The use of ozone therapy for the treatment and post-surgical management of patients treated with bilateral extraction of the included third mandibular molars

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Abstract

The use of ozone in medicine and dentistry is well-supported in the scientific literature, particularly for its antibacterial, antiviral, anti-inflammatory, and anti-edema effects. These benefits are achieved through reductions in pro-inflammatory substances, stimulation of neoangiogenesis, and enhanced production of antioxidant enzymes. Additionally, ozone is pain-relieving by inactivating algogenic mediators and inducing endorphin release. Although ozone application devices are standard in conventional medicine, they are less so in dentistry and often have reduced performance. This study aims to evaluate the effectiveness of a specific ozone therapy device in managing postoperative pain and promoting healing in patients undergoing impacted third-molar extractions. Materials and methods: Patients scheduled for the extraction of impacted third molars were enrolled in a randomized split-mouth study to receive either ozone therapy or conventional antibiotic treatment. The Visual Analog Scale (VAS) assessed pain intensity and healing progress. Results: Patients treated with ozone therapy reported significantly lower pain levels and demonstrated qualitatively improved healing compared to the control group, with statistical significance. Conclusions: The study supports the use of ozone therapy in routine dental surgical practice, highlighting its favorable cost/benefit profile. Ozone therapy can be beneficial for impacted third-molar surgeries and broader applications in oral surgery.

Keywords: Ozone therapy in dentistry, OZONE DTA equipment, Third molar extraction and soft tissue healing.

Introduction

The use of ozone in dentistry is a topic of discussion in the scientific literature (1-3). A recent review of the literature was performed by El Malagy et al. (4), with the results showing apparent efficacy in vitro and negligible efficacy in vivo. However, the antibacterial and generally non-toxic action was highlighted in a work published by Bocci et al. (5). The system through which ozone acts is well described and is linked to its antibacterial properties; ozone's oxidant potential causes the breakdown of bacterial and fungal cell walls and cytoplasmic membranes by destroying glycoproteins, glycolipids, and other amino acids. The anti-inflammatory effect of ozone is highlighted in a work conducted by Hidalgo-Tallon F.J. et al. (6). In particular, how ozone acts at the cellular level is well described; it exerts an anti-inflammatory effect by reducing the activation of the nuclear factor kappa B (NF–κB) pathway, thus decreasing the production of

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cytokines such as IL–1, IL–2, IL–6, and tumor necrosis factor-alpha (TNF-α) while stimulating the production of cytokines such as IL–4, IL–10, IL–13, and transforming growth factor–beta (TGF–β). The action of ozone also concerns the increase in the release of oxygen in the tissues by red blood cells, as described by Alfaro et al. in their publication (7).

Therefore, since we found contrasting works in the literature, it is also essential to evaluate how the methods of administration and the fields of applications can influence the final judgment regarding effectiveness. There can be differences in the administration methods in dentistry and the consequent ozone concentration in situ depending on the technology used for the application (8). In oral surgery, the postoperative inflammation that occurs after the extraction of the included third molars represents the complication involving the most significant patient discomfort. Pain, swelling, trismus caused by muscle spasms (9), and infection of the site with alveolitis (10) are responsible for a partial loss of function and a negative impact on the lives of the patients (11-12). The pain reaches maximum intensity 3-5 hours after surgery, persists for about 2-3 days, and gradually decreases until 7 days (13-14). The swelling reaches its peak intensity within 12-48 hours, resolving between 5 and 7 days after surgery. Local or systemic corticosteroids and non-steroidal anti-inflammatory drugs are often recommended (15,16). However, side effects such as gastrointestinal irritation, systemic bleeding, and (17) allergic reactions can sometimes occur. A poster presented at C.D.U.O. 2024 in Trieste (Italy) by Bizzocca M and other researchers showed that there is a correlation between the number of the patient's platelets and the speed and mode of healing after extraction of the lower thirds (18). In particular, the number of platelets was correlated, in any case, within the numerical range considered normal concerning the type of healing measured with the same VAS. As platelets increase, the healing quality significantly improves, and pain on postoperative days is statistically significantly reduced.

For this reason, over the years, non-pharmacological therapies have been proposed, such as ozone therapy 9, to improve postoperative symptoms and avoid the undesirable effects of synthetic drugs. In oral surgery, ozone can be helpful in promoting hemostasis, improving local oxygen intake, and inhibiting bacterial growth 10. Numerous studies have shown the antibacterial properties of ozone, as well as its effectiveness in the treatment of infections 11. Such treatment showed good patient tolerance, ease of execution, no side effects or adverse reactions, and high medical–social efficiency. In work by Damario et al. (19), it was demonstrated that the use of ozone is essential not only in pedodontic therapy but also in improving the healing of soft tissues in oral surgery and oral pathology. In another study conducted by Mampieri G et al. (20), very encouraging results were published on the use of ozone in treating peri-implantitis, both in vitro and in vivo. Although the authors point out that further, more extensive studies need to be conducted, ozone therapy appears to have statistically significant positive effects on subjects treated for implantitis and on contaminated titanium disks treated in vitro studies. We can, therefore, say that the substantial premise for the use and study of ozone in dentistry is a demonstrated effectiveness in various applications, as shown by studies in the literature; the meager cost and non-invasiveness of this type of treatment encourage studies to delve into possible dental application fields. Our study aimed to evaluate the effect and benefits of ozone therapy in the post-surgical management of patients treated with bilateral extraction of the included third mandibular molars.

Materials and methods

Our research involved conducting a randomized, single-blind, controlled clinical trial involving patients requiring third-molar surgery. This study was conducted at one clinical center in conformity with the Good Clinical Practice guidelines, following the ethical principles of the World Medical Association Declaration of Helsinki for medical research involving human subjects, as revised in Fortaleza (2013). This clinical study aimed to evaluate the effects of ozone therapy compared to standard postoperative systemic antibiotic treatment.

