Dentin hypersensitivity treatment with ozonated oil: a randomized controlled triple-blind clinical trial

Tratamento de hipersensibilidade dentinária com óleo ozonizado: um ensaio clínico randomizado controlado triplo-cego

Tratamento de hipersensibilidade dentinaria con aceite ozonizado: ensayo clínico aleatorizado, controlado, triple ciego

Abstract
The present study aimed to assess dentin hypersensitivity (DH) level and quality of life in patients before and after treatment with ozonated oil compared with extra virgin oil. This is a randomized triple-blind controlled clinical trial, consisting of patients with dentin hypersensitivity which was stimulated by evaporative and thermal stimuli. DH level was measured using a numerical rating scale. The patients were treated with ozonated oil and olive oil. Data were measured at baseline, immediately, and 4 weeks after treatment. The Dentine Hypersensitivity Experience Questionnaire (DHEQ-15) and the Oral Health Impact Profile (OHIP-14) were applied at baseline and 4 weeks after treatment. The sample consisted of 8 women and 3 men, with an average age of 23.82 years. The test group was 40 teeth while the control group consisted of 36 teeth, with the most prevalent tooth being the incisor (52.6%). There was a significant reduction in the DH level and an improvement in the quality of life after treatment. Among the sample, 90.1% reported an improvement in the final result. Both ozonated oil and olive oil were effective in reducing dentin hypersensitivity level and improving oral health-related quality of life 30 days after treatment.

Keywords: Dentin sensitivity; Ozone; Pain measurement; Quality of life; Randomized clinical trial.

Resumo
O presente estudo teve como objetivo avaliar o nível de hipersensibilidade dentinária (HD) e a qualidade de vida em pacientes antes e após o tratamento com óleo ozonizado em comparação com o óleo extra virgem. Este é um ensaio clínico randomizado, triplo-cego, controlado, composto por pacientes com hipersensibilidade dentinária estimulada por estímulos evaporativos e térmicos. O nível de HD foi medido por meio de uma escala de avaliação numérica. Os pacientes foram tratados com óleo ozonizado e azeite de oliva. Os dados foram medidos no início do estudo,
Dentin hypersensitivity (DH) is characterized as an acute and brief pain when dentin is exposed to thermal, evaporative, tactile, osmotic, or chemical stimuli and cannot be attributed to any form of dental defect or pathology (Canadian Advisory Board on Dentin Hypersensitivity, 2003; Cunha-Cruz, et al., 2011). It is a pain that disappears immediately after the removal of the generating stimulus (Sobral & Garone, 1999).

The most accepted theory to explain cervical dentinal hypersensitivity is the “hydrodynamic theory”, in which the rapid movement of fluid inside the dentinal tubules stimulates odontoblasts and nerve cells present inside the tubules or even in the pulp chamber. Thus, with the increase of hydrodynamic stimuli inside the tubules, the nociceptives are activated, causing the characteristic pain (Brännström & Garberoglio, 1980; Moretzsohn & Campos, 2001).

The prevalence varies in different studies, in which it is reported that DH occurs more in adults, being more common in people between 20 and 40 years old, with a peak of greater occurrence at the end of the third decade (Vale & Bramante, 1997). Population studies indicate that this type of painful manifestation affects one in seven adult patients and can result in behavioral and emotional changes (Grippo, 1991; Vale & Bramante, 1997; Moretzsohn & Campos, 2001; Sgolastra, et al., 2011).

Quality of life is the individual's perception of his insertion in life in the context of the culture and value systems in which he lives and concerning his goals, expectations, standards and concerns (Farquhar, 1995; Fleck, 2000). The condition of oral health is a factor of great interference for it (Bulgareli, et al., 2018). One of these conditions is the influence of DH on people's daily lives. There are some instruments to assess the quality of life related to oral health, which can be generic, such as the Oral Health Impact Profile (OHIP-14) (Slade, 1997; Afonso, et al., 2018) or specific, such as the Dentine Hypersensitivity Experience Questionnaire (DHEQ-15) (Douglas-de-Oliveira, et al., 2018).
There are currently several types of hypersensitive teeth treatments, such as desensitizing toothpaste, laser therapy, varnishes and cyanoacrylate (Lima, et al., 2017). Since the great challenge to be overcome is to find a substance that effectively eliminates the painful sensation and does not relapse, thus improving the quality of life (Boiko, et al., 2010).

Ozone application (Fernandes, et al., 2021) is an alternative for the treatment of dentin hypersensitivity (Lena & Marianne, 2017). However, the literature is scarce on the effectiveness of ozonated oil on DH. The objective of this work was to compare the effectiveness of ozonated oil with extra virgin oil in reducing the DH level. As a secondary objective, it was investigated the oral health related quality of life after treatment and the most prevalent affected tooth was confirmed.

