



# A Comparative Study of Pain and Healing in Post-Dental Extraction Sockets Treated with Ozonated Water/Oil and Normal Saline

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## Abstract

**Aim** A comparative study of pain and healing in post-dental extraction sockets treated with ozonated water/oil and normal saline.

**Purpose** The present study was conducted to evaluate the efficacy of ozonated water/oil in reducing pain and enhancing healing and swelling following dental extractions and surgical removal of impacted mandibular third molars.

**Patients and Methods** Clinical trial was conducted involving 50 individuals requiring two-stage bilateral removal of tooth of which 25 patients were for asymptomatic bilateral extractions and 25 patients for surgical removal of asymptomatic bilaterally similar impacted mandibular third molars. The patients were divided into two groups following a split-mouth design: In group I, sterile ozonated water was irrigated in the sockets after extraction for 2 min on study side and normal saline on the control side following extraction. In group II, transalveolar extractions/surgical extraction of impacted mandibular III molars were carried out under copious irrigation with sterile ozonated water on study side and normal saline irrigation on control side evaluated by independent observer on 2nd, 4th and 7th day for the efficacy of ozonated water/oil in reducing pain and enhancing healing in post-dental extraction sockets.

**Results** The use of ozonated water/oil increased the healing rate in all extraction cases, except in 4% of cases in which they did not show any effect of healing in extraction sockets on 7th postoperative day. The use of ozonated

water/oil did not show any effects on the healing rate in impaction cases in all postoperative days. The use of ozonated water/oil showed decreased incidence of pain in subjects of both extraction and impaction cases.

**Keywords** O<sub>3</sub> · Ozone · Ozonated water · Ozonated oil

## Introduction

Surgical extraction of the third molars, or of teeth, is widely carried out in dental practice. The extraction of tooth may range from relatively easy to extremely difficulty depending upon the location, angulations, density of the bone and various other features [1]. Depending on the range, there will be increase in pain and swelling and also effects on healing. This is because when there is increase in the range of difficulty, there will be more excessive damage to the adjacent soft and hard tissues [2, 3].

The pain will increase as soon as the effects of local anesthesia wear off in 3–5 h after the procedure and swelling will also be aggravated within 12–48 h. To prevent the pain and its associated effects, the use of local or systemic corticosteroids and non-steroidal anti-inflammatory drugs is often recommended. However, the majority of these may manifest side effects such as a tendency to systemic bleeding, gastrointestinal irritation, and allergic reactions [4].

Non-medication methods have been used to minimize tissue injury after third molar extraction which includes compression, cryotherapy, and the application of lasers.

Ozone therapy is one of the non-medication method used in dentistry, which is recently gaining a place in everyday dental practice and is used in almost all dental applications [5].

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Medical-grade ozone is a mixture of pure O<sub>2</sub> and pure O<sub>3</sub> in the ratio of 0.1–5% of O<sub>3</sub> and 95–99.5% of O<sub>2</sub>. Due to the instability of the O<sub>3</sub> molecule, medical grade ozone must be prepared immediately before use.

German chemist Christian Frederick Schonbein is credited with the discovery of ozone in 1840. Zurich dentist Dr Fisch first investigated the medicinal value of ozone in 1933 in infected wounds and periodontal infections. The first ozone generator was developed by Werner Von Siemens in Germany in 1857. In 1957, the first patent on an ozone generator was registered [6].

Use of ozone in Endodontics as a root canal disinfectant, storing solution for avulsed teeth, in Periodontics for periodontal infections to reduce the inflammation, in Prosthetic dentistry as a denture cleaning solution, mouth washes along with chlorhexidine, to treat ulcers and infected wounds is well established. The role of ozone in maxillofacial surgery is the present topic of study where only a few reports are available in the literature [7].

Few studies suggest the use of ozonated water as cooling agent and rinsing medium to reduce the infectious and inflammatory post-operative complications in third molar osteotomies. A review by Dr Stubinger et al. mentioned the positive effect of ozone on oral soft and hard tissues [8].

The present study was conducted to evaluate the efficacy of ozonated water/oil in reducing pain and enhancing healing and swelling following dental extractions and surgical removal of impacted mandibular third molar.