Study Design

In this study, we employed a randomized split-mouth design to ensure that each participant acted as their control, thereby minimizing variability and enhancing the reliability of our findings. In total, 45 patients were enrolled, resulting in 90 dental extractions. The randomization allowed for an equitable distribution of extractions between the two treatment groups, ensuring that each patient served as their control. This design allows for a direct comparison of the effects of topical ozone therapy and systemic antibiotics within the same patient, thereby controlling for individual differences and providing more valid conclusions regarding the efficacy of the treatments.

According to the Pell and Gregory classification, the extractions comprised classes II and III. The molars included in the study were primarily vertical (30 molars), mesioinclined (25 molars), distoinclined (20 molars), and horizontal (15 molars), but not inverted. Among the patients selected were 24 women and 21 men. The average age was 31, and all patients were from Central Italy. Due to privacy regulations and ethical considerations, we could not collect comprehensive data on variability in ethnicity and socioeconomic status. All patients were instructed to avoid anti-inflammatory drugs or antibiotics 5 days h before the procedure to avoid interference with the study outcomes. Although a formal sample size calculation was not conducted, the number of patients was determined based on availability and logistical resources. Our choice of a sample size of 90 aligns with previous studies in the scientific literature that have examined similar treatments in the context of postoperative pain management, such as the study of Kazancioglu HO et al. (2014) (29).

Using the split-mouth design, the test group received topical ozone (OZONE DTA) without postoperative systemic antibiotics. In contrast, the control group was treated only with systemic antibiotics (Augmentin) without topical ozone. Randomization facilitated the placement of 90 extractions, divided equally into 45 for the test group and 45 for the control group. After obtaining the informed consent of the enrolled patients, a suitable medical history, health records, and appropriate radiographic examinations were collected. All subjects underwent orthopantomography before the surgery. In cases where

a more comprehensive analysis was deemed necessary (e.g., to evaluate the relationships between the roots of the included third molars and the inferior alveolar nerve), a cone beam computed tomography (CBCT) scan with a small field of view (FOV) was performed. To enhance oral health before the surgical procedures, all patients underwent a professional oral hygiene session seven days before the study commenced. They were instructed on proper home oral hygiene techniques to maintain optimal oral health.

Additionally, two days before each extraction, the patients were reassessed, and all reported a Full Mouth Bleeding Score (FMBS) and a Full Mouth Plaque Score (FMPS) of less than 20%. The period between the first and the second extraction was three weeks to prevent the postoperative outcome parameters of one extraction from affecting the other. All patients were prescribed analgesic treatment for 2 days. The evaluating surgeon was unaware of the treatment assignment for the entire study.

The rationale for comparing systemic antibiotic therapy with ozone therapy alone is based on the urgent need to limit antibiotic use in clinical practice, particularly in light of the increasing emergence of antibiotic-resistant bacterial species. Lewis (2008) states, "With the emergence of bacterial species resistant to antibiotics, there is a need to become vigilant about their prescription." Thus, this study evaluates whether ozone therapy, recognized for its antimicrobial, anti-inflammatory, and healing-promoting properties, can be an effective alternative to systemic antibiotics in minor oral surgery. By exploring ozone as a standalone treatment, we aim to contribute to ongoing efforts to reduce antibiotic prescriptions without compromising patient safety or surgical outcomes (31).

Criteria for inclusion

Patients requiring bilateral surgical removal of included lower third molars
Patients without particular systemic pathologies
18 to 45 years of age
Molars with similar difficulty index evaluated with the Pell and Gregory classification

Criteria for exclusion

Patients with systemic diseases or allergies or those who were unwilling to participate in the study
Non-cooperative patients
Smokers (> 10 sig/die)

Primary Variables evaluated

Opening of the postoperative mouth;
Pain;
Swelling.

Secondary Variables evaluated

The number of analgesic doses required by each group on postoperative days 3 to 5.

Data Collection procedures

Postoperative pain was evaluated using the VAS (18):
0 (no pain);
1-3 (average pain);
4-7 (moderate pain);
8-10 (severe pain).

The opening of the mouth was assessed in millimeters using a gauge that measured the inter-decision distance:
1 (less than 2cm);
2 (between 2 and 4 cm);
3 (above 5 cm).

Swelling was assessed by measuring the points shown in the diagram (Figure 1):
0 (none);
1 (slight);
2 (moderate);
3 (elevated).

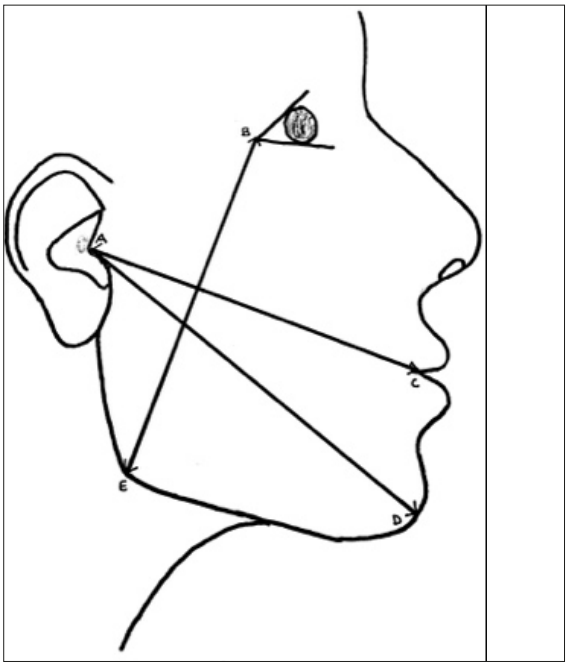

Figure 1. A) Point furthest from the tragus; B) angle of the eye; C) lateral point of the labial line; D) pogonion; E) angle of the jaw.

The resulting facial swelling was calculated as the difference between the average postoperative and preoperative swelling:
Postoperative (AC+AD+BE) - Preoperative (AC+AD+BE).
Here, (AC) is from the posterior point of the tragus to the lateral point on the angle of the mouth; (AD) is from the posterior point of the tragus to the soft tissue of the pogonion; and (BE) is from the lateral eye angle to the lowest point on the angle of the mandible.