2. Methodology

Ethics and study design

This quantitative study (Mohajan, 2020) was approved by the Research Ethics Committee of the Universidade Federal dos Vales do Jequitinhonha e Mucuri (UFVJM) under protocol 2.995.865, fulfilling all the requirements for researching human beings according to the statement of Helsinki, 1975, revised in 2013, and it adheres to CONSORT guidelines. Registration number RBR-3nqhfy on the website http://www.ensaiosclinicos.gov.br/rg/RBR-3nqhfy/.

This is a randomized triple-blind controlled clinical trial, with the sample consisting of patients who complained of DH. This study was carried out at the Surgery and Periodontics Clinic of the Dentistry Department of the Faculty of Biological and Health Sciences of the UFVJM.

Sample size and characteristics

To determine the sample size, the calculation was used to compare the average of the two groups. Calculations with a 5% significance level and 80% power determined that 34 hypersensitive teeth would be sufficient to detect a 2mm difference in the visual analog scale between the groups. 2.96mm standard deviation was obtained in a similar previous study (Patel, et al., 2013). Thus, the minimum necessary was 34 hypersensitive teeth per group.

Patients with complaints of DH in daily activities and with a clinical diagnosis of DH were selected. The diagnosis was done through air-jet applied from the triple syringe and flexible cotton swabs in contact with ice cubes.

Patients should be aged between 18 and 60 years with good general and oral health conditions. Also, the participant should not have been using desensitizing agents, not having undergone scaling and polishing or periodontal treatment in the last 3 months, respond to the stimulus of the air jet from the triple syringe on the numerical rating scale ≥ 5, respond to the stimulation of the flexible cotton swabs in continuous contact with ice cubes for 10 seconds on the numerical rating scale ≥ 5, consented to participate in the research. And have at least 1 hypersensitive tooth in 2 different hemiarchs.

Patients with restorations and carious lesions in the exposed dentin of hypersensitive teeth; presenting with gingival inflammation and who frequently used painkillers, anti-inflammatories and antidepressants were excluded. Patients were instructed in the hygiene technique, using a soft brush and toothpaste without desensitizing agents for the period of study.

Interventions

Patients underwent two treatment groups which selection was determined by lottery drawn. In the test group, the teeth were subjected to test treatment (Ozone Oil; São Paulo, Brazil), using ozonated oil. In the control group, the teeth were subjected to control treatment, using extra virgin vegetable oil (Azeite Gallo Extra Virgem; GalloWorldwide; Abrantes, Portugal). The products were applied in the quantity of 0.5ml only once in the sensitive area for 5 minutes with the aid of a microbrush and under relative isolation with cotton wool rolls (Patel, et al., 2013). Then, the tooth was dried with gauze. All
the procedures described above were performed by only one operator previously trained. Before the beginning of the research, a pilot study was carried out with 2 participants who did not enter the final sample.

The interventions were performed under strict control within the biosafety norms. It was adopted the usage of barriers on surfaces and personal protective equipment, such as gloves, masks and protective eyewear during all procedures. It was performed cleaning, sterilization and disinfection of dental instruments, devices, equipment and surfaces. All staff had hand hygiene before and after each intervention. Before treatment, intraoral antisepsis was performed with 0.12% chlorhexidine rinse for 1 minute.

**Randomization, concealment of allocation and masking procedures**

Randomization was performed by an independent researcher who assigned a letter to each treatment and a number to each hemiarch of the patient's mouth. Each treatment and each hemiarch were selected by lottery drawn. This allocation was kept secret within opaque, sealed envelopes for each subject. Only at the time of application of the oil, the envelopes were opened, ensuring the allocation was concealed. Each patient received both types of treatment in different hemiarchs: one with ozonated oil and the other with vegetable oil. Such measures were necessary to avoid external interference.

Masking was facilitated by the fact that the oils have similar color, consistency and taste. The patients received the same procedure ritual in both hemiarchs. Patients were unable to know what type of treatment they received on each side of the mouth. The operator was also blinded to the types of oil used, as he received the oils in a dappen pot without identification and with sufficient quantity for the procedure. Also, the evaluator who was masked to the interventions, performed the pre- and post-treatment evaluations. Patients were instructed not to undergo dental procedures in order not to interfere with the results of the research, except in situations of real need, during the 4 weeks after intervention.

**DH Stimulation**

DH was stimulated through evaporative and thermal tests. Initially, an air jet was applied for 3 seconds to teeth previously isolated from the rest by utility wax. The thermal test was done by applying cold: flexible cotton swabs from the ice cubes applied to the cervical of the teeth for 3 seconds. One minute interval between the application of each stimulus was used. During the entire study period, all stimuli were performed by a single previously trained researcher.