The aim of the study is to study the efficacy of ozonated water/oil in reducing pain and enhancing healing in post-dental extraction sockets. Furthermore observations included: to study the effect of ozonated water/oil on pain in post-extraction sockets, to study the effect of ozonated water/oil in healing process in post-dental extraction sockets, to study the effect of ozonated water/oil on swelling following surgical removal of impacted mandibular third molar.

## Materials and Methods

A sample consisting of 50 subjects of various age groups was included in the study.

### Inclusion Criteria

Healthy patients above 18 years of age of both the genders, patients requiring bilateral extractions for Orthodontic purpose, patient requiring bilateral transalveolar extractions, bilaterally similar impacted mandibular III molars.

### Exclusion Criteria

Patients who are medically compromised, pregnant and lactating women, alcoholics and substance abusers, patients who are on treatment with ACE inhibitors and patients who are on oral contraceptives, patients who are on immunosuppressive drugs.

Ethical clearance with IRB no–VDC/IEC/2014–30 was given for the study.

### Materials Used

Virgin olive oil which was Ozonated before the procedure, sterile water which was Ozonated before the procedure, Normal saline.

Virgin grade olive oil was ozonated by using medical grade ozone generator (Universal Ozone generators, Mumbai, India) at concentration of 65 mcg/ml for 4 h before the procedure; sterile water was ozonated using medical grade ozone generator at concentration of 65 mcg/ml for 15 min.

Patients were divided into two groups.

- Group I: Included patients requiring bilateral normal extractions (therapeutic).
- Group II: Includes patients requiring transalveolar extraction/surgical extraction of bilaterally similar impacted mandibular III molars.

A split mouth study design was used, where the study side and the control side were randomly selected by a coin toss method. Patient was blinded to the information on the study side and control side. A period of 2 weeks was given before proceeding onto the opposite side. All the cases were done under local anesthesia (2% lignocaine HCL with adrenaline 1:1, 00,000). In group I, sterile ozonated water was irrigated in the sockets for 2 mins on study side [9] and normal saline on the control side following extraction. In group II, transalveolar extractions/surgical extraction of impacted mandibular III molars were carried out under copious irrigation with sterile ozonated water on study side and normal saline irrigation on control side. On the study side ozonated oil [10] was applied on the socket and tissue around before placing pressure pack Sockets were irrigated with ozonated water and examined on 2nd, 4th and 7th post-operative days. Patient was prescribed medication and provided with standard post-operative instructions. Antibiotics: Caps. Amoxicillin 500 mg TID for 5 days and in allergic patients Clindamycin 600 mg BD for 5 days, Rescue pain medication: Tab Ibuprofen 400 mg SOS. Patients in group I were prescribed only the rescue pain medication.

## Evaluation

Evaluations were done on 2nd, 4th and 7th postoperative days for.

*Healing:* Wound healing was evaluated using following observation of presence or absence of blood clot, granulation tissue or fibrous tissue over the socket and condition of wound epithelium with a scale [11].

- 1 Significantly worse than control,
- 2 Same as control,
- 3 Significantly better than control.

*Pain:* Severity of the pain was measured by visual analog scale [1]

*Pain medication consumed:* Number of rescue pain medication taken during the evaluation period was noted for study side and control side.

*Swelling:* The postoperative swelling was measured by a tape measure in centimeters from tragus of the ear to the corner of the mouth in all the postoperative evaluations [12].

## Results

The study comprised of 50 subjects, of which 25 patients were for surgical removal of asymptomatic bilaterally similar impacted mandibular third molars; and 25 patients for asymptomatic bilateral extractions (orthodontic purpose). The sample comprised of 38 males and 12 females with mean age of 26.6 years (range 18–40 years). After the procedure, patients were recalled postoperatively on days 2, 4, and 7 and evaluated for healing, swelling, pain and number of analgesics taken.

### Healing

Healing was evaluated using following observation of presence or absence of blood clot, granulation tissue or fibrous tissue over the socket and condition of wound epithelium, there was a significant difference in the healing of extraction sockets between 2nd and 4th day, 2nd and 7th day, 4th and 7th day. 96% of the extraction cases had healing more than that on the control side at 4th and 7th postoperative days. The rest 4% of extraction sockets had healing comparable with the control side after 7th postoperative day.