Surgery description

Patients in the study and control groups underwent surgical extraction of the teeth under local anesthesia by a single surgeon. The preoperative opening of the mouth and swelling of the face were detected in millimeters before surgery.

Only one tooth was removed at a time three weeks apart to allow postoperative symptom resolution after the first extraction.

The surgical procedure was standardized for all patients: the surgical site was prepared with Betadine solution, the anesthesia used was SEPTANEST (4% articaine with 1:200,000 epinephrine injection solution), a mucoperiostal flap was incised with surgical exposure, the tooth was extracted after removal of the overlying bone using a surgical handpiece under saline irrigation, and closure of the wound was performed with 3-0 silk sutures.

The average surgical time was recorded from the time of the incision to the last suture for the surgical wound closure.
Post-extractive injury management varied between the study and control groups following the research approach:

- The control group received a simple antibiotic therapy. Augmentin was prescribed to be taken after surgery, 2 times a day for 7 days.
- The test group received topical ozone before surgery and into the post-extractive alveolus via the OZONE DTA machinery without antibiotics.

Figure 2. OZONE DTA equipment for ozone supply.

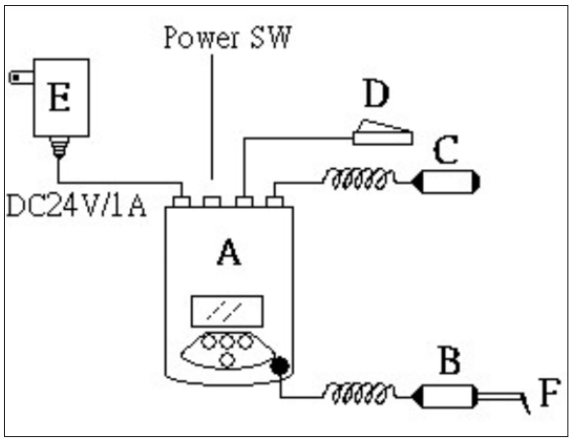

Figure 3. Component illustration. A: Control box. B: Ozone-generating handpiece. C: Safety rod (patient ground). D: Foot pedal. E: Power. F: Probe.

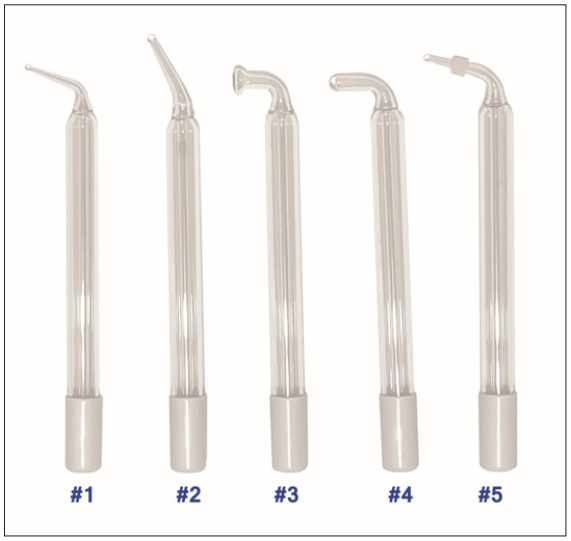

Figure 4. Probes used on the handpiece.

The application of ozone using the OZONE DTA involves several steps to ensure both efficacy and patient comfort. The treatment area was initially prepared by cleaning and isolating it to prevent contamination. The handpiece of the OZONE DTA was then positioned directly over the treatment area. The handpiece is designed to deliver ozone precisely where needed, maximizing the bactericidal effects while minimizing exposure to surrounding tissues (Figure 3).

The handpiece has several probes (Figure 4):
#1 Probe: Probe pointed at 10°. For the treatment of gingivitis.

#2 Probe: Probe pointed at 50°, for the treatment of gingivitis.

#3 Probe: Flat probe. For treatment of the skin and mucous membrane.

#4 Probe: Conical probe. For alveolar therapies after tooth extraction.

#5 Probe: Probe pointed 10° with conical plastic for root canal treatments.

However, in this study, only probes #4 and #5 were used because we selected the appropriate probe based on the cavity size and shape. Probe #4 was used to treat larger cavities resulting from tooth extractions. Its conical shape facilitates effective ozone diffusion within the cavity, ensuring thorough ozone penetration. While probe #5 is designed specifically for endodontic applications such as root canal treatments, it allows precise placement and optimal ozone dispersion within smaller cavities, such as the apical root portion of the extraction socket. Therefore, it was used for smaller or more intricate cavities to maximize ozone efficacy. The duration of ozone application varied depending on the clinical scenario, but typically, it was from 1 to 5 minutes per site. Treatment settings involved adjusting the output power between levels 3 and 6, with treatment durations ranging from 1 to 3 minutes for non-bleeding cavities. In cases of bleeding cavities, the output power was increased to level 12, and the treatment time was extended to approximately 5 minutes, which was adjusted according to the severity of the bleeding. Generally, this brief exposure is sufficient to reduce bacterial load significantly, as ozone is a powerful oxidizing agent that

disrupts bacterial cell walls and inactivates microbial enzymes. During the application, patients did not experience any pain or discomfort, as the procedure is non-invasive and the ozone concentration used was carefully controlled. The OZONE DTA apparatus has safety features to monitor ozone levels and ensure they remain within the therapeutic range. This ensured that the treatment was safe for the patients. Both the control and study groups received postoperative analgesics for 2 days; additional analgesic intakes were recorded on the third, fourth, or fifth postoperative day in patients from both groups. A researcher blinded to the study and control groups evaluated the following parameters: postoperative pain, swelling, and maximum opening of the mouth at baseline (post-surgery), T0 (2 days after surgery), and T1 (7 days after surgery).

Statistical analysis

Mean values and standard deviations (SD) were calculated for each parameter on the study and control sides. Given the split-mouth study design, comparisons between the study and control sides were performed using paired T-tests. Statistical significance was set at $P < 0.05$. A two-way ANOVA with repeated measures was used to compare mean values between sexes and groups. Data was analyzed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 45 patients (21 males and 24 females) were recruited. The average age for males was 33.33, and for females, it was 29.33 (Table 1). All patients were non-smokers, except one patient who smoked less than three cigarettes per day.