The air jet was applied to each tooth for 3 seconds at 0.5 cm distance, with neighboring teeth isolated with utility wax. The flexible cotton swabs came into contact with the ice for 10 seconds before being applied to each sensitive tooth of the hemiarch for 3 seconds. The stimuli were removed earlier than expected if the sensitivity was unbearable. All the results found were recorded in the individual patient record.

The evaluator was trained for the execution of clinical exams and calibrated by the test–retest method, with an interval of 12 days. In total, 30 hypersensitivity teeth were selected, and the examiner assessed them through evaporative and thermal tests. The agreement index was calculated through the intraclass correlation coefficient, of which the result was ICC = 0.879.

**Evaluation parameters**

The initial assessment was considered as a baseline. All other subsequent assessments were done by the same researcher. In the form, treatment A (test) or B (control) was noted and only at the end of the study, both the operator and the evaluator know the type of treatment used.

The DH level was measured using a numerical rating scale, ranging from 0 to 10. After each stimulus, the evaluator asked which number on the scale best represented the pain the patient felt at the time of the tests. Data were obtained at baseline, immediately after interventions and 4 weeks after treatment.
The Brazilian version of DHEQ-15 was used to assess oral health related quality of life, applied at baseline and 30 days after treatment (Douglas-de-Oliveira, et al., 2018). This instrument contains 15 items grouped into 5 dimensions: restrictions, adaptation, social impact, emotional impact, identity, and must be answered on a Likert scale of 1 to 7 points. The final score ranges from 15 to 105 points, with a higher score indicating the worse quality of life related to oral health. Besides, the Brazilian version of OHIP-14 was also used. This version includes only two questions for each of the seven domains: Functional limitation, Physical pain, Psychological discomfort, Physical disability, Psychological disability, Social disability and Disadvantage (Slade, 1997; Afonso, et al., 2017).

At the end of the study, participants were informed about the results found. Research patients who presented residual hypersensitivity were treated by using cyanocrylate glue (Flecha, et al., 2013).

**Statistical analysis**

The results were analyzed using the Statistical Package for Social Science software (SPSS version 25.0). Descriptive statistics analyzes were performed to obtain frequencies, means and standard deviations. The normality of the data was verified by the Shapiro-Wilk test. The association between variables was verified by the Friedman (with Bonferroni posthoc) and Wilcoxon tests. The level of significance was set at 95% (p <0.050).

3. Results

The sample consisted of 8 (72.7%) women and 3 (27.3%) men, with a mean age of 23.82 years and a standard deviation of 6.63. The test group was composed of 40 (52.6%) teeth while the control group was composed of 36 (47.4%) teeth. The most prevalent tooth was incisor with 52.6% (n = 40) (Table 1). Among the 11 patients, 10 (90.1%) reported an improvement in the final result and 1 (9.9%) reported that there was a worsening of the initial presentations.

| Tooth     | n  | %  |
|-----------|----|----|
| Molar     | 3  | 3.9|
| Premolar  | 12 | 15.8|
| Canine    | 21 | 27.6|
| Incisor   | 40 | 52.6|

Table 1. Tooth Prevalence with Hypersensitivity

Source: Authors.

There was a statistically significant difference for DH level stimulated by air jet for test treatment (p = 0.001) after 30 days. Control treatment also obtained a statistically significant result after 30 days (p <0.001). Control group showed a good result immediately after the treatments (<0.001) (Table 2).
Table 2. Evaluation of air-stimulated dentin hypersensitivity.

| AIR JET   | Baseline (T0) | Immediate (T1) | 30 Days (T2) | p*         | Post-hoc |
|-----------|---------------|----------------|--------------|------------|----------|
|           | Mean  SD      | Mean  SD       | Mean  SD     |            |          |
| Test      | 3.88 2.26     | 3.00 2.12      | 2.33 1.55    | 0.001      | T0 x T1:0.057 T0 x T2:0.001 T2 x T1:0.721 |
| Control   | 4.89 2.20     | 3.47 1.94      | 2.58 1.82    | <0.001     | T0 x T1:0.024 T0 x T2:0.001 T2 x T1:0.102 |
| p**       | 0.073         | 0.387          | 0.625        |            |          |

*Friedman test, Bonferroni post hoc test, ** Wilcoxon test. Source: Authors.

There was a statistically significant difference for DH stimulated with ice for test (p <0.001) and control (<0.001) groups after treatments (Table 3).

Table 3. Evaluation of DH stimulated with flexible cotton swabs in contact with ice

| ICE       | Baseline (T0) | Immediate (T1) | 30 days (T2) | p*        | Post-hoc |
|-----------|---------------|----------------|--------------|-----------|----------|
|           | Mean  SD      | Mean  SD       | Mean  SD     |           |          |
| Test      | 7.03 1.42     | 5.68 1.77      | 4.78 2.25    | <0.001    | T0 x T1:0.001 T0 x T2:<0.001 T2 x T1:0.865 |
| Control   | 7.08 1.90     | 5.86 2.01      | 4.92 2.07    | <0.001    | T0 x T1:0.008 T0 x T2:<0.001 T2 x T1:0.102 |
| p**       | 0.452         | 0.560          | 0.709        |           |          |

*Friedman test, Bonferroni post hoc test, ** Wilcoxon test. Source: Authors.

