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# Aqueous *versus* gaseous ozone, what is the most effective adjunct to periodontal treatment? A systematic review

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**Abstract**

**Objective:** To assess the effectiveness of using aqueous and gaseous ozone in the gingival tissues of periodontitis patients.

**Materials and Methods:** Two independent reviewers searched electronic databases (Lilacs, PubMed, Scopus, and Web of Science) using keywords specific to the topic. The variables extracted from each selected article included: type of study, sample size, population, periodontal parameters and age. The eligibility criteria included randomized clinical trials analyzing the effectiveness of ozone (aqueous or gaseous) as an adjunct to periodontal treatment.

**Results:** After applying the inclusion and exclusion criteria, 1,203 articles were initially selected from the databases. From 926 studies selected by the title, 11 articles were considered appropriate for the present study, with the majority being classified with a low risk of bias. It was found that the two forms of ozone (aqueous and gaseous) provided clinical benefits to the treatment of periodontitis, but aqueous ozone is safer regarding toxicity.

**Conclusion:** Given the results obtained, when compared to a negative control group, aqueous ozone was superior, and when compared to chlorhexidine (CHX), aqueous ozone had similar effects as adjunct in the periodontal treatment.

**Clinical relevance:** Using aqueous ozone can help to safely eliminate bacterial pathogens, improving the periodontal treatment, without side effects, compared to CHX.

*Keywords: Periodontal disease. Ozone. Periodontitis. Systematic review.*

## Introduction

Periodontal diseases comprise a series of inflammatory conditions that affect the supporting structures of teeth (gingivae, bone, and periodontal ligament), which may lead to tooth loss and contribute to systemic inflammation (Bartold, 2018). According to the research program named Global Burden of Disease Study (GBD), periodontitis is the sixth most prevalent disease in the world, with 11.2% (± 743 million) people affected among the world population (Yan *et al*., 2020). In Brazil, moderate to severe periodontitis has a prevalence of 15.3% in the population, and severe periodontitis has a prevalence of 5.8% (Vettore *et al*., 2013).

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Initially, periodontal treatment is performed by means of scaling and root planing and control of dental biofilm (etiological factor). This method consists of removing the dental calculus and adapting the oral environment to control periodontal diseases. However, in some cases, there is a need to use adjunctive agents to conventional periodontal therapy, in order to potentiate the treatment. Among these supporting agents are: laser therapy, antibiotic therapy, photodynamic therapy and the use of chlorhexidine (Smiley *et al*., 2015).

Besides mechanical and chemical treatment alternatives, such as scaling and root planing (SRP) or the use of oral antiseptics such as chlorhexidine (CHX), the field of dentistry has been innovating periodontal treatment techniques. Thus, studies indicate the use of ozone as a potential alternative antiseptic agent, aiming to reduce and

control microorganisms in the gingival sulcus (Kshitish *et al*., 2010; Huth *et al*., 2011; Carinci *et al*., 2015; Issac *et al*., 2015; Suh *et al*., 2019; Uraz *et al*., 2019).

Ozone is a triatomic molecule composed of three oxygen atoms, being used both in medicine and dentistry. It can be used for the treatment of more than 260 different pathologies. In dentistry, ozone has been used for the elimination of bacterial pathogens, disinfection of the periodontal pocket, bone disinfection, caries prevention, endodontic treatment, tooth sensitivity, temporomandibular joint treatment, and gingival recession, among others (Saini, 2011; Gupta and Mansi, 2012).

Although the application of ozone presents several benefits, such as non-invasiveness, simplicity, and low time consumption, it should be noted that inhaling it can be toxic to the pulmonary system and other organs (Naik *et al*., 2016; Srikanth *et al*., 2013). However, as ozone has different forms of presentation (gaseous, aqueous, and oily), it offers various resources for the treatment of different pathologies.

Ozone therapy has been increasingly promoted in dentistry, especially in the field of periodontics, mainly because ozone seems to have some antimicrobial activity against periodontal pathogens (Huth *et al*., 2011; Gupta and Deepa, 2016). The aqueous and gaseous forms are the most used modalities in the treatment of periodontal disease, due to their bactericidal and bacteriostatic properties. They represent a safe and effective method in therapeutic doses and, if used properly, hardly present any adverse reactions (Kumar *et al*., 2014; Naik *et al*., 2016).

