Original Research Article

Assessing Oral Health Related Quality of Life after third molar extraction with ozonized water: a randomized triple blind spit-mouth clinical trial

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ABSTRACT

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| **Purpose** The present study evaluated the oral health related quality of life of patients that were submitted to removal of lower third molars with alveolar irrigation using double distilled ozonized water or only double distilled water during the surgical procedure. **Methods** In this split mouth study, 21 patients were randomized into group 1 (T1 – side of the mouth that received ozonized double-distilled water during surgical procedure) and group 2 (T2 – group that received double-distilled water only during surgical procedure). Each patient was submitted to 2 surgical procedures, at least 4 weeks apart from each other. A questionnaire on OHRQoL was completed by each patient after the surgical procedure and 7 days after, as well as another questionnaire after suture removal. **Results**It was included 8 men and 12 women. For social isolation dimension, the ozonized water showed better results than control group (p = 0.043). Eighty percent of patients in test group reported pain and edema as a cause of social isolation after surgery (p = 0.013). Ability to feed and variations in diet dimension shows that 5% (n = 1) of patients in T1 did not notice any change in these skills, while none of the patients at T2 recovered from surgery without any change in their eating ability and diet.**Conclusion** Ozone therapy can positively affect patients' OHRQoL in terms of pain and swelling and satisfaction with treatment. |

*Keywords: Third molar, Ozone, Quality of life, Oral Surgery*

1. INTRODUCTION

The extractions of impacted third molars are surgical procedures that can cause postoperative discomfort, such as pain, edema and trismus, consequently affecting the patient's oral health-related quality of life (OHRQoL), causing biological and social impacts, influencing routine obligations for several days after the surgery (Chaudhry et al., 2021; Duarte-Rodrigues et al., 2018; Glória et al., 2020). In view of the impacts of oral conditions on the patient's well-being and the effectiveness of the treatment performed, the use of instruments that assess these impacts can be an ally of the professional in the success of the treatments. In this context, the questionnaires for assessing the quality of life (QoL), in addition to estimating the quality, effectiveness and efficiency of methods of treatment, also assess their physical, psychosocial, and social consequences in these individuals (Duarte-Rodrigues et al., 2018).

In the control and management of postoperative discomforts in dentistry, such as edema, pain, trismus, sensitivity and alveolitis (de Santana-Santos et al., 2013) ozone is a non-drug alternative with a strong antimicrobial and healing action has been widely used in medicine and in dentistry. It is available in various forms, such as gas, gel and water, which can be applied to tissues parenterally and through topic applications (Glória et al., 2020). In addition to its antibacterial, immunostimulating, analgesic, and antihypnotic properties, ozone also has detoxicating, bioenergizing, and biosynthetic properties, as well as improved wound healing (Ahmedi et al., 2023). Its oxidizing potential induces the destruction of cell walls and cytoplasmic membranes of bacteria and fungi. In this process, ozone attacks glycoproteins, glycolipids and other amino acids, in addition to inhibiting and blocking the cell's enzymatic control system, resulting in increased membrane permeability, causing the death of these bacteria and fungi (Garg et al., 2022; Vats et al., 2022).

In view of the therapeutic properties of the ozone, as well as the need for better control of pain, edema and oral trismus after surgical interventions, the aim of this study was to evaluate changes in the OHRQoL after surgery of the mandibular third molar with alveolar irrigation using double distilled ozonized water or only double distilled water during the surgical procedure in a randomized triple-blind, split-mouth clinical trial.

2. material and methods

This study was carried out at the Surgery and Periodontics Clinic of the Federal University of the Jequitinhonha and Mucuri Valleys (UFVJM- Brazil), from January to March 2018. The protocol was approved by the UFVJM Research Ethics Committee (protocol 2174074) and was performed in accordance with the Helsinki Declaration of 1975, revised in 2013. All participants signed an informed consent form (ICF) before the beginning of this study. This clinical trial was registered with ClinicalTrials (NCT3501225) and developed in accordance with CONSORT (Ghosh et al., 2020).

This controlled, randomized, triple blind clinical trial used the split-mouth study design, in which patients who had surgical indication for removal of impacted third mandibular molars, classification II B (Pell-Gregory), underwent a surgical procedure with double distilled ozonized water (T1) or double distilled water only (T2) as an irrigating solution, according to randomization. A questionnaire on oral health related quality of life was applied to the participants after the surgical procedures and 7 days after.