There was a statistically significant difference when comparing Functional limitation (p = 0.003) (OHIP-14); Social disability (p = 0.010) (OHIP-14); Restrictions (p = 0.046) (DHEQ-15) and total value (p = 0.046) (DHEQ-15) between baseline and 30 days of treatment (Table 4).
Discus

In the present study, both ozonated oil and olive oil were effective in reducing sensitivity, suggesting that ozonated oil is not more efficient than olive oil for the treatment of DH. Likewise, placebo olive oil also showed a significant reduction in post-surgical root DH and no significant difference was found between ozonated olive oil and placebo olive oil (Patel et al., 2013). The decrease in DH level after treatment by both oils may be due to the presence of polyurethane in their compositions (Mastrantonio & Ramalho, 2003). It has been shown that polyurethane can induce bone neoformation in addition to the formation of collagen and mineralized tissue (matrix of collagen and hydroxyapatite crystals) which makes it biocompatible with dentin, which also has hydroxyapatite crystals and fibers in its collagens composition (Mastrantonio & Ramalho, 2003; Goldberg, et al., 2011; Zhang, et al., 2019). With this, possibly induction of mineralized tissue occurs when the oil comes in contact with the dental element, where the dentinal tubule tends to decrease its diameter and consequently decrease the sensitivity. Studies are needed to confirm this hypothesis.

An in vitro study (Veena, et al., 2020) observed that adjuvant application of a desensitizing agent containing arginine, with ozonized oil, had a synergistic effect, where the latter causes the opening of the dentinal tubules allowing a more compact penetration of the former and, therefore, can be an approach of potentially more effective treatment in the management of DH. According to the authors, this study was the first of its kind to evaluate the effects of the adjuvant use of a desensitizing paste containing arginine with ozone on the occlusion of the dentinal tubule, and suggest that further studies are needed to clinically validate the likely superior effect and of this synergistic combination in the management of DH.

The results observed herein corroborate in the literature indicating that the treatment of hypersensitive teeth with ozone technology reduces the DH level, however, this effect is not different from the placebo treatment (Dähnhardt, et al., 2008; Azarpazhooh, et al., 2009; Elgalaid, 2010).

The functional limitation and restrictions domains, which decreased significantly after 4 weeks, may be due to the inability of the patient with DH not to be able to consume certain foods, due to a painful sensation at the time of chewing (Aguiar, et al., 2005). After treatment, as the DH level decreases, there is no longer dietary restrictions, consequently improving the oral health quality of life.

| Table 4. Evaluation of quality of life after treatment of dentin hypersensitivity |
|-----------------------------------------------|
|                                | BASELINE |             | 30 DAYS |         |
|                                | Mean     | SD         | Mean    | SD      | p*     |
| Functional limitation          | 3.27     | 1.01       | 3.00    | 1.10    | 0.003  |
| Physical pain                  | 6.18     | 1.40       | 5.27    | 1.49    | 0.103  |
| Psychological discomfort       | 4.64     | 1.43       | 3.73    | 1.74    | 0.121  |
| Physical disability            | 3.82     | 1.83       | 3.64    | 1.36    | 0.720  |
| Psychological disability       | 3.00     | 0.89       | 2.82    | 1.08    | 0.599  |
| Social disability              | 3.27     | 0.90       | 2.18    | 0.40    | 0.010  |
| Social disadvantage            | 2.73     | 1.10       | 2.45    | 0.82    | 0.380  |
| Total                          | 26.91    | 5.92       | 23.09   | 5.63    | 0.246  |
| Restrictions                   | 16.91    | 2.63       | 13.73   | 5.04    | 0.046  |
| Adaptation                     | 15.82    | 4.05       | 13.36   | 4.67    | 0.098  |
| Social impact                  | 11.82    | 4.00       | 10.45   | 4.23    | 0.175  |
| Emotional impact               | 14.64    | 2.94       | 11.82   | 4.14    | 0.074  |
| Identity                       | 9.45     | 2.84       | 7.45    | 4.16    | 0.090  |
| Total                          | 68.64    | 12.36      | 56.82   | 20.14   | 0.046  |

*Wilcoxon test. Source: Authors.

4. Discussion

In the present study, both ozonated oil and olive oil were effective in reducing sensitivity, suggesting that ozonated oil is not more efficient than olive oil for the treatment of DH. Likewise, placebo olive oil also showed a significant reduction in post-surgical root DH and no significant difference was found between ozonated olive oil and placebo olive oil (Patel et al., 2013).