There was no significant difference in the healing of impaction cases at all the post-operative days. Healing at the study side was found to be equal with the control side with a score of 2; the results are shown in Table 1 and Table 2.

### Swelling

Swelling was assessed on 2, 4 and 7 post-operative days. No swelling was observed on the study and control side in any of the extraction cases.

No statistically significant difference was observed between the study and control sides at all post-operative days in impaction cases as shown in Table 3 and Table 4.

### Pain

The degree of pain that the patients experienced on the study side was significantly lower than that on the control side at all evaluations among extraction cases. All the subjects both at study side and the control side had no experience of pain on 7th postoperative day

In impaction cases, the degree of pain that the patients experienced on the study side was significantly lower than that on the control side at all evaluations except on 7th postoperative day where it was equal on both the sides (Table 5 and Table 6).

### Number of Analgesics Taken

Medication taken was recorded by the patient in pain diary. The mean number of analgesics taken for pain in impaction cases at control side and study side was 5.6 and 4.1, respectively. It was found that significantly fewer analgesics were taken for the study side when compared to the control side both in impaction and extraction cases.

## Discussion

Extraction of teeth and surgical removal of impacted mandibular III molars are one of the most common minor surgical procedures performed in maxillofacial surgery. Local signs of inflammation, which include pain, swelling, and trismus, usually present after surgical removal of teeth. Various factors contribute to post-operative swelling, pain and trismus. Some of them are soft tissue handling, method of osteotomy, difficulty of impaction (amount of bone removal and surgical time taken for removal). Postoperative sequel and complications after surgical removal of teeth and their management have been an area of interest since ages.

Many studies have been conducted to understand the effects of various therapeutic agents and non-medication therapies in managing these post-operative complications.

Considering the importance given to the clinical usage of ozone, a prospective study was undertaken to know its efficacy in controlling the postoperative problems following teeth removal. A sample size of 50 subjects (25 with

**Table 1** Comparison of healing at different postoperative days in extracted cases

S.No	Healing			Chi-square value	P value	
	Postoperative day	Less than control	Equal to control			More than control
1	2nd day	1 (4.0%)	16 (64.0%)	8 (32.0%)	22.235	.000
	4th day	0 (0%)	1 (4.0%)	24 (96.0%)		
2	2nd day	1 (4.0%)	16 (64.0%)	8 (32.0%)	22.235	.000
	7th day	0 (0%)	1 (4.0%)	24 (96.0%)		
3	4th day	0 (0%)	1 (4.0%)	24 (96.0%)	–	–
	7th day	0 (0%)	1 (4.0%)	24 (96.0%)		

**Table 2** Comparison of healing at different postoperative days in extracted cases in both groups

Postoperative days	Groups	Healing			Chi-square value	P value
		Less than control	Equal to control	More than control		
2nd day	Test side	1 (4%)	16 (64%)	8 (32%)	10.976	.000
	Control side	0	25 (100%)	0		
4th day	Test side	–	1 (4%)	24 (96%)	46.154	.000
	Control side	–	25 (100%)	0		
7th day	Test side	–	1(4%)	24 (96%)	40.154	.000
	Control side	–	25 (100%)	0		

**Table 3** Comparison of swelling at the test and control sockets among impacted cases

	Groups	n	Mean	Std. deviation	t value	p value
2nd day	Test group	25	11.9120	1.67763	– .522	.604
	Control	25	12.1600	1.68077	– .522	.604
4th day	Test group	25	11.3240	1.62308	– .506	.615
	Control	25	11.5600	1.67680	– .506	.615
7th day	Test group	25	10.7520	1.44831	– .473	.638
	Control	25	10.9520	1.53978	– .473	.638

**Table 4** Comparison of swelling at different postoperative days in impaction cases

S no	Postoperative days	n	Mean	std. deviation	t value	p value
1	2nd day	25	11.9120	1.67763	1.259	.214
	4th day	25	11.3240	1.62308		
2	2nd day	25	11.9120	1.67763	2.617	.012
	4th day	25	10.7520	1.44831		
3	2nd day	25	11.3240	1.62308	1.315	.195
	4th day	25	10.7520	1.44831		

asymptomatic bilaterally similar impacted mandibular III molars and 25 with bilateral asymptomatic extraction) was selected. Asymptomatic bilateral impactions with similar Pedersons difficulty index were included to eliminate bias.

