Like edema, the transient jaw stiffness usually reaches its peak on the 2nd day and resolves by the end of the 1st week. It is diagnosed from clinical examination of the maximal interincisal distance (MID) <40–45 mm caused by contracture and not by obstructive joint impingement.[28] The factors contributing to trismus are: (1) Low-grade infection post administration of local anesthetic agents. (2) Multiple needle penetrations correlate with a greater incidence of post-injection trismus, especially if the barbed needle, and the most commonly involved muscle is medial pterygoid during inferior alveolar nerve (IAN) block. (3) Elevation of flap beyond the external oblique ridge at the insertion of temporalis muscle. (4) At times, the patient hurts his/her tongue or cheek under the effect of anesthesia resulting in reflex trismus.[29]

In present study showed that before surgery no significant differences were found between the two groups, on the third postoperative day, the mean of the mouth opening of the antibiotic group(control group) was significantly higher than the ozone gel group (study group), also at the seventh post-operative day, the mean of mouth opening of the antibiotic group was significantly higher than that of the ozone gel group. The results of the present study were not in line with Erdemci et al [30] who found ozone gel therapy provided excellent patient comfort , in turn, trismus, and in accordance with Alkholy S.S. et al., [5] and Ricardo Pedro da Silva. [22] Showed in his study a non-significant effect of ozone gel on the trismus.

Oral soft tissue healing is a dynamic and complicated process of returning cellular structures and tissue layers [31] the healing of oral epithelial tissue is also a complex process that uses the interactions between keratinocytes and extracellular matrix- as a result of cell migration, proliferation, differentiation and restoring the structure and function of this tissue. [32] Ozone gel can kill and destroys bacteria [33] and activate

cellular metabolism [34] and exhibiting intercellular ATP concentration and cytokines expression.[35] This concept affects positively the healing of soft tissue injury, especially the transforming growth factor-B1 (TGF-B1). [36] The activation of these growth factors, and local antioxidant mechanisms besides the antimicrobial efficacy enhance oral soft tissue repair and reduce post-operative disturbance and pain. [37]

In present study showed that the healing of soft tissue was significantly higher in an antibiotic group (control group) than the ozone gel group (study group). The results of the present study were not in similar to Filippi A [38] who found that the ozone gel can accelerate the healing mechanism and improve soft tissue repair and healing after surgical extraction of impacted lower third molars. Filippi A[38] in his study observed at the initial phase of surgery ozone gel possibly prevents wound contamination and modulates the cellular and humoral immunity. Such a phase activates the macrophage and stimulates synthesis of biologically active substances. Like-wise, the biosynthetic and analgesic properties of ozone facilitate soft tissue healing by increasing the PO2 in tissues and activating the process of intercellular aerobic antihypoxic action. This eases transportation of oxygen by inhibiting RBCs aggregation[33] . In my study, the evaluation of soft tissue healing on 7th day was based on the criteria given by (Gonshor) [13] . I revealed statistically non-significant effect of ozone gel on soft tissue healing after surgical removal of impacted lower third molars .

Dry socket (DS) is one of the most common complications following third molar surgery. Its exact etiology and pathogenesis, despite various approaches to this pathology, are still not known. DS was originally described as a consequence of the disintegration of blood clots during days 2 –4 after the tooth extraction, it is appearance has been described based on the clinical symptoms, such as a dry alveola covered with a layer of necrotic, yellow--gray tissue, halitosis, and high intensity of pain that radiates to the neck and ear. [39] although rare, other symptoms are lymphadenitis, headache, insomnia, and trismus. It is mostly prevalent in surgical extraction of mandibular third molars. [40] According to the insufficient experience of surgeons [41] amount of trauma during surgery[42] smoking habits [43] inappropriate irrigation during surgery [44] oral contraceptive use[45] and preoperative infection [46] the incidence of DS increase. Various studies had reported different incidence of DS in surgical removal of impacted mandibular third molar between 5% and 30%.[47] systematic and locally application of antibacterial, anti-inflammatory, antifibrinolytic, and clot support agents had been proposed for treatment. [39]. All of the mentioned influences revealed meaningful correlation with incidence of DS. Yet, prevention is more effective in DS. Identification of risk factors and eliminating them along with pharmacological prophylaxis had resulted in a significant decrease in incidence of DS. [48]

The present study showed that there were no statistically significant differences between the groups concerning dry socket and this finding is in disagreement with Cruz Guerra et al., [49] and Ahmedi J. et al., [50] who found in their study ozone had a positive effect on reducing the development of dry socket after surgical removal of impacted lower third molars.

CONCLUSIONS

This study concluded that the use of ozone gel is useful for the reduction of postoperative pain and swelling. While the use of ozone gel did not affect on trismus, dry socket and soft tissue healing after surgical removal of impacted lower third molars.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest relevant to this article.

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