However, there are many uncertainties about using ozone and which chemical derivative is most effective for clinical dental use (Issac *et al*., 2015). Undoubtedly, the applicability of ozone is increasing, as research is showing positive results in the individuals tested (Srikanth *et al*., 2013; Suh *et al*., 2019). Thus, the present study aimed to verify, by means of a systematic review of the literature, the efficacy of using aqueous or gaseous ozone in the gingival tissues of periodontitis patients.

## Materials and Methods

### *Protocol and registration*

A systematic literature review was performed, registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the identification number CRD42020166320, and conducted according to the recommendations of the Statement of Preferred Items for Systematic Reviews and Meta-analysis (PRISMA) (Moher *et al*., 2009; Hutton *et al*., 2015; Liberatti *et al*., 2009). The search period was from April to August 2020.

### *Focused question*

In this systematic review, the following question was addressed: *Considering the forms of aqueous or gaseous ozone, which chemical agent is most effective for the periodontal treatment?*

### *Eligibility criteria*

The strategy chosen was PICOS, as follows:

Population (P): permanent human teeth with periodontitis. Intervention (I): application of ozone in periodontal treatment. Comparison (C): conventional periodontal treatment associated with ozone (aqueous or gaseous) associated or not with the alternative use of chlorhexidine (positive control) or 0.9% saline solution (negative control). Outcome (O): efficacy of ozone as an adjunct therapy in periodontal treatment; and Study design(S): clinical trials, case-control studies and cohort studies.

### *Selection criteria*

The studies were selected according to the following criteria:

#### *Inclusion criteria*

1. Randomized clinical trials comparing the results of aqueous and gaseous ozone in periodontitis patients.
2. Randomized clinical trials with patients to which ozone therapy was used in periodontal pockets larger than 4 mm.
3. Comparative studies between aqueous and gaseous ozone, using a positive control group in the treatment of periodontitis.
4. Only articles in English language.

#### *Exclusion criteria*

1. Narrative or systematic reviews, meta-analyses, comments, editorials, letters to the editor, study protocols, case reports, or case series.
2. Studies on the use of ozone therapy in oil, and/or other pathologies unrelated to periodontal disease.
3. Lack of coherence in the studies researched, with a dubious and difficult to understand methodology.
4. Studies that did not present statistical analysis on the clinical findings.
5. Studies evaluating healthy teeth in periodontitis patients.

### *Search strategy*

The Lilacs, PubMed, Scopus, and Web of Science databases were searched again before submitting this study for publication, through the Rayyan QCRI platform and using the Endnote software to export the articles from the databases (Ouzzani *et al*., 2016). Two independent reviewers (L.C.D. and V.C.S.) analyzed the data, and MeSH terms were used in the search along with other keywords (Appendix 1). The articles searched had no distinction of year and language, respecting the PICO format (Stone, 2002; Akobeng, 2005). For the search, a Kappa concordance index (0.90) of researchers was performed regarding the adequacy of studies in relation to the inclusion and exclusion criteria.

### *Selection of studies*

A study selection strategy was developed through a manual search based on the references from manuscripts previously selected and other review articles. Two independent researchers (L.C.D. and V.C.S.) read the titles and abstracts of the studies identified in the research, and any disagreements were resolved by means of a discussion. In case of disagreement, another independent reviewer (M.S.T.) was consulted to reach a consensus.

### *Data collection*

After reading the abstracts, the studies that met the inclusion and exclusion criteria were read in full. Three different independent researchers (L.C.D., V.C.S., and D.J.G.) extracted the data. The variables extracted from each selected article included the type of study, sample size, population, details of clinical periodontal parameters, sex, average age, the chemical agent used, and the presence or absence of a control group. The data were included on an Excel spreadsheet to store the information found/selected.