Table 1.

Variables of the study	Test and Control Groups (Split-Mouth Design)
Patients	45
Male	21 (46,7%)
Female	24 (53,3%)
Mean age	31 y

The average time for the surgical procedures was 20+/- 12 and 22+/-14 minutes for the control and study groups, respectively. The study results indicate (Table 2) that the average differences between the sexes were not significant and that gender was not an important confounding factor.

The study group showed a statistically significant reduction in postoperative pain scores at the baseline and the second and seventh postoperative days; the mean pain scores in the control and study groups were, respectively, 7,48 and 5,45 on the baseline, 5,15 and 2,97 on the second postoperative day, and 0,94 and 0,06 on the seventh postoperative day (p=0,0001) (Table 3) (Figure 5).

Patients in the test group also showed reduced swelling compared to the control group. The average postoperative swelling for the study group was 123.19,

Table 2.

	Pain (VAS)			Facial Swelling			Mouth Opening		
	Baseline	Day 2 (T0)	Day 7 (T1)	Baseline	Day 2 (T0)	Day 7 (T1)	Baseline	Day 2 (T0)	Day 7 (T1)
Control Group Male n=21	7,44 ± 0,63	4,94 ± 0,93	0,81± 0,40	141,38 ± 5,30	128,13± 6,35	112,31 ± 3,14	22,88 ± 2,87	31± 1,97	42,69 ± 2,96
Control Group Female n=24	7,53 ± 0,51	7,35 ± 0,70	1,06 ± 0,56	141,59 ± 5,59	126,71 ±7,65	112,82 ± 3,54	20,41 ± 3,33	27,76 ± 2,94	40,35 ± 2,78
Test Group Male n=21	5,5 ± 0,52	2,88 ± 0,72	0,06 ± 0,25	112,19 ± 1,7	113,38 ± 2,96	104,13 ± 2,00	30,94 ± 3,71	37,56 ± 4,03	47 ± 3,43
Test Group Female n=21	5,41 ± 0,62	3,06 ± 0,83	0,06 ± 0,24	123,94 ± 2,66	114,35 ± 2,42	104,94 ± 1,95	27,70 ± 3,80	33,76 ± 3,51	44,35 ± 3,12

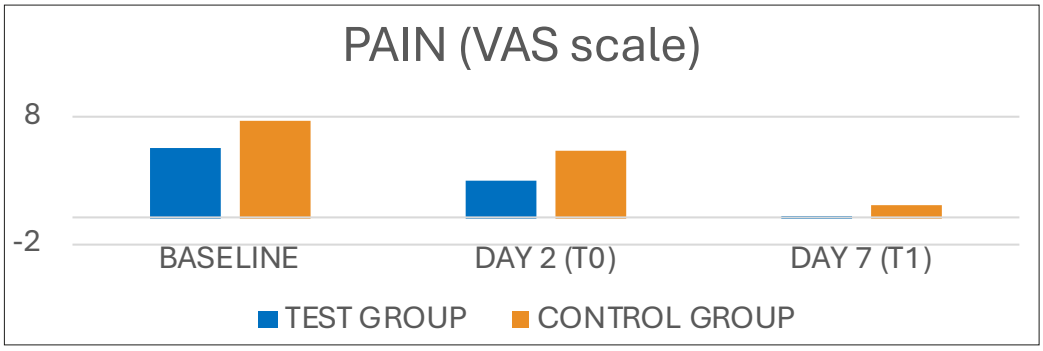

Figure 5.

113.88, and 104.55 mm at the baseline, second, and seventh days, respectively, compared to the 141.48, 127.39, and 112.58 mm recorded for the control group (p=0.0001) (Table 3) (Figure 6).
A comparison of the maximum opening of the mouth revealed that patients in the study group recorded 29.27, 35.61, and 45.64 mm in baseline evaluations, changes of 2.61 and 7.00 per day, while the control showed 21.61, 29.33, and 41.48 mm, respectively. These results were also statistically significant with P = 0.0001 showing a better maximum mouth opening in the study group than in the control group (Table 3) (Figure 7).
Age and sex are the two study variables other than the predictive variables. It was found that age was not correlated with the result variables. Therefore, age was not considered in the final analysis. The average requirement for analgesics based on clinical observation on days 3, 4, and 5 was higher for the control group, 3, 1,32±0,48, and 1,06±0,24, respectively, compared to the study group, which was 3, 1, and 0 (Table 4).

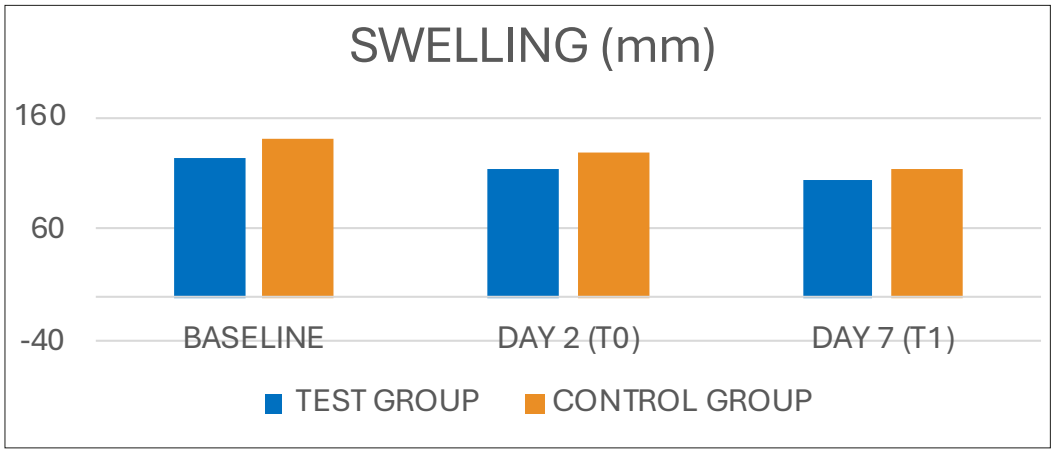

Figure 6.