The decrease in DH level after treatment by both oils may be due to the presence of polyurethane in their compositions (Mastrantonio & Ramalho, 2003). It has been shown that polyurethane can induce bone neoformation in addition to the formation of collagen and mineralized tissue (matrix of collagen and hydroxyapatite crystals) which makes it biocompatible with dentin, which also has hydroxyapatite crystals and fibers in its collagens composition (Mastrantonio & Ramalho, 2003; Goldberg, et al., 2011; Zhang, et al., 2019). With this, possibly induction of mineralized tissue occurs when the oil comes in contact with the dental element, where the dentinal tubule tends to decrease its diameter and consequently decrease the sensitivity. Studies are needed to confirm this hypothesis.

An in vitro study (Veena, et al., 2020) observed that adjuvant application of a desensitizing agent containing arginine, with ozonized oil, had a synergistic effect, where the latter causes the opening of the dentinal tubules allowing a more compact penetration of the former and, therefore, can be an approach of potentially more effective treatment in the management of DH. According to the authors, this study was the first of its kind to evaluate the effects of the adjuvant use of a desensitizing paste containing arginine with ozone on the occlusion of the dentinal tubule, and suggest that further studies are needed to clinically validate the likely superior effect and of this synergistic combination in the management of DH.

The results observed herein corroborate in the literature indicating that the treatment of hypersensitive teeth with ozone technology reduces the DH level, however, this effect is not different from the placebo treatment (Dähnhardt, et al., 2008; Azarpazhooh, et al., 2009; Elgalaid, 2010).

The functional limitation and restrictions domains, which decreased significantly after 4 weeks, may be due to the inability of the patient with DH not to be able to consume certain foods, due to a painful sensation at the time of chewing (Aguiar, et al., 2005). After treatment, as the DH level decreases, there is no longer dietary restrictions, consequently improving the oral health quality of life.
Significant improvement was also observed in the social disability domain which is related to the individual's sociability (such as eating and socializing with other people) (Melo, et al., 2015). Probably, as a consequence of the treatment, the DH level decreased and the individual could be able to make social interaction without so much hassle.

The total DHEQ-15 score indicates that there was an improvement concerning the quality of life related to oral health. This is probably because DH treatment is effective, corroborating the findings in the literature that state that DH treatment improves the quality of life of individuals (Boiko, et al., 2010; Lima, et al., 2017; Douglas-de-Oliveira, et al., 2018).

The present study also demonstrated that the most prevalent tooth was the incisor, confirmed by the literature that shows the incisors as the most affected by DH because they naturally exhibit less enamel thickness when compared to other groups of teeth (Barroso, et al., 2019; Silva, et al., 2019). Also, studies have pointed out the incisors as more prevalent because they present greater wear with loss of enamel and dentin (Alcântara, et al., 2018).

In the present study, most of the sample was composed of women, which confirms the literature, which shows a higher prevalence of DH in this group (Silva, et al., 2011). This difference between men and women can result from oral health problems from social, economic, cultural and historical contexts. It is reported that, for a long time, women developed a cultural role of health-seeking behavior; therefore, they are more inclined to visit their dentist (Bulgareli, et al., 2018; Lim, et al., 2019). Men are less concerned with the impact of oral conditions on their quality of life, to the point of reporting the problem only when the condition is already quite advanced, with physical changes and pain, becoming more significant (Borrell & Artazcoz, 2008; Bulgareli, et al., 2018). The present result may also be attributed to the fact that women are more demanding in the aesthetic appearance of the smile, which makes them more sensitive to the presence of dental caries, in addition to hormonal conditions and a higher prevalence of systemic diseases that can influence their oral health (Bulgareli, et al., 2018).

The patients' routine was a limiting factor for this research since all patients had very limited hours due to academic or work routine, which made it difficult to have more therapy sessions with test/control oils. Lack of knowledge of the concentration of ozone in the oil can also be considered a limiting factor. Future studies should have a greater number of therapy sessions since the tooth with DH had little contact with the oils. Further studies are also needed to investigate the ability of Polyurethane to mineralize dentin.

Numerous studies suggest the benefits of ozone. Ozone therapy reaffirms itself as a promising preventive and therapeutic approach with wide application in Dentistry. It is a less invasive treatment method, without discomfort or pain. It also minimizes the patient's anxiety and stress level as it reduces the duration of treatment. Ozone has successfully evolved in oral and dental treatment. However, the beneficial role of ozone in the treatment of different oral and dental forms has still limited conditions. Future studies are needed in order to determine its potential risks, mainly due to toxicity, as well as the feasibility of its use compared to existing therapies. The results obtained so far need further corroboration and validation in different environments. It is extremely important that usage and security parameters are well defined regardless of the specialty to be applied, as well as the cost / benefit (Di Mauro, et al., 2019; Prestes, et al., 2020; Sen & Sen, 2020; Shekhar, et al., 2021; Silva, et al., 2021).