### *Risk of bias in individual studies and quality of evidence*

Two separate reviewers (C.A.O. and J.P.C.) assessed the risk of bias in the selected studies using the SYRCLE criteria (risk of bias tool for animal/human studies), which is the Cochrane tool for assessing the risk of bias (Higgins *et al*., 2011). A third reviewer (M.S.T.) resolved cases of disagreement. Thus, methodological quality scores of data were used according to the following predetermined criteria: generation of a random sequence, blinding of allocation, blinding of participants and professionals, blinding of outcome evaluators, incomplete outcomes, report of selective outcomes, and other sources of bias. The quality of evidence was assessed as low, high, or uncertain risk bias for each study (Hutton *et al*., 2015; Hooijmans *et al*., 2014).

## Results

Figure 1 shows the research strategy's flowchart. The study selection was performed in two phases. Firstly, through the use of the Rayyan QCRI application (https://rayyan.qcri.org/users/sign_in), the studies identified in the research (n = 1,203), were read according to their title and abstract independently and through blinding of the two reviewers (L.C.D. and V.C.S.), in order to identify eligible studies for this review. At the end of the individual selection of eligible articles by the two reviewers, the third reviewer (D.J.G.) demonstrated the results. There was a total of 8 articles in conflict during the selection, which were resolved in the presence of the third