Table 3.

	Pain (VAS)			Facial Swelling			Mouth Opening			
	Baseline	Day 2 (T0)	Day 7 (T1)	Baseline	Day 2 (T0)	Day 7 (T1)	Pre-Op	Baseline	Day 2 (T0)	Day 7 (T1)
Control Group	7,48 ± 0,57	5,15 ± 0,83	0,94 ± 0,50	141,48 ± 5,37	127,39 ± 6,98	112,58 ± 3,30	47,03 ± 4,75	21,61 ± 3,32	29,33 ± 2,98	41,48 ± 3,06
Test Group	5,45 ± 0,56	2,97 ± 0,77	0,06 ± 0,24	123,19 ± 2,44	113,88 ± 2,70	104,55 ± 1,99	47,21 ± 4,57	29,27 ± 4,05	35,61 ± 4,18	45,64 ± 3,49

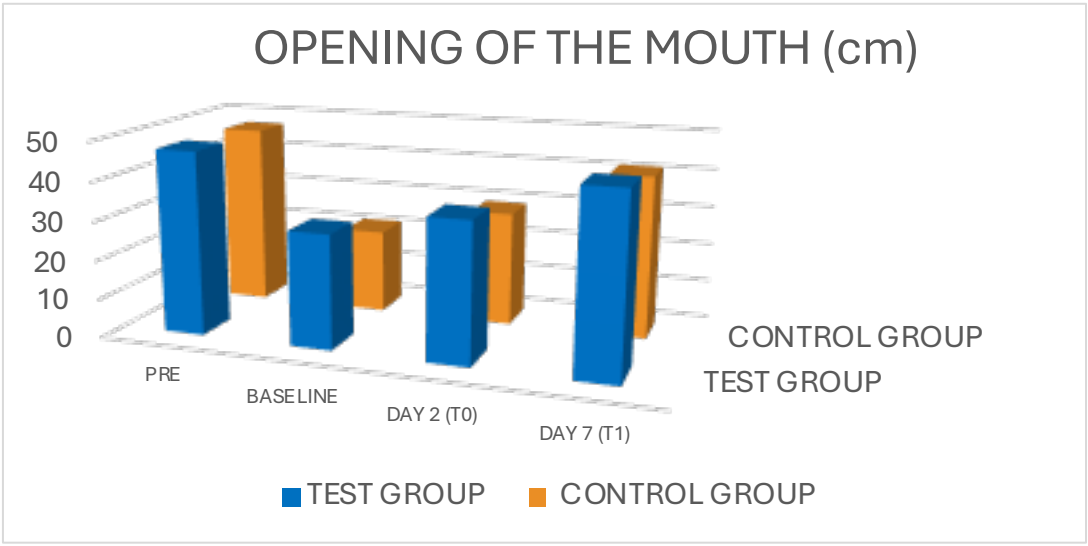

Figure 7.

Table 4.

	Day 1	Day 2	Day 3	Day 4	Day 5
Control Group	3	3	3	1,32 ± 0,48	1,06 ± 0,24
Test Group	3	3	3	1	0

table benefits include reduced pain and swelling, improved mouth opening, and accelerated wound healing. The decrease in pain consequently reduces the additional use of analgesics and, therefore, the side effects associated with non-steroidal anti-inflammatory drugs and antibiotic abuse.

Discussion

This clinical study aimed to test the effects of ozonotherapy compared to routine postoperative systemic antibiotics. The main aim was to see if patient comfort improved with topical use of ozone, so we studied and compared postoperative pain, facial swelling, and mouth opening in both groups. These three parameters represent the most common complications after extracting third molars. They occur due to inflammation resulting from tissue injury or infection of the surgical wound. Generally, such complications are prevented by administering analgesics, antibiotics (19), glucocorticoids, and topical chlorhexidine gel. However, such drugs often involve systemic or local adverse reactions. This study used topical intraoral ozone as an alternative to conventional therapies. The healing of hard and soft tissues in oral surgery is a topic discussed in the use of static magnetic fields (20), which, although studied in terms of their effect on improving the differentiation of osteoblasts, demonstrated an excellent ability to influence soft tissues in vitro positively. More practical and widespread is the use of ozone. Several studies have shown different forms of ozone administration in oral surgery, such as aqueous solution, gel, and extraoral gas, which showed excellent results in wound healing in the study by Kazancioglu et al. (21). In addition, the gel form offers (22) advantages such as ease of application, a higher concentration of ozone molecules, and stability of the compound for a longer duration. The gel contains ozone in the form of ozonides that release active ozone over time when in contact with the wound surface at body temperature (23). This study showed a statistically significant reduction in the incidence and severity of postoperative pain, swelling, and trismus in the study group. Surgical trauma leads to over-regulation of biochemical mediators of pain and inflammation, such as prostaglandins, histamine, bradykinin, and serotonin. However, in our study, we observed that VAS scores, which reflect postoperative pain, were considerably lower on the side of the study where ozone treatment was used locally. The reduction in postoperative pain can be attributed to the anti-inflammatory property of ozone that leads to a reduction in the release of algogenic chemical mediators (24). It was also interesting to note a considerable reduction in the intake of analgesics in the study group, especially on the third, fourth, and fifth days. Inflammatory processes triggered by soft tissue manipulation, bone removal, or infection are responsible for postoperative swelling. It is directly proportional to the duration of the intervention; therefore, for our study, cases of equal difficulty were chosen to attempt to standardize the duration of the intervention. Edema reaches its peak at 48-72 hours after surgery. For this reason, ozone was applied for three days after extraction. Indeed, a significant reduction in postoperative swelling was observed in the study group. The reduced inflammation observed can be attributed to ozone's ability to modulate cellular and humoral immunity by activating macrophages and stimulating the synthesis of biologically active substances, respectively 20. The analgesic properties of this substance, which are associated with better wound healing, also explain the reduction in trismus in the study group compared to the control group. In a study by Koray et al., that analyzed post-extractive trismus after applying hyaluronic spray, a beneficial effect was established. However, the treatment required application for 7 days and did not eliminate pain 21. The antimicrobial action of ozone extends to a broad spectrum of bactericidal, viricidal, and fungicidal effects (25). The bactericidal mechanism occurs through the destruction of the cell membrane and the oxidative disintegration of cellular contents. In viruses, it alters the action of reverse transcriptase that synthesizes viral proteins, while in fungi, it inhibits cell growth in selective stages. Ozone toxicity has been extensively studied. Inhalation of ozone can lead to toxic side effects such as upper respiratory tract irritation, vomiting, headaches, and sometimes stroke (26, 27). Ozone poisoning can be managed by placing the patient on their back and administering vitamin E and n-acetylcysteine (28-29). However, Huth et al. showed that the aqueous form of ozone showed lower cytotoxicity than gaseous ozone and conventional antimicrobials such as chlorhexidine digluconate (CHX) 2%, 0.2%; sodium hypochlorite (NaOCl) 5.25%, 2.25%; and hydrogen peroxide (H2O2) 3% (30).