In the present study, sterile water was used as a carrier and coolant for irrigation in surgical cases because ozone in gaseous form is 1.6-fold denser and tenfold more soluble in

aqueous solutions, and it reacts immediately as soon as it is dissolved in biological water (physiological saline, plasma, lymph, urine). Very few studies have been reported in literature regarding capacity of ozone in healing of intraoral wounds [13].

$O_3 + \text{biomolecules} \rightarrow O_2 + \text{free radicals}$ ,

**Table 5** Comparison of pain at the test and control sockets among impacted cases

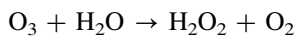
S no	Group	Mean	Std. deviation	t value	p value
Pain 2nd day	Test	4.9000	1.04083	– 5.552	.000
	Control	6.3800	.83267		
Pain 4th day	Test	.9600	1.48549	– 3.914	.000
	Control	2.5800	1.44106		
Pain 7th day	Test	.2400	.54237	.144	.886
	Control	.2200	.43493		

**Table 6** Comparison of pain at the test and control sockets among extracted cases

S no	Group	Mean	Std. deviation	t value	p value
Pain 2nd day	Test	3.0000	.95743	– 5.552	.000
	Control	3.9600	.97809		
Pain 4th day	Test	.1600	.45000	– 3.914	.000
	Control	.3800	.71122		
Pain 7th day	Test	.0000	.00000 <sup>a</sup>	.144	.886
	Control	.0000	.00000 <sup>a</sup>		

Because of its instability ozone is dissolved in sterile water before being used as therapeutic agent

Stubinger, in his review, stated that ozone is anti-bacterial, anti-fungal, anti-viral and also acts as a disinfectant. However, it does not have the same strength on all microbes. It acts by inhibiting the metabolic activity and cell wall of bacteria. This antimicrobial property of ozone can be used for its advantage as a good therapeutic agent in oral cavity. When ozone is used, it dissociates into bimolecular form and free radical.



Thus, it reacts with water and forms hydrogen peroxide. Similarly, glutathione peroxidase, catalase and super oxide dismutase are formed which leads to increased phagocytosis [8]. None of the cases in the present study reported with any postoperative infections.

Huth et al., in their study concluded that the aqueous form of ozone, as a potential antiseptic agent, showed less cytotoxicity than gaseous ozone or established antimicrobials (chlorhexidine digluconate 2%, 0.2%, sodium hypochlorite 5.25%, 2.25%, hydrogen peroxide 3%) under most conditions [14]. Therefore, aqueous ozone maintains optimal cell biological characteristics in terms of biocompatibility for oral application. Considering this finding, ozonated sterile water was used as a coolant and irrigant in the present study and no adverse events related to its use have been identified

Velio. A Bocci et al., proved the reaction of ozone with oil. They stated that unsaturated lipid substrates react with gaseous O<sub>2</sub>/O<sub>3</sub> mixture leading to therapeutically active ozonated derivatives [15]. Briefly, the postulated mechanism known as Criegee reaction provides that ozone combines with an unsaturated bond to form an initial,

unstable primary ozonide which readily decomposes to form a zwitterions and a carbonyl fragment. In anhydrous environment these substrates combine to give the typical cyclic trioxolane derivative. Therapeutic point of view, the ozonide compositions have the capacity to deliver active O<sub>2</sub> and/or other useful species deep within the lesion without causing primary skin irritation. In this study, ozonated olive oil (Virgin grade) was utilized as a dental dressing on the socket after impactions and extractions.

Ozonation was done by medical grade ozone generator (universal ozone generators) with an oxygen cylinder connected to it. Oxygen is passed through generator with a pressure of 1LPM and in which Ultraviolet System causes to dissociate oxygen molecules leading to formation of ozone molecules with a concentration of 65 mcg/ml to ozonate water/oil.

After extraction was done on the study side, ozonated sterile water was used to irrigate extraction sockets for 2 min. There is evidence that ozonized water, not being an isotonic solution, does not have any negative effect on the vitality of the remaining cells on the socket wall surface when used as irrigation for 2 min from the study conducted by Ebensberger u, et al. [9].