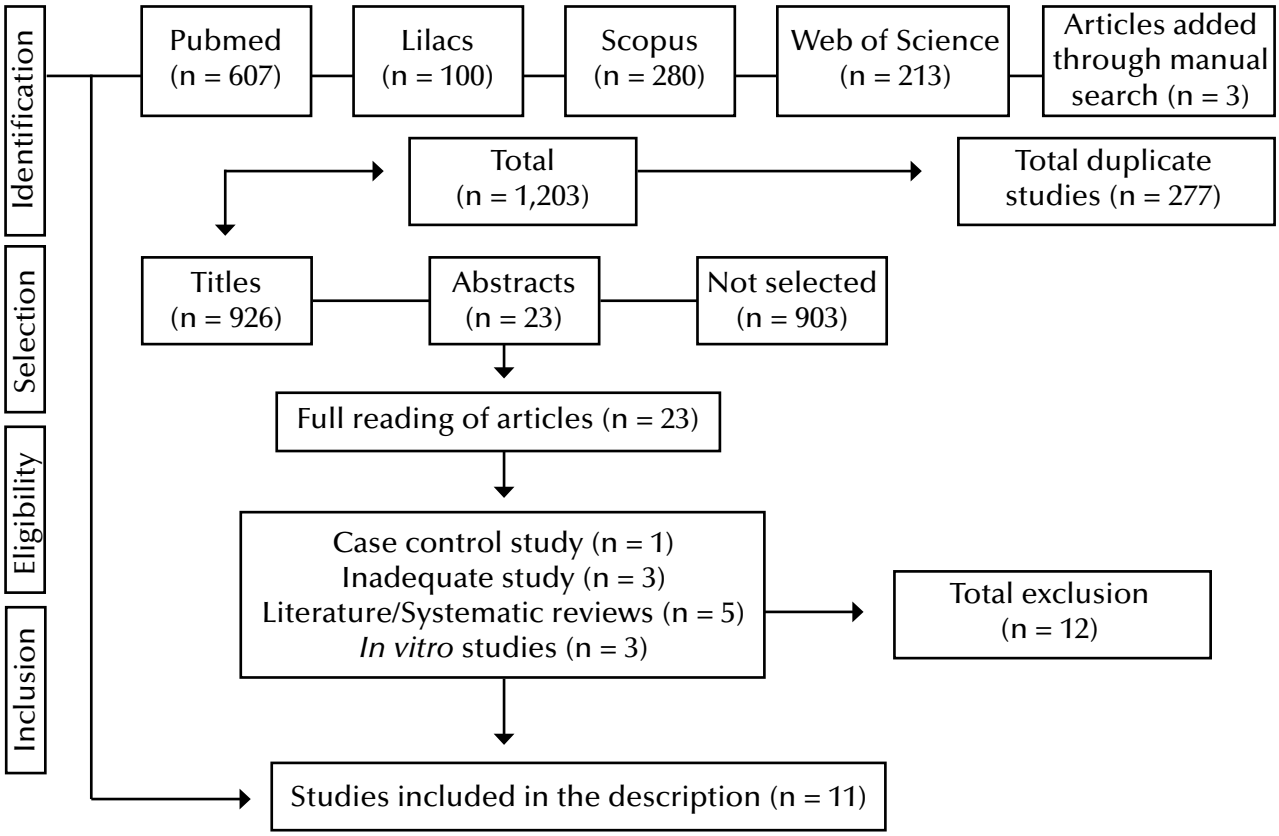


***Figure 1. Flowchart of the research strategy.***

reviewer (D.J.G.). Upon solving the conflicts, 23 articles were selected according to their title and abstract. In the second phase, the same reviewers (L.C.D. and V.C.S.) performed the complete reading of the 23 articles, also independently and applying the eligibility and exclusion criteria. Doubts or disagreements were resolved by analyzing each study and discussion in the presence of the third reviewer, to obtain consensus (D.J.G.). At both times, a team of three experts (C.A.O., M.C.W., J.P.C.) cross-examined all the information. Any disagreements regarding eligibility were discussed between the research team and the coordinator (M.S.T.). Twelve (12) studies were excluded for the following reasons: six studies were narrative or systematic reviews, meta-analyses, comments, editorials, letters to the editor, study protocols, case reports, or case series; three studies were performed *in vitro*; one study lacked coherence or had a dubious or difficult to understand methodology; one study was about the use of ozone therapy in oil and/or other pathologies unrelated to periodontal disease; one study lacked access to the full text. In the end, 11 studies were used to perform this article (Table 1).

The study included 11 articles containing the clinical research of patients diagnosed with periodontitis and treated with the use of aqueous or gaseous ozone along with a control group.

**Table 1.** Articles excluded after applying the exclusion criteria.

| Reference | First author, year | Exclusion reason |
|---|---|---|
| 1 | Kshitish and Laxman, 2010 | Included |
| 2 | Skurska *et al.*, 2010 | 1, 3 |
| 3 | Huth *et al.*, 2011 | 1, 2 |
| 4 | Eick *et al.*, 2012 | 1, 2 |
| 5 | Hayakumo *et al.*, 2013 | Included |
| 6 | Katti and Chava, 2013 | Included |
| 7 | Yilmaz *et al.*, 2013 | 1, 5 |
| 8 | Hayakumo *et al.*, 2014 | 1, 2 |
| 9 | Saini, 2014 | 1 |
| 10 | Al Habashneh *et al.*, 2015 | Included |
| 11 | Carinci *et al.*, 2015 | 1 |
| 12 | Eregowda, 2015 | 1 |
| 13 | Issac *et al.*, 2015 | Included |
| 14 | Gupta and Deepa, 2016 | 1 |
| 15 | Naik *et al.*, 2016 | 1 |
| 16 | Pandya *et al.*, 2016 | Included |
| 17 | Gandhi *et al.*, 2019 | 4 |
| 18 | Kaur *et al.*, 2019 | Included |
| 19 | Seydamir-Dengizeh *et al.*, 2019 | Included |
| 20 | Suh *et al.*, 2019 | 1 |
| 21 | Tasdemir *et al.*, 2019 | Included |
| 22 | Uraz *et al.*, 2019 | Included |
| 23 | Vasthavi *et al.*, 2020 | Included |

(1) Narrative or systematic reviews, meta-analyzes, comments, editorials, letters to the editor, study protocols, case reports, or case series. (2) In vitro studies. (3) Lack of coherence in the studies researched, or doubtful or difficult to understand methodology. (4) Studies on the use of ozone therapy in oil and/or other pathologies unrelated to periodontal disease. (5) Full text not accessible.

As presented in Table 2, from the 11 studies analyzed, 3 showed better results in relation to aqueous ozone. However, none of the articles directly compared the two agents (liquid and gaseous), but both were used separately, being compared only with the control group (saline solution) and CLX (chlorhexidine solution, positive control). The risk of bias in randomized clinical trials was evaluated using the Cochrane tool that assesses seven different types of biases. Each article, based on specific criteria, was classified as "low", "high", or "uncertain" risk of bias.