In our study, there were no episodes of toxic or allergic reactions. In summary, ozone used as post-surgical therapy showed significant advantages in the study group and improved patient comfort. Such improvements suggest that the use of this therapy may reduce the need for unnecessary antibiotics and painkillers by limiting the side effects associated with NSAIDs. A split-mouth study design was utilized to reduce biases related to the subjectivity of postoperative symptoms. In addition, casual randomization and blind evaluation minimized the risk of further bias.

Conclusion

Ozonotherapy represents a promising and valid alternative to traditional antibiotics administered postoperatively in third-molar surgeries. This study has demonstrated that patients treated with topical ozone experience significantly reduced postoperative swelling, pain, and trismus compared to those receiving systemic antibiotics alone. The benefits observed include a reduction in the common discomforts associated with third molar extractions and an overall enhancement in patient comfort and recovery. The simplicity of use and the absence of side effects make ozonotherapy a particularly appealing option. Traditional postoperative treatments often involve the administration of corticosteroids and non-steroidal anti-inflammatory drugs, which can lead to gastrointestinal irritation,

systemic bleeding, and allergic reactions. In contrast, ozonotherapy avoids these potential adverse effects while effectively managing postoperative symptoms. The data collected in this study show an apparent reduction in pain, as evidenced by lower Visual Analogue Scale (VAS) scores and a decrease in the need for additional analgesics among patients treated with ozone. The swelling was also significantly lower in the ozone group, contributing to a quicker return to normal facial function and appearance.

Moreover, the patients in the ozone group exhibited better mouth opening postoperatively, indicating a faster resolution of trismus. The findings suggest that ozonotherapy provides a high level of efficacy in controlling postoperative discomfort and promotes faster wound healing. The reduced need for antibiotics is critical in the context of increasing antibiotic resistance and the growing emphasis on minimizing antibiotic use. Given these advantages, ozonotherapy is expected to be increasingly adopted in clinical practice. Its ease of application, safety profile, and effectiveness position it as a valuable tool in the management of postoperative care following third molar extractions. Future research and broader clinical trials will further establish its role and expand its use in other dental and medical treatment areas. In summary, ozone therapy offers a viable and beneficial alternative to systemic antibiotics for postoperative management in oral surgery. Its ability to reduce pain, swelling, and trismus without the side effects associated with traditional pharmacological treatments underscores its potential to improve patient outcomes and enhance the overall quality of postoperative care. We expect increasingly widespread use of ozone given this technique's advantages, such as its simplicity of use, the absence of side effects, and reductions in the administration of postoperative drugs and their related systemic side effects.

Declarations

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There was no founding in this article