5. Conclusions

It was concluded that both ozonated oil and extra virgin oil were effective for the treatment of DH. Also, oil treatment improved oral health related quality of life. Given the importance of the subject, it is necessary to develop new research to expand knowledge about the effectiveness of ozonated oil on DH.

The results obtained herein need further corroboration and validation in different conditions. Randomized clinical trials may offer the best levels of evidence.
Acknowledgments

The authors thank Ozone Oil for making its product available for our research.

References

Afonso, A., Silva, L., Meneses, R. & Frias-Bulhosa, J. (2017). Oral health-related quality of life: Portuguese linguistic and cultural adaptation of ohip-14. *Psicologia Saúde & Doenças*, 18 (2), 374-388. dx.doi.org/10.15309/17pd180208

Aguir, F. H. B., Giovanni, E. M., Monteiro, F. H. L., Villalba, H., Melo, J. J. de & Tortamano, N. (2005). Dentin hypersensitivity - Causes and treatment. A review. *Revista do Instituto de Ciências da Saúde*, 23 (1), 67-71. http://repositorio.unamp.wp-content/uploads/2020/12/V23_N1_2005_p67-72-1.pdf

Alcântara, P. M., Barroso, N. F. F., Botelho, A. M., Douglas-de-Oliveira, D. W., Gonçalves, P. F. & Flecha, O. D. (2018). Associated factors to cervical dentin hypersensitivity in adults: a transversal study. *BMC Oral Health*, 18 (1), 155. https://doi.org/10.1186/s12903-018-0616-1

Azarpazhooh, A., Limeback, H., Lawrence, HP. & Fillery, E. D. (2009). Evaluating the effect of an ozone delivery system on the reversal of dentin hypersensitivity: a randomized, double-blinded clinical trial. *Journal of Endodontics*, 35 (1), 1-9. https://doi.org/10.1016/j.joen.2008.10.001

Barroso, N. F. F., Alcântara, P. M., Botelho, A. M., Douglas-de-Oliveira, D. W., Gonçalves, P. F. & Flecha, O. D. (2019). Prevalence of self-reported versus diagnosed dental hypersensitivity: a cross-sectional study and ROC curve analysis. *Acta Odontologica Scandinavica*, 77 (3), 219-223. https://doi.org/10.1080/00016357.2018.1536804

Boiko, O. V., Baker, S. R., Gibson, B. J., Locker, D., Sufi, F., Barlow, A. P. & Robinson, P. G. (2010). Construction and validation of the quality of life measure for dentine hypersensitivity (DHEQ). *Journal of Clinical Periodontology*, 37 (11), 973-980. https://doi.org/10.1111/j.1600-051X.2010.01618.x

Borrell, C. & Artazcoz, L. (2008). Las desigualdades de género en salud: retos para el futuro. *Revista Española de Salud Pública*, 82 (3), 241-249. https://socioescisci.es/ciencia.php?pid=S1135-57272008000300001&script=sci_arttext&tlng=pt

Brännström, M. & Garberoglio, R. (1980). Occlusion o dentinal tubules under superficial attrited dentine. *Swedish Dental Journal*, 4 (3), 87-91. https:pubmed.ncbi.nlm.nih.gov/6933708/

Bulgareli, J. V., Faria, E. T., Cortellazzi, K. L., Guerra, L. M., Meneghim, M. C., Ambrosano, G. M. B., Frias, A. C. & Pereira, A. C. (2018). Factors influencing the impact of oral health on the daily activities of adolescents, adults and older adults. *Revista de Saúde Pública*, 52, 44. https://doi.org/10.11606/s1518-8787.2018052000042

Canadian Advisory Board on Dentin Hypersensitivity. (2003). Consensus-based recommendations for the diagnosis and management of dentin hypersensitivity. *Journal Canadian Dental Association*, 69 (4), 221-226. https://www.cda-adc.ca/jcda/vol-69-issue-4/221.pdf

Cunha-Cruz J, Stout, J. R., Heaton, L. J. & Wataha, J. C. *Northwest PRECEDENT*. (2011). Dentin hypersensitivity and oxalates: a systematic review. *Journal of Dental Research*, 90 (3), 304-310. https://doi.org/10.1177/0022034510389179

Dähnhardt, J. E, Gyga, M., Martignoni, B., Suter, P. & Lussi A. (2008). Treating sensitive cervical areas with ozone. A prospective controlled clinical trial. *American Journal of Dentistry*, 21 (2), 74-76. http://eurpoeppmc.org/article/med/18578171

Di Mauro R., Cantarella G., Bernardini R., Di Rosa M., Barbagallo I., Distefano A., Longhitano L., Vicario N., Nicolosi D., Lazzarino G., Tibullo D., Gulino M. E., Spampinato M., Avola R. & Li Volti G. (2019). The Biochemical and Pharmacological Properties of Ozone: The Smell of Protection in Acute and Chronic Diseases. *International Journal of Molecular Sciences*, 20 (3), 634. https://doi.org/10.3390/ijms2003634