**2.1 Sample calculation and selection**

The sample size was calculated to compare the mean values which considered standard pain deviation 3.32 mm (Altman et al., 2001) and the difference to be detected between the groups stipulated at 3 mm, 95% significance level and 80% test power, determining 19 patients. Two patients were added to cover any dropouts. Patients were recruited between November 2017 and February 2018.

The patients selected for this study were between 18 and 30 years old, did not report any systemic diseases and had surgical indication for the removal of impacted lower third molars, classification II B, which were radiographically evaluated before surgical procedures (Pell-Gregory) (9). Patients with contraindications to ozone therapy (patients with absence or decrease of the G6PD enzyme, pregnant or lactating women, and patients with very recent acute hemorrhage), local infection, pericoronitis and smokers were excluded (Hems et al., 2005). The surgeries were scheduled in 2 separate clinical sessions, at least 4 weeks apart from each other.

**2.2 Randomization, masking, and allocation of volunteers**

The selected patients were numbered from 1 to 21. By drawing lots, group 1 was assigned to receive ozonized water and group 2, double distilled water. The volunteers were randomly assigned to one of the two groups using an accurate dice; if an odd number was drawn, the subject was allocated to group 1; and an even number to group 2. The information on the type of intervention used was unknown by the patient, surgeon, clinical investigator (patient follow-up and outcome measures) and statistician. The side to be operated on was also randomized by rolling an accurate die; an odd number indicated surgery on the right side; even number, left side. In this sequence, the dice was rolled twice per patient. The results of the drawings were placed in two opaque envelopes, sealed, and properly identified with the patient's code. The envelopes were opened just a few moments before the surgery procedure. Thus, allocation concealment was achieved.

**2.3 Ozonized double-distilled water**

Ozonized double-distilled water was prepared 5 min prior to the surgical procedures by an external collaborator using the model MedPlus ozone generator (Philozon®, Santa Catarina, Brazil) regulated at 40 μg /mL for 5 min of bubbling in 250 ml of double-distilled water (Sanobiol, Pouso Alegre, Brazil). The final concentration was 8.0 μg /mL.

**2.4 Surgical intervention**

All surgeries were performed under local anesthesia (2% lidocaine and epinephrine 1: 100,000) using the regional technique of blocking the inferior alveolar and lingual nerves with anesthetic complementation of the buccal nerve. All operations were performed by the same surgeon with experience in oral surgery, under strict control and within biosafety rules. In order to reduce differences in the level of intraoperative trauma, the same surgical procedure was adopted for both sides. After incision and removal of soft tissue, a low rotation osteotomy (30,000 rpm) was performed using drill 8 (350,000 rpm) and with 702C stainless steel carbide drills (dental drills) (Dabi Atlante®), under constant irrigation with 10cc (ruthe) hypodermic glass syringe attached to a 10mm steel needle (BD) with double distilled water or ozonized double distilled-water according to randomization, followed by aspiration. Then, the third molars were extracted with the aid of the straight Seldin lever, careful curettage, bone regularization and cleaning of the surgical area through abundant irrigation followed by aspiration. Suture was performed with silk thread (4.0) in isolated points and removed after 7 days. All patients received postoperative instructions and were prescribed sodium dipyrone (500 mg), 1 tablet every 6 h in case of pain; and nimesulide (100 mg), 1 tablet every 12 h for 3 days.

**2.5 Postoperative quality of life (baseline)**

All individuals were instructed and completed a questionnaire on postoperative oral health-related quality of life. The questionnaire used was the same as that described by Savin; Ogden, 1997 and adapted by Sancho-Puchades et al., 2012. The questionnaire assesses the following items: social isolation; isolation from work and physical appearance, which possible responses consisted of "yes" or "no"; and variations in eating ability and diet; speech ability and sleep impairment which possible responses consisted of “not at all”, “a little”, “quite a lot” and “very much”.

**2.6 Quality of life after 7 days and after suture removal**

All individuals were instructed and completed the same questionnaire to assess OHRQoL on the seventh day after the surgical procedure and another questionnaire on the same day, after suture removal. This second, also described by Savin; Ogden, 1997 and adapted by Sancho-Puchades et al., 2012 consists of the following items: pain and discomfort when removing the suture, which possible responses consisted of “not at all”, “a little”, “quite a lot” and “very much”, and satisfaction with the treatment, which possible responses consisted of “yes” or “no”.