Conflicts of interest

The authors declare no conflicts of interest

References

1. Saini R. Ozone therapy in dentistry: a strategic review. J Nat Sci Biol Med. 2: 151, 2011
2. Gupta G, Mansi B. Ozone therapy in periodontics. J Med Life 5: 59, 2012
3. Shilpa Reddy A, Narender Reddy, Sainath Dinapadu, et al. Role of Ozone Therapy in Minimal Intervention Dentistry and Endodontics - A Review. J Int Oral Health. 5:102, 2013.
4. El Meligy OA, Elemam NM, Talaat IM. Ozone Therapy in Medicine and Dentistry: A Review of the Literature. Dent J (Basel). 2023 Aug 7;11(8):187. doi: 10.3390/dj11080187. PMID: 37623283; PMCID: PMC10453584.
5. Saccomanno, S., Mummolo, S., Laganà, D., ... Marzo, G., Quinzi, V. The digital diagnostic approach to stafne's bone cavity (Sbc): From a review of the literature to the description of a clinical case. Open Dentistry Journal, 2021, 15(Special Issue), pp. 111–119
6. Bocci V. Is it true that ozone is always toxic? The end of a dogma. Toxicol. Appl. Pharmacol. 2006;216:493–504. doi: 10.1016/j.taap.2006.06.00
7. Hidalgo-Tallón F.J., Torres-Morera L.M., Baeza-Noci J., Carrillo-Izquierdo M.D., Pinto-Bonilla R. Updated Review on Ozone Therapy in Pain Medicine. Front. Physiol. 2022;13:840623. doi: 10.3389/fphys.2022.84062
8. Mummolo, S., Ortu, E., Necozione, S., Monaco, A., Marzo, G. Relationship between mastication and cognitive function in elderly in L'Aquila. International Journal of Clinical and Experimental Medicine, 2014, 7(4), pp. 1040–1046
9. Alfaro M.F., Walby W.F., Adams W.C., Schelegle E.S. Breath condensate levels of 8-isoprostane and leukotriene B4 after ozone inhalation are greater in sensitive versus nonsensitive subjects. Exp. Lung Res. 2007;33:115–133. doi: 10.1080/01902140701364367
10. Pizzolante, T., Memè, L., Ciccariello, A., ... Inchingolo, F., Mummolo, S. Complications of zygomatic implantol-ogy: observational clinical study Bulletin of Stomatology and Maxillofacial Surgery, 2024, 20(4), pp. 73–80
11. Barone A, Marconcini S, Giacomelli L, Ris- poli L, Calvo JL, Covani U. A randomized clinical evaluation of ultra-sound bone surgery versus traditional rotary instruments in lower third molar extraction. J Oral Max- illofac Surg 2010;68:330–6.
12. Chuang SK, Perrott DH, Susarla SM, Dodson TB. Risk factors for inflammatory complications following third mo-lar surgery in adults. J Oral Maxillofac Surg 2008;66:2213–2218.
13. Strappa, E.M., Memè, L., Cerea, M., Roy, M., Bambini, F.
14. Custom-made additively manufactured subperiosteal implant
15. Minerva Dental and Oral Science, 2022, 71(6), pp. 353–360
16. Shugars DA, Gentile MA, Ahmad N, et al. Assessment of oral health-related quality of life before and after third molar surgery. J Oral Maxillofac Surg 2006;64:1721–1730.
17. Iacomino, E., Rastelli, S., Capogreco, M., ... Grivetto, F., D'amario, M. Pterygoid implants in severe posterior maxillary atrophy: a case report. ORAL and Implantology, 2024, 16(2), pp. 88–94
18. Guerra, D., Severino, M., Caruso, S., Rastelli, S., Gatto, R. The importance of using physical tridimensional models for the management and planning of extended osseous odontogenic lesions Dentistry Journal, 2021, 9(11), 134
19. Pizzolante, T., Rasicci, P., Saggiomo, A.P., ... Capogreco, M., Mummolo, S. Buccal Fat Pad Flap and Buccal Advancement Flap for Closure of Oroantral Fistula: A Systematic Review and a Case Report. ORAL and Implantology, 2024, 16(2), pp. 50–61
20. Memè, L., Bambini, F., Pizzolante, T., ... Bianchi, A., Mummolo, S. Osteonecrosis of the jaw in patients with metastatic renal carcinoma: systematic review and meta-analysis. ORAL and Implantology, 2024, 16(2), pp. 79–87
21. Arcuri, C., Petro, E., Sollecchia, G., Mummolo, S., Marzo, G. Laser in periodontal pockets: In vivo and in vitro study. Journal of Biological Regulators and Homeostatic Agents, 2020, 34(3), pp. 139–146
22. Tecco, S., Baldini, A., Mummolo, S., ... Marzo, G., Gherlone, E.F. Frenulectomy of the tongue and the influence of rehabilitation exercises on the sEMG activity of masticatory muscles. Journal of Electromyography and Kinesiolo-gy, 2015, 25(4), pp. 619–628
23. Dinoi, M.T., Mummolo, S., Monaco, A., ... Campanella, V., Marzo, G. Correction to: Orthodontic treatment of the transposition of a maxillary canine and a first premolar: a case report (Journal of Medical Case Reports (2015) 9 (48) DOI: 10.1186/s13256-015-0521-z) Journal of Medical Case Reports, 2019, 13(1), 68
24. Slade GD, Foy SP, Shugars DA, Phillips C, White RP Jr. The impact of third molar symptoms, pain, and swell-ing on oral health-related quality of life. J Oral Maxillofac Surg 2004;62:1118–1124.
25. Markovic AB, Todorovic L. Postoperative analgesia after third molar surgery: contribution of the use of long-acting local anaesthetics, low-power laser and diclofenac. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;102:4–8.
26. Lago ML, Dinitz FM, Serna RC, Gude- Sampedro F,Gandara Rey JM,Garcıa-Garcıa A. Relationships between surgical difficulty and postoperative pain in lower third molar extractions. J Oral Maxillofac Surg 2007;65:979–83.