Douglas-De-Oliveira, D. W., Lages, F. S., Paiva, S. M., Cromley, J. G., Robinson, P. G. & Cota, L. O. M. (2018). Cross-cultural adaptation of the Brazilian version of the Dentine Hypersensitivity Experience Questionnaire (DHEQ-15). *Brazilian Oral Research*, 32:e37. https://doi.org/10.1590/1807-3107bor...2018.vol32.0037

Douglas-de-Oliveira, D. W., Vitor, G. P., Silveira, J. O., Martins, C. C., Costa, F. O. & Cota, L. O. M. (2018). Effect of dentin hypersensitivity treatment on oral health related quality of life - A systematic review and meta-analysis. *Journal of Dentistry*, 71, 1-8. https://doi.org/10.1016/j.jdental.2017.12.007

Elgaid, T. (2010). Ozone treatment had no effect on tooth hypersensitivity. *Evidence-Based Dentistry*, 11 (3), 70. https://doi.org/10.1038/ejd.6400732

Farquhar, M. (1995). Definitions of quality of life: a taxonomy. *Journal of Advanced Nursing*, 22 (3), 502-508. https://doi.org/10.1046/j.1365-2648.1995.22030502.x

Fernandes, K. G. C., Kozusny-Andreani, D. I., Tim, C. R., Bazan, L. G., Moreti, L. C. T., Simonato, L. E. & Garcia, L. A. (2021). Ozonotherapy as a coadjuvant in the irrigation of the radicular channels system. *Research, Society and Development*, 10 (1), e40210111855. http://dx.doi.org/10.33448/rsd-v10i1.11855

Flecha, O. D., Azvedo, C. G. S., Matos, F. R., Vieira-Barbosa, N. M., Ramos-Jorge, M. L., Gonçalves, P. F. & Koga Silva, E. M. (2013). Cyanoacrylate versus laser in the treatment of dentin hypersensitivity: a controlled, randomized, double-masked and non-inferiority clinical trial. *Journal of Periodontology*, 84 (3), 287-294. https://doi.org/10.1902/jpo.2012.120165

Fleck, M. P. A. (2000). The World Health Organization instrument to evaluate quality of life (WHOQOL-100): characteristics and perspectives. *Ciência & Saúde Coletiva*, 5 (1), 33-38. https://doi.org/10.1590/S1413-81232000000100004

Goldberg, M., Kulkarni, A.B., Young, M. & Boskey, A. (2011). Dentin: structure, composition and mineralization. *Frontiers in Bioscience (Elite Edition)*, 3, 711-735. https://doi.org/10.2741/e281
Grippo, J. O. (1991). Abstractions: a new classification of hard tissue lesions of teeth. *Journal of Esthetic Dentistry, 3* (1), 14-19. https://doi.org/10.1111/j.1708-8240.1991.tb00799.x.

Lena, K. & Marianne, K. (2017). Ozone Treatment on Dentin Hypersensitivity Surfaces - A Pilot Study. *The Open Dentistry Journal, 11*, 65-70. https://doi:10.2174/1874210601711010065

Lim, M. T., Lim, Y. M. F., Tong, S. F. & Sivasampu, S. (2019). Age, sex and primary care setting differences in patients’ perception of community healthcare seeking behaviour towards health services. *PLoS One, 14* (10), e0224260. https://doi:10.1371/journal.pone.0224260

Lima, T. C., Vieira-Barbosa, N. M., Azevedo, C. G. S., de Matos, F. R., Douglas-de-Oliveira, D. W., de Oliveira, E. S., Ramos-Jorge, M. L., Gonçalves, P. F. & Flecha, O. D. (2017). Oral Health-Related Quality of Life Before and After Treatment of Dentin Hypersensitivity With Cyanoacrylate and Laser. *Journal of Periodontology, 88* (2), 166-172. https://doi.org/10.1902/jop.2016.160216

Mastrandonio, S. S. & Ramalho, L. T. O. (2003). Mouse connective tissue reaction to polyurethane derived from castor oil. *Revista de Odontologia da UNESP, 32* (1), 31-37. https://revodontolunesp.com.br/article/588017a1718c9d0a4098b4814/pdf/rou-32-1-31

Melo, T. L., Silva, M. J. C. N., Sousa, B. M., Freitas, S. A. A., Pereira, E. M. & Pereira, A. F. V. (2015). Dentin sensitivity and the impact on the quality of life of patients with chronic periodontitis at the Federal University of Maranhão. *Arquivos em Odontologia, 51* (4), 179-185. http://revodontodo.bvsalud.org/scielo.php?script=sci_arttext&pid=S151605332015000300002