The values ​​were obtained by adding the scores of each subscale and the total sum at the baseline and 7 days post-intervention.

**2.7 Data analysis**

The results were entered and analyzed using the Statistical Package for the Social Science Software (SPSS version 25.0). This process was carried out by two people (one typed in and the other verified). The envelope containing the data for each patient received a corresponding number in the database. The statistical analysis was initially performed with the groups coded as Treatment 1 and Treatment 2. The decoding envelope for this information was assessed after the completion of the clinical trial and statistical analysis. Thus, the statistician was blinded for the type of treatment until all analyses were done. Descriptive statistics were analyzed to obtain the mean and standard deviation. The association between categorical variables was verified using the chi-square test. The significance level was 95% (p <0.05).

3. results and discussion

Twenty of the 20 participants, 8 men and 12 women, with an average age of 20.9 years, returned the completed questionnaires and attended the follow-up appointments. Twenty impacted teeth were included in each group. The mean time of surgery was 15.65 (± 6.94) minutes for group 1 and 15.90 (± 5.56) minutes for group 2, without any complications. The results of the questionnaire are shown in Table 1.

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| Table 1. Oral Health related quality of life questionnaire according to group. |
|  | Ozonized Distilled Water |  | Distilled Water |  |
|  | Non (%) | Yesn (%) |  | Non (%) | Yesn (%) | p |
| Social isolation  |  |  |  |  |  |  |
| 1a. Did you keep your usual social activities?  | 5 (25.0) | 15 (75.0) |  | 7 (35.0) | 13 (65.0) | 0.687 |
| 1b. Have you continued practicing your favorite sport or hobbies?  | 11 (55.0) | 9 (45.0) |  | 7 (35.0) | 13 (65.0) | 0.043 |
| **Please mark the reason for social isolation:** |  |  |  |  |  |  |
| 1c. pain and/or swelling  | 9 (45.0) | 11 (55.0) |  | 4 (20.0) | 16 (80.0) | 0.013 |
| 1d. physical appearance  | 13 (65.0) | 7 (35.0) |  | 11 (55.0) | 9 (45.0) | 0.081 |
| 1e. bad mood  | 14 (70.0) | 6 (30.0) |  | 17 (85.0) | 3 (15.0) | 0.004 |
| 1f. malaise  | 15 (75.0) | 5 (25.0) |  | 15 (75.0) | 5 (25.0) | 0.999 |
| Working isolation |  |  |  |  |  |  |
| 2a. Did you ask for sick leave or discontinued your work?  | 15 (75.0) | 5 (25.0) |  | 14 (70.0) | 6 (30.0) | 0.091 |
| 2c. Did the extraction affect your performance at work?  | 17 (85.0) | 3 (15.0) |  | 16 (80.0) | 4 (20.0) | 0.999 |
| 2d. Did someone accompany you?  | 19 (95.0) | 1 (5.0) |  | 19 (95.0) | 1 (5.0) | 0.999 |
| 2e. Does this person discontinued his/her work to do so?  | 20 (100.0) | 0 (0.0) |  | 19 (95.0) | 1 (5.0) | - |
| Eating ability and diet variations.  | Not at all n (%) | A little n (%) | Quite a lotn (%) | Very muchn (%) |  | Not at all n (%) | A little n (%) | Quite a lotn (%) | Very muchn (%) |  |
| 3a. Did you continue with your usual diet?  | 12 (60.0) | 0 (0.0) | 8 (40.0) | 0 (0.0) |  | 12 (60.0) | 0 (0.0) | 8 (40.0) | 0 (0.0) 0.456 | 0.456 |
| 3b. Did you notice any changes in taste perception?  | 11 (55.0) | 7 (35.0) | 2 (10.0) | 0 (0.0) |  | 8 (42.1) | 8 (42.1) | 1 (5.3) | 2 (10.5) 0.357 | 0.357 |
| 3d. Did you notice any changes in chewing ability?  | 1 (5.0) | 11(55.0) | 4 (20.0) | 4 (20.0) |  | 0 (0.0) | 12 (60.0) | 6 (30.0) | 2 (10.0) 0.001 | 0.001 |
| 3e. Did you have problems opening your mouth?  | 6 (30.0) | 8(40.0) | 2 (10.0) | 4 (20.0) |  | 4 (20.0) | 10 (50.0) | 4 (20.0) | 2 (10.0) 0.016 | 0.016 |
| Speaking ability |  |  |  |  |  |  |  |  |  |  |
| 4a. Have you noticed any changes in your voice?  | 13 (65.0) | 7 (35.0) | 0 (0.0) | 0 (0.0) |  | 14 (70.0) | 6 (30.0) | 0 (0.0) | 0 (0.0) 0.001 | 0.001 |
| 4b. Have you noticed any changes in speech?  | 9 (45.0) | 7 (35.0) | 2 (10.0) | 2 (10.0) |  | 7 (35.0) | 10 (50.0) | 3 (15.0) | 0 (0.0) 0.053 | 0.053 |
| 4c. When you talk to other people, do they understand you?  | 1 (5.6) | 2 (11.1) | 8 (44.4) | 7 (38.9) |  | 2 (10.0) | 2 (10.0) | 5 (25.0) | 11 (55.0) 0.130 | 0.130 |
| Sleep impairment |  |  |  |  |  |  |  |  |  |  |
| 5a. Have you had difficulty falling asleep?  | 14 (70.0) | 3 (15.0) | 2 (10.0) | 1 (5.0) |  | 14 (70.0) | 5 (25.0) | 1 (5.0) | 0 (0.0) <0.001 | <0.001 |
| 5b. Have you experienced interruptions in sleep?  | 14 (70.0) | 4 (20.0) | 1 (5.0) | 1 (5.0) |  | 15 (78.9.0) | 3 (15.8.0) | 1 (5.3.0) | 0 (0.0) <0.001 | <0.001 |
| 5c. Have you felt drowsy? | 13 (65.0) | 5 (25.0) | 2 (10.0) | 0 (0.0) |  | 15 (75.0) | 3 (15.0) | 2 (10.0) | 0 (0.0) <0.001 | <0.001 |
| **Physical appearance** | Non (%) | Yesn (%) |  | Non (%) | Yesn (%) |  |
| 6a. Have you noticed changes in your physical appearance?  | 13 (65.0) | 7 (35.0) |  | 11 (55.0) | 9 (45.0) | 0.081 |
| 6b. Is it what you expected?  | 4 (21.1) | 15 (78.9) |  | 5 (25.0) | 15 (75.0) | 0.226 |