**Table 2.** Summary of the characteristics of the 11 studies included in this review.

| Reference | Year | Type of study | Sex | Number of participants and groups | Average age (years) | Probing depth | Diagnosis | Type of treatment | Most effective chemical agent |
|---|---|---|---|---|---|---|---|---|---|
| Kshitish and Laxman | 2010 | Randomized clinical and microbiological | F/M | 16 individuals 2 time intervals | ND (20-60 years) | ND | Generalized chronic periodontitis | TG: Aqueous ozone CG: 0.2% CHX | Aqueous ozone |
| Hayakumo *et al*. | 2013 | Randomized controlled | F/M | 22 individuals 2 groups | 45.9 ± 14.8 years | ≥ 4mm | Mild to moderate chronic periodontitis | TG: SRP + NBW3 CG: SRP + normal water | NBW3 |
| Katti and Chava | 2013 | Randomized clinical | F/M | 30 individuals 2 groups | ND (20-60 years) | ≥ 5mm | Chronic periodontitis | CG: Saline solution TG: aqueous ozone | Aqueous ozone |
| Al Habashneh *et al*. | 2015 | Randomized controlled clinical | ND | 41 individuals 2 groups | 39.7 ± 13.7 years (TG) 39.0 ± 10.2 years (CG) | > 5mm | Chronic periodontitis | CG: SRP + distilled water TG: SRP + aqueous ozone | Similar effect between the two groups |
| Issac *et al*. | 2015 | Clinical microbiological | F/M | 30 individuals 2 groups | ND (35-55 years) | ≥ 6mm | Chronic periodontitis | CG: Only SRP TG: SRP + aqueous ozone | No effect |
| Pandya *et al*. | 2016 | Clinical microbiological split-mouth | F/M | 10 individuals 4 groups | ND (20-65 years) | 5-8mm | Generalized periodontitis | TG: SRP + 0.2% CHX TG: SRP + aqueous ozone TG: SRP + saline CG: Only SRP | 0.2% CHX |
| Kaur *et al*. | 2019 | Randomized clinical | F/M | 20 individuals 2 groups | ND (30-60 years) | 4-6mm | Chronic periodontitis | TG: 0.2% CHX. CG: aqueous ozone | Aqueous ozone |
| Seydanur Dengizek, *et al*. | 2019 | Randomized clinical | ND | 40 individuals 2 groups | 42,4±6,7 years | 4-6mm | Chronic periodontitis | TG: SRP + gaseous ozone CG: SRP + placebo | Similar effect between the two groups |
| Tasdemir *et al*. | 2019 | Randomized clinical | F/M | 36 individuals 2 groups | 43.7±10.2 years | ≥ 5mm | Moderate to severe generalized periodontitis | TG: SRP + topical gaseous ozone CG: SRP + placebo | No effect |
| Uraz *et al*. | 2019 | Randomized clinical microbiological and biochemical | F/M | 18 individuals 2 groups | 40±6.51 Years | ≥ 5mm | Generalized chronic periodontitis | TG: SRP + gaseous ozone CG: Only SRP | Similar effect between the two groups |
| Vasthavi *et al*. | 2020 | Randomized clinical microbial | ND | 24 individuals 2 groups | ND (30-65 years) | > 5mm | Generalized chronic periodontitis | TG: SRP + aqueous ozone CG: SRP + distilled water | Similar effect between the two groups |

F/M: female and male; ND: not described; TG: test group; CG: control group; CHX: chlorhexidine; NBW3: ozone nano-bubble water; SRP: scaling and root planing.

When evaluating irrigation with ozonated water or gas, some periodontal parameters were analyzed, such as the biofilm index, probing depth, and level of clinical attachment, showing reductions in most of them. However, some of the parameters showed a similarity of results to other associated chemical agents, after the follow-up of a few days or months. Table 3 shows the clinical characteristics of the study participants.