Mohajan, H. K. (2020). Quantitative Research: A Successful Investigation in Natural and Social Sciences. *Journal of Economic Development, Environment and People, 9* (4), 50-79. http://www.ceeol.com/search/article-detail?id=9359590

Moretzsohn, M. & Campos, I. (2001). Hipersensibilidade dentinária: Ainda um problema? *Revista Brasileira de Odontologia, 58* (4), 232-234. https://revoss.bvsalud.org/portal/resource/pt/llil296781

Patel, P. V., Patel, A., Kumar, S. & Holmes, J. C. (2013). Evaluation of ozonated olive oil with or without adjunctive application of calcium sodium phosphosilicate on, post-surgical root dentin hypersensitivity: a randomized, double-blinded, controlled, clinical trial. *Minerva Stomatologica, 62* (5), 147-161. https://pubmed.ncbi.nlm.nih.gov/23715201/

Prestes, L. V., Turci, R. F. P., Grunow, A. C. S., Peressin, H. M., Tecilla, K. & Boleta-Ceranto, D. C. F. (2020). Aplicabilidade da ozonioterapia na odontologia: uma revisão de literatura. *Revistas Ciências da Saúde da UNIFAR, 24* (3), 203-208. https://doi.org/10.25110/arqsaude.v24a.2020.7950

Sen S. & Sen S. Ozone therapy a new vista in dentistry: integrated review. (2020). *Medical Gas Research*, 10 (4), 189-192. https://doi:10.4103/2045-9912.304226

Sgoalastra, F., Petrucci, A., Gatto, R. & Monaco, A. (2011). Effectiveness of laser in dentinal hypersensitivity treatment: a systematic review. *Journal of Endodontics, 37* (3), 297-303. https://doi.org/10.1016/j.joen.2010.11.034

Shekhar A., Srivastava S., Kumar Bhati L., Chaturvedi A., Singh S., Agarwal B. & Arora K. (2021). An evaluation of the effect of ozone therapy on tissues surrounding dental implants. *International Immunopharmacology, 96*:107588. https://doi.org/10.1016/j.intimp.2021.107588

Silva, B. S., Carvalho, R. E., Asfoka, K. K., Coelho Júnior, L. G. T. M., Gomes, S. G. F. & Caldas Júnior, A. F. (2011). The Occurrence and Risk Factors of Dentin Hypersensitivity. *Revista de Cirurgia e Traumatologia Bucal-Maxilo-Facial, 11* (1), 99-105. http://revodontodo.bvsalud.org/scielo.php?script=sci_abstract&pid=S1808-52102011000100014&lng=pt&nrm=iss&tlng=en

Silva H., M. da, Oliveira E. C. M., Lira L. M. S. s. de, Rocha L. M. B. M., Gains E. P. L., Marinho R. R. B. & Lima E. K. N. S. (2021). Aplicação da ozonoterapia na odontologia: revisão integrativa. *Revista Eletrônica Acervo Saúde, 13* (8), e8648. https://doi.org/10.25248/rees.e8648.2021

Silva, M. S., Lima, A. N. A. N., Pereira, M. M. A., Mendes, R. F. & Prado Júnior, R. R. (2019). Prevalence and predictive factors of dentin hypersensitivity in Brazilian adolescents. *Journal of Clinical Periodontology, 46* (4), 448-456. https://doi.org/10.1111/jcpe.13097

Slade, G. D. (1997). Derivation and validation of a short-form oral health impact profile. *Community Dentistry and Oral Epidemiology, 25* (4), 284-290. https://doi.org/10.1111/j.1600-0528.1997.tb00941.x

Sobral, M. A. P. & Garone Netto, N. (1999). Clinical aspects about the etiology of cervical dentin hypersensitivity. *Revista de Odontologia da Universidade de São Paulo, 13* (2), 189-195. https://doi.org/10.1590/S0103-06631999000200014

Vale, I. S. & Bramante, A. S. (1997). Dentin hypersensitivity: diagnosis and treatment. *Revista de Odontologia da Universidade de São Paulo, 11* (3), 207-213. https://doi.org/10.1590/S0103-06631997000300009

Veen H. R., Afigith Mathew C., Daniel R. A., Shubha P., Sreeparvathy R. & Pradhan N. (2020). An in vitro analysis of the effect of adjunctive use of ozonated oil with a desensitizing agent on dentinal tubule occlusion. *Journal of Oral Biology Craniofacial Research, 10* (4), 727-732. https://doi:10.1016/j.jobcr.2020.10.001

Zhang, Y., Huang, K., Yuan, Q., Gu, Z. & Wu, G. (2019). Development of Arg-Based Biodegradable Poly(ester urea) Urethanes and Its Biomedical Application for Bone Repair. *Journal of Biomedical Nanotechnology, 13* (9), 1909-1922. https://doi.org/10.1166/jbn.2019.2818