27. Memè, L., Bambini, F., Pizzolante, T., ... Bianchi, A., Mummolo, S. Evaluation of a single non-surgical ap-proach in the management of periimplantitis: glycine powder air-polishing versus ultrasonic device. ORAL and Implantolo-gy, 2024, 16(2), pp. 67–78
28. Bamgbose BO, Akinwande JA, Adeyemo WL, Ladeinde AL, Arotiba GT, Ogunlewe MO. Effects of co-administered dexamethasone and diclofenac potassium on pain, swelling and trismus following third molar surgery. Head Face Med 2005;1:11.
29. Bambini, F., De Stefano, C.A., Giannetti, L., Memè, L., Pellecchia, M.
30. Influence of biphosphonates on the integration process of endosseous implants evaluated using single photon emission computerize tomography (spect) I Valutazione scintigrafica con metodica SPECT dell'effetto dei bifosfonati sul processo di osseointegrazione implantare
31. Minerva Stomatologica, 2003, 52(6), pp. 331–338
32. K. Chaudhry, N. Rustagi, R. Bali et al., "Efficacy of adjuvant ozone therapy in reducing postsurgical complications following impacted mandibular third-molar surgery: a systematic review and meta-analysis," Journal of the American Den-tal Association, vol. 152, 2021.
33. Rastelli, S., D'amario, M., Iacomino, E., ... Guerra, D., Capogreco, M. Early diagnosis of Sjögren's syndrome: the role of biopsy of the minor salivary glands. Journal of Biological Regulators and Homeostatic Agents, 2022, 36, pp. 81–86
34. Falisi, G., Qorri, E., Botticelli, G., ... Mondragon, M., Di Giacomo, P. Stabilization of the lower denture through the use of fine mini-implants: retrospective study. European Journal of Musculoskeletal Diseases, 2024, 13(2), pp. S1–S7
35. Rastelli, S., Capogreco, M., D'amario, M., ... Severino, M., Iacomino, E. PTERIGOID IMPLANTS: A viable al-ternative for the rehabilitation of the posterior sectors of the atrophic maxilla ORAL and Implantology, 2024, 16(1), pp. 38–43
36. Severino, M., Caruso, S., Rastelli, S., ... Nota, A., Tecco, S. Hand-carried ultrasonography instrumentation in the diagnosis of temporomandibular joint dysfunction. Methods and Protocols, 2021, 4(4), 81
37. Saccomanno, S., Mummolo, S., Giancaspro, S., ... Marzo, G., Quinzi, V. Catering work profession and medi-co-oral health: A study on 603 subjects. Healthcare (Switzerland), 2021, 9(5), 582
38. Baysan A, Lynch E. Clinical reversal of root caries using ozone: 6-month results. Am J Dent 2007;20:203–8
39. D'Amario, M., Di Carlo, M., Natale, S.M., Memè, L., Marzo, G., Matarazzo, G., Capogreco, M. Application of Ozone Therapy in Paediatric Dentistry (2022) Applied Sciences (Switzerland), 12 (21), art. no. 11100
40. Bambini, F., Santarelli, A., Putignano, A., Procaccini, M., Orsini, G., Memè, L., Sartini, D., Emanuelli, M., Lo Muzio, L. Use of supercharged cover screw as static magnetic field generator for bone healing, 1st part: In vitro en-hancement of osteoblast-like cell differentiation (2017) Journal of Biological Regulators and Homeostatic Agents, 31 (1), pp. 215-220.
41. Mampieri, G., Alushi, A., Di Girolamo, M., Rasicci, P., Capogreco, M., Marino, R., Memè, L. Ozone therapy new protocols and innovations: a systematic review (2022) Journal of Biological Regulators and Homeostatic Agents, 36, pp. 117-121.
42. Mummolo, S., Marchetti, E., Albani, F., ... Tecco, S., Marzo, G. Comparison between rapid and slow palatal expansion: Evaluation of selected periodontal indices Head and Face Medicine, 2014, 10(1), 30
43. Baysan A, Lynch E. Clinical reversal of root caries using ozone: 6-month results. Am J Dent 2007;20:203–8.
44. Bambini, F., Greci, L., Memè, L., ... Procaccini, M., Lo Muzio, L.
45. Raloxifene covalently bonded to titanium implants by interfacing with (3-aminopropyl)-triethoxysilane affects osteoblast-like cell gene expression
46. International Journal of Immunopathology and Pharmacology, 2006, 19(4), pp. 905–914
47. Elvis AM, Ekta JS. Ozone therapy: a clinical review. J Nat Sci Biol Med. 2011;2: 66–70.
48. Bocci V. Biological and clinical effects of ozone Has ozone therapy a future in medicine? Br J Biomed Sci. 1999;56:270–9.
49. Cusenza, I., Pensa, V., Rastelli, S., ... D'orto, B., Nagni, M. Conscious sedation in dentistry: narrative review. ORAL and Implantology, 2024, 16(1), pp. 7–13
50. Kim K, Brar P, Jakubowski J, et al. The use of corticosteroids and nonsteroidal anti- inflammatory medication for the management of pain and inflammation after third molar surgery: A review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 107:630, 2009
51. Falisi, G., Paolo, C.D., Rastelli, C., ... Gatto, R., Botticelli, G. Ultrashort Implants, Alternative Prosthetic Reha-bilitation in Mandibular Atrophies in Fragile Subjects: A Retrospective Study Healthcare, 2021, 9(2), pp. 1–9
52. Manica, U., Izzi, F., Palmacci, M., ... Balbi, B., Nagni, M. Implant-prosthetic rehabilitation of an agenesis lateral incisor: a case report and literature review. ORAL and Implantology, 2024, 16(1), pp. 14–18
53. Marchetti, E., Pizzolante, T., Americo, L.M., ... Quinzi, V., Mummolo, S.Periodontology Part 4: Periodontal dis-ease in children and adolescents. European Journal of Paediatric Dentistry, 2022, 23(4), pp. 332–335
54. Di Paolo, C., Qorri, E., Falisi, G., ... Inchingolo, F., Di Giacomo, P. RA.DI.CA. Splint Therapy in the Manage-ment of Temporomandibular Joint Displacement without Reduction Journal of Personalized Medicine, 2023, 13(7), 1095
55. Bernardi, S., Mummolo, S., Zeka, K., ... Continenza, M.A., Marzo, G. Use and Evaluation of a Cooling Aid in Laser-Assisted Dental Surgery: An Innovative Study. Photomedicine and Laser Surgery, 2016, 34(6), pp. 258–262
56. Pennazza, G., Marchetti, E., Santonico, M., ... D'Amico, A., Di Natale, C. Application of a quartz microbalance based gas sensor array for the study of halitosis. Journal of Breath Research, 2008, 2(1), 017009
57. Guerra, D., D'amario, M., Lacarbonara, M., ... Lupi, E., Capogreco, M. 3D printed anatomical models in the preliminary planification and execution of complex implanplacement: a case report Journal of Biological Regulators and Homeostatic Agents, 2022, 36(2), pp. 65–70
58. Bambini, F., Pellecchia, M., Meme, L., ... Procaccini, M., Lo Muzio, L.
59. Anti-inflammatory cytokines in peri-implant soft tissues: A preliminary study on humans using cDNA microarray technology
60. European Journal of Inflammation, 2007, 5(3), pp. 121–127
61. Marchetti, E., Ratta, S., Mummolo, S., ... Bedini, R., Marzo, G. Mechanical Reliability Evaluation of an Oral Im-plant-Abutment System According to UNI en ISO 14801 Fatigue Test Protocol Implant Dentistry, 2016, 25(5), pp. 613–618
62. Bernardi, S., Mummolo, S., Varvara, G., ... Marzo, G., Macchiarelli, G. Bio-morphological evaluation of perio-dontal ligament fibroblasts on mineralized dentin graft: An in vitro study Journal of Biological Regulators and Homeostatic Agents, 2019, 33(1), pp. 275–280
63. Marchetti, E., Ratta, S., Mummolo, S., ... Bedini, R., Marzo, G. Evaluation of an endosseous oral implant sys-tem according to UNI en ISO 14801 fatigue test protocol Implant Dentistry, 2014, 23(6), pp. 665–671
64. Memè, L., Grilli, F., Pizzolante, T., ... Sampalmieri, F., Mummolo, S. Clinical and histomorphometric compari-son of autologous dentin graft versus a deproteinized bovine bone graft for Socket Preservation. ORAL and Implantology, 2024, 16(2), pp. 101–106