**Table 3.** Clinical characteristics of the study volunteers.

| Reference | Plaque index | Gingival index | Mean PD | BOP | Mean clinical attachment level | Number of sites | |
|---|---|---|---|---|---|---|---|
| | | | | | | PD ≥ 5mm | PD ≥ 6mm |
| Kshitish and Laxman, 2010 | Day 0:<br>»Aqueous ozone: 1.39 ± 0.27<br>»0.2% CHX: 1.23 ± 0.31<br>Day 7:<br>»Aqueous ozone: 1.23 ± 0.40<br>»0.2% CHX: 1.18 ± 0.29 | Day 0:<br>»Aqueous ozone: 1.17 ± 0.43<br>»0.2% CHX: 1.21 ± 0.45<br>Day 7:<br>»Aqueous ozone: 0.83 ± 0.26<br>»0.2% CHX: 0.98 ± 0.35 | ND | ND | ND | ND | ND |
| Hayakumo *et al*., 2013 | ND | ND | 4 weeks:<br>»NBW3: 0.34 ± 0.2<br>»WATER: 0.17 ± 0.1<br>8 weeks:<br>»NBW3: 0.29 ± 0.2<br>»WATER: 0.14 ± 0.2 | Baseline:<br>»NBW3: 32.95±15.7<br>»WATER: 30.20±14.8<br>4 weeks:<br>»NBW3: 15.69±12.5<br>»WATER: 8.98±9.2<br>8 weeks:<br>»NBW3: 13.47±9.2<br>»WATER: 6.97±10.8 | 4 weeks:<br>»NBW3: 0.31 ± 0.1<br>»WATER: 0.10 ± 0.2<br>8 weeks:<br>»NBW3: 0.27 ± 0.2<br>»WATER: 0.09 ± 0.2 | ND | ND |
| Katti and Chava, 2013 | Baseline:<br>»Saline solution: 1.76 ± 0.39<br>»Aqueous ozone: 1.70 ± 0.39<br>Day 15:<br>»Saline solution: 1.28 ± 0.33<br>»Aqueous ozone: 1.23 ± 0.30<br>Day 30:<br>»Saline solution: 1.35 ± 0.34<br>»Aqueous ozone: 1.20 ± 0.279 | Baseline:<br>»Saline solution: 2.13 ± 0.52<br>»Aqueous ozone: 2.04 ± 0.49<br>Day 15:<br>»Saline solution: 1.55 ± 0.42<br>»Aqueous ozone: 1.44 ± 0.36<br>Day 30:<br>»Saline solution: 1.48 ± 0.35<br>»Aqueous ozone: 1.30 ± 0.30 | Baseline:<br>»Saline solution:<br>M: 5.4 ± 1.2<br>D: 5.7 ± 1.5<br>»Aqueous ozone:<br>M: 5.4 ± 0.92<br>D: 6.0 ± 1.4<br>Day 15:<br>»Saline solution:<br>M: 4.7 ± 1.0<br>D: 5.1 ± 1.3<br>»Aqueous ozone:<br>M: 4.0 ± 0.9<br>D: 4.9 ± 1.5<br>Day 30:<br>»Saline solution:<br>M: 4.7 ± 1.1<br>D: 5.0 ± 1.3<br>»Aqueous ozone:<br>M: 4.0 ± 0.9<br>D: 4.7 ± 1.6 | ND | Baseline:<br>»Saline solution:<br>M: 4.8 ± 1.7<br>D: 4.9 ± 2.0<br>Buccal: 4.8 ± 2.2<br>»Aqueous ozone:<br>M: 4.8 ± 1.9<br>D: 5.4 ± 1.5<br>Buccal: 4.1 ± 1.6<br>Day 15:<br>»Saline solution:<br>M: 4.2 ± 1.4<br>D: 4.6 ± 2.0<br>Buccal: 4.2 ± 1.9<br>»Aqueous ozone:<br>M: 3.5 ± 1.6<br>D: 4.2 ± 1.5<br>Buccal: 3.3 ± 1.5<br>Day 30:<br>»Saline solution:<br>M: 4.2 ± 1.4<br>D: 4.6 ± 2.0<br>Buccal: 4.2 ± 1.9<br>»Aqueous ozone:<br>M: 3.5 ± 1.5<br>D: 4.0 ± 1.4<br>Buccal: 3.3 ± 1.5 | ND | ND |

PD: Probing depth; BOP: bleeding on probing; CHX: Chlorhexidine; ND: Not described; NBW3: ozone nano-bubble water; M: Mesial; D: Distal; SRP: Scaling and root planning.