There was an improved healing on test sides than in control sides in extraction cases when reviewed on post-operative 2nd 4th and 7th days. But in impactions, as described by the Filippi, A. in healthy patients, osteotomies of third molars using ozonized water for irrigation showed no difference in postoperative outcome in comparison with the use of sterile isotonic saline [16]. Corroborating with his findings, there was no significant difference observed in healing after III molar surgeries on the study and control

sides in the present study. Healing reviewed on 2nd 4th and 7th post-op days was similar on both the sides.

The lack of any significant difference may be attributed to close approximation of flaps by suturing after osteotomy of third molars or increased retraction and increased soft tissue traction leading to decreased efficacy of ozonated water/oil.

Kim, Noh, Han, et al. in their animal study found that topical form of O<sub>3</sub> can accelerate acute cutaneous wound repair in guinea pig model by promoting collagen synthesis and fibroblast proliferation at the injury site and by increasing the expression of growth factors such as PDGF, TGF- $\beta$ , and VEGF [17].

Bocci, V et al. in their study concluded that the influence of ozone leads to a higher expression of cytokines that are important for wound healing, especially TGF- $\beta$ , an important substance for regulation and coordination in the initial wound healing phase. TGF- $\beta$  has a marked influence on cell proliferation, chemotaxis (monocytes and fibroblasts), angiogenesis, synthesis of extracellular matrix and collagen synthesis [18].

Filippi, A in his study stated that wound receives more oxygen when ozonized water is applied. Thereby shortening of initial wound healing time enhancement of phagocytic activity defending cells, accelerated migration of epithelial cells, activation of fibroblasts and importance for collagen synthesis are examples given by him for enhanced wound healing [16].

Subjective discomfort has been found to be significantly higher after the surgical removal of the impacted mandibular third molars, than after the routine extractions of other teeth. The size of swelling depends on the degree of tissue trauma and patient's variability, microbial flora in the oral cavity, and individual response differences. The degree of pain also depends on tissue trauma. Usually, it is necessary to treat the pain after extraction with pain relief medications for a period of 2–3 days. In this study patients were advised to take rescue pain medication when the incidence of pain occurred and to pen down in a proforma which was given to each patient to compare pain in study side with control side. In the proforma patient was advised to note the incidence, severity of pain, adverse events, and amount of rescue pain medication taken [19, 20].

Pain intensity and the degree of inflammation can vary between patients. For this reason, a split-mouth design was chosen for the study to eliminate bias in the collection of information, unlike when tests and controls are different individuals. Pain intensity measurement was taken through VAS score on 2nd and 4th and 7th days, on 10 units in combination with a graphic rating scale.

Pain following surgical extraction of impacted mandibular third molars and therapeutic extractions was evaluated and it was found that the VAS score for pain and

the number of analgesics taken were significantly higher for the control side than for the study side at all assessment sessions, on postoperative days 2, 4 and 7.

The mean number of analgesics taken for pain by impaction cases on control side and study side was 5.6 and 4.1, respectively. It was found that significantly fewer analgesics were taken for the study side when compared to the control side both in impaction and extraction cases.

The degree of pain that the patients experienced on the study side was significantly lower than that on the negative control side at all evaluations in both extraction and impaction cases except on the 7th postoperative day when it was equal on both the sides.

In the present study, facial swelling was evaluated with a tape measure measuring from tragus of ear to the corner of the mouth as described by Schultze-Mosgau et al. [12]. There was no significant difference between the study side and the control side at all the postoperative days in impaction cases. No swelling was observed either at the control side or at the test side for extraction cases.

The results of this study corroborate with the findings of Okazancioglu et al. [1] and Filipovic-Zore et al. [22], even though the exact mechanism of pain control by ozone is not clear [23–25].

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**Compliance with Ethical Standards**

**Conflict of interest** The authors declare that they have no conflict of interest.

**Consent to Participate** Yes all the patients gave consent for participation.

**Consent for Publication** Yes all the patients gave consent for publication.

**Data Availability** Yes all the data are available.

**Ethics Approval** IRB no–VDC/IEC/2014–30.

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