Regarding “social isolation”, the ozonized distilled water showed better results for discontinued the practice of sports or hobbies than distilled water (p = 0.043). 80% of patients that underwent distilled water reported pain and edema as a cause of social isolation after surgery (p = 0.013). "Bad mood" as a cause of social isolation was greater in patients that received ozonized water when compared to patients that received distilled water (p = 0.004). There were no differences between the groups taking into account the domain working isolation.

"Ability to feed and variations in diet" shows that 5% (n = 1) of patients in T1 did not notice any change in these skills, while none of the patients at T2 recovered from surgery without any change in their eating ability and diet. On the other hand, 20% (n = 4) of patients in T1 reported "a lot" in their eating ability and diet variations, while only 10% (n = 2) of patients in T2 reported the same (p = 0.001). Thirty percent (n = 6) reported that during T1, they did not have any difficulty opening their mouths while only 20% (n = 4) of patients in T2 reported the same. Twenty percent (n = 4) of patients in T1 reported "quite a lot" on the same issue while only 10% (n = 2) of patients in T2 (p = 0.016) reported the same.

In speech ability, 65% (n = 13) reported no changes in voice in T1, while 70% (n = 14) reported the same in T2. Meanwhile, 35% of patients (n = 7) in T1 reported noticing a few changes in their voice, while 30% of patients (n = 6) reported the same in T2 (p = 0.001). In “sleep impairment”, most patients in T2 reported having difficulty falling asleep (5%, p = 0.001), but they did not experience any interruptions in sleep (75%, p = 0.001) and did not feel sleepy after the surgical procedure (75%, p = 0.001). The "physical appearance" statistics were not significant.

The results of “Pain and discomfort at suture removal” and “Satisfaction with the treatment” are shown in Table 2. There was a difference between the two groups regarding anxiety caused by suture removal appointment, and 100% of the patients in the ozone group (T1) reported that they would repeat this kind of treatment and that their problem has been resolved.