**Table 3. (Continuation)** Clinical characteristics of the study volunteers.

| Reference | Plaque index | Gingival index | Mean PD | BOP | Mean clinical attachment level | Number of sites | |
|---|---|---|---|---|---|---|---|
| | | | | | | PD ≥ 5mm | PD ≥ 6mm |
| Al Habashneh *et al*., 2015 | Aqueous ozone: 1.6 ± 0.5<br>Distilled water: 1.5 ± 0.6 | Baseline:<br>»Aqueous ozone: 1.6 ± 0.5<br>»Distilled water: 1.6 ± 0.5<br>Three months after treatment:<br>»Aqueous ozone: 1.5 ± 0.6<br>»Distilled water: 1.3 ± 0.6 | Aqueous ozone: 2.8 ± 0.4<br>Distilled water: 2.4 ± 0.4 | Baseline:<br>»Aqueous ozone: 75.0 ± 26.0<br>»Distilled water: 72.0 ± 28.0<br>Three months after treatment:<br>»Aqueous ozone: 23.0 ± 20.0<br>»Distilled water: 26.0 ± 24.0 | Aqueous ozone: 1.5 ± 1.2<br>Distilled water: 1.7 ± 1.2 | More than 2 sites | ND |
| Issac *et al*., 2015 | ND | Aqueous ozone:<br>»Baseline: 1.88 ± 0.33<br>»Four weeks: 0.73 ± 0.27<br>SRP only:<br>»Baseline: 2.00 ± 0.21<br>»Four weeks: 1.13 ± 0.33 | Aqueous ozone:<br>»Baseline: 6.43 ± 0.7 3<br>»4 weeks: 3.9 3 ± 1.72<br>Only SRP:<br>»Baseline: 6.67 ± 0.88<br>»4 weeks: 5.67 ± 1.06 | ND | Aqueous ozone:<br>»Baseline: 6.90 ± 0.92<br>»4 weeks: 4.40 ± 1.85<br>Only SRP:<br>»Baseline: 6.80 ± 1.06<br>»4 weeks: 5.73 ± 1.11 | ND | 2 sites |
| Pandya *et al*., 2016 | ND | Day 30:<br>SRP + CHX: 1.31000 ± 0.47714<br>SRP + Aqueous ozone: 0.89500±0.46812<br>SRP + Saline solution: 0.48800±0.22827<br>SRP alone: 0.35500±0.30772 | Day 30:<br>SRP + CHX: 1.87600 ± 0.56038<br>SRP + Aqueous ozone: 1.46100 ± 0.63278<br>SRP + Saline solution: 0.81200 ± 0.67199<br>SRP alone: 0.61900 ± 0.31918 | ND | ND | ND | ND |
| Kaur *et al*., 2019 | 1 week:<br>»CHX: 2.00<br>»Aqueous ozone: 1,675<br>4 weeks:<br>»CHX: 1.90<br>»Aqueous ozone: 1.475<br>3 months:<br>»CHX: 2.25<br>»Aqueous ozone: 1.70 | Baseline:<br>»CHX: 2.25<br>»Aqueous ozone: 2.40<br>4 weeks:<br>»CHX: 1.60<br>»Aqueous ozone: 1.75<br>3 months:<br>»CHX: 1.15<br>»Aqueous ozone: 1.05 | 4 weeks:<br>»CHX: 3.75<br>»Aqueous ozone: 3.85<br>3 months:<br>»CHX: 3. 10<br>»Aqueous ozone: 2.95 | ND | 4 weeks:<br>»CHX: 7.60<br>»Aqueous ozone: 7.80<br>3 months:<br>»CHX: 7.05<br>»Aqueous ozone: 7.00 | ND | ND |
| Seydanur Dengizek, *et al*., 2019 | SRP + Gaseous ozone:<br>»Baseline: 2.5 ± 0.6<br>»1 month after treatment: 0.6 ± 0.2<br>SRP + placebo:<br>»Baseline: 2.4 ± 0.6<br>»1 month after treatment: 0.6 ± 0.2 | SRP + Gaseous ozone:<br>»Baseline: 2.3 ± 0.7<br>»1 month after treatment: 0.8 ± 0.2<br>SRP + placebo:<br>»Baseline: 2.1 ± 0.6<br>»1 month after treatment: 0.9 ± 0.2 | SRP + Gaseous ozone:<br>»Baseline: 3.8 ± 0.8<br>»1 month after treatment: 3.0 ± 0.6<br>SRP + placebo:<br>»Baseline: 3.6 ± 0.8<br>»1 month after treatment: 3.0 ± 0.8 | ND | SRP + Gaseous ozone:<br>»Baseline: 4.4 ± 1.1<br>»1 month after treatment: 4.0 ± 0.7<br>SRP + placebo:<br>»Baseline: 4.1 ± 0.8<br>»1 month after treatment: 3.8 ± 0.8 | ND | ND |