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| --- | --- | --- | --- | --- |
|  | Ozonized Distilled Water |  | Distilled Water |  |
|  | Not at alln (%) | A little n (%) | Quite a lotn (%) | Very much n (%) |  | Not at alln (%) | A little n (%) | Quite a lotn (%) | Very much n (%) | **p** |
| Pain and discomfort at suture removal.  |  |  |  |  |  |  |  |  |  |  |
| 7a. Has suture removal been uncomfortable?  | 13 (65.0) | 7 (35.0) | 0 (0.0) | 0 (0.0) |  | 15 (75.0) | 5 (25.0) | 0 (0.0) | 0 (0.0) | 0.787 |
| 7b. Has the appointment for suture removal caused you anxiety?  | 12 (60.0) | 6 (30.0) | 2 (10.0) | 0 (0.0) |  | 12 (60.0) | 8 (40.0) | 0 (0.0) | 0 (0.0) | 0.024 |
| Satisfaction with treatment | No n (%) | Yesn (%) |  | No n (%) | Yesn (%) |  |
| 8a. Are you satisfied with treatment?  | 1 (5.0) | 19 (95.0) |  | 2 (10.0) | 18 (90.0) | 0.732 |
| 8b. Would you recommend it?  | 1 (5.0) | 19 (95.0) |  | 1 (5.0) | 19 (95.0) | 0.999 |
| 8c. Would you repeat it?  | 0 (0.0) | 20 (100.0) |  | 1 (5.0) | 19 (95.0) | - |
| 8d. Do you feel that the problem causing you seek treatment has been solved?  | 0 (0.0) | 20 (100.0) |  | 1 (5.0) | 19 (95.0) | - |

**Table 2.** Pain and satisfaction according to the group.

In the analyses between groups, a greater number of patients did not follow the practice of their favorite sport or hobby after the surgical procedure with ozonized water as an irrigating solution. This discrepancy may be since, for most patients, the first irrigation method to be drawn was ozonized water, which justifies greater postoperative psychological trauma and, consequently, less practice of physical activities. Patients might have been more careful, therefore less active, after the first procedure than after the second surgical procedure.

Eighty percent of the patients in T2 (double-distilled water) reported the presence of pain and swelling, while only 55% of the patients in T1 reported the same. Ozone therapy not only has an antibacterial effect, it also reacts with blood components (erythrocytes, leukocytes, endothelial cells, and the vascular system) and positively affects oxygen metabolism, cellular energy, immuno-modulatory properties, antioxidant defense system and microcirculation (Boczkowska-Radziwon et al., 2022). Kazancioglu et al., 2014 suggested that such effects of ozone therapy are similar to the biostimulatory properties of low-level laser therapy (LLLT), which is widely studied and used to control some postoperative complications. Thus, it is recommended that the ozonized water be compared to LLLT after third molars surgeries in other RCTs.

The statistical data regarding the problems with mouth opening were not significant. Sivalingam et al., 2017 in a clinical trial that used topical ozonized gel to fill the alveolar socket after extraction of impacted third molars found excellent results regarding mouth opening on days 1 and 3 after the surgical procedure. This result suggests that a greater contact of ozone with the affected area brings more satisfactory responses since ozone modulates cellular immunity through the activation of macrophages and the stimulation of the synthesis of biologically active substances. Such action reduces inflammation and improves healing (Nagayoshi et al., 2004). Ozone affects the unity of bacterial cell envelope by oxidation of phospholipids and lipoproteins. According to Vats et al., 2022, a low concentration of even 0.1 ppm is capable to inactivate bacterial cells including spores, and can also suppress fungal cell growth (Garg et al., 2022).

Some advantages of using ozone therapy in OHRQoL observed in the present study refer mainly to the lower presence of pain and swelling, by the patient's perception, and by the general satisfaction with the results of the treatment. Less pain means less use of analgesics and, consequently, fewer side effects associated with drug therapies (Nagayoshi et al., 2004).

The use of a non-validated questionnaire is a limitation of this study, since it does not provide us with scores, but more qualitative data. Another limitation that is always present in QoL studies is that such data are subjective, based on the patients' perception2. However, it was possible to evaluate some aspects of OHRQoL in patients undergoing extraction of lower third molars.

4. Conclusion

Ozone therapy has been shown to positively affect patients' OHRQoL in terms of pain and swelling and satisfaction with treatment. Further studies are suggested relating the use of ozone in an attempt to offer a better QoL after surgical procedures in dentistry.

Consent

"All authors declare that ‘written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal."

Ethical approval

 “All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.”

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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