PD: Probing depth; BOP: bleeding on probing; CHX: Chlorhexidine; ND: Not described; NBW3: ozone nano-bubble water; M: Mesial; D: Distal; SRP: Scaling and root planning.

**Table 3. (Continuation)** Clinical characteristics of the study volunteers.

| Reference | Plaque index | Gingival index | Mean PD | BOP | Mean clinical attachment level | Number of sites | |
|---|---|---|---|---|---|---|---|
| | | | | | | PD ≥ 5mm | PD ≥ 6mm |
| Tasdemir *et al.*, 2019 | SRP + Topical gaseous ozone: »Baseline: 2.34 (0.4) »3 months of treatment: 1.2 (0.5) SRP + placebo: »Baseline: 2.42 (0.4) »3 months of treatment: 1.1 (0.5) | SRP + Topical gaseous ozone: »Baseline: 2.21 (0.4) »3 months of treatment: 1.15 (0.4) SRP + placebo: »Baseline: 2.30 (0.4) »3 months of treatment: 1.22 (0.4) | SRP + Topical gaseous ozone: »Baseline: 3.24 (0.7) »3 months of treatment: 1.97 (0.5) SRP + placebo: »Baseline: 3.17 (0.6) »3 months of treatment: 2.01 (0.5) | SRP + Topical gaseous ozone: »Baseline: 90 (5.7) »3 months of treatment: 32.9 (12.5) SRP + placebo: »Baseline: 92 (6.8) »3 months of treatment: 31.1 (11.9) | SRP + Topical gaseous ozone: »Baseline: 3.9 (0.6) »3 months of treatment: 4.2 (0.4) SRP + placebo: »Baseline: 3.7 (0.5) »3 months of treatment: 4.3 (0.3) | 6 sites | ND |
| Uraz *et al.*, 2019 | SRP + Gaseous ozone: »Baseline: 1.23 ± 0.46 »3 months of treatment: 0.73 ± 0.30 Only SRP: »Baseline: 1.27 ± 0.43 »3 months of treatment: 0.78 ± 0.34 | SRP + Gaseous ozone: »Baseline: 1.58 ± 0.33 »3 months of treatment: 1.03 ± 0.28 Only SRP: »Baseline: 1.61 ± 0.32 »3 months of treatment: 1.14 ± 0.24 | SRP + Gaseous ozone: »Baseline: 5.87 ± 1.13 »3 months of treatment: 3.96 ± 0.95 Only SRP: »Baseline: 5.91 ± 1.05 »3 months of treatment: 3.98 ± 0.92 | SRP + Gaseous ozone: »Baseline: 69.44 ± 12.54 »3 months of treatment: 15.55 ± 18.60 Only SRP: »Baseline: 67.42 ± 18.95 »3 months of treatment: 19.44 ± 22.15 | ND | ≥ 3 sites | ND |
| Vasthavi *et al.*, 2020 | SRP + Aqueous ozone: »Baseline: 2.5058 ± 0.31822 »Day 14: 1.8250 ± 0.58029 »Day 21: 1.8517 ± 0.55440 »2 months of treatment: 1.4164 ± 0.37263 SRP + distilled water: »Baseline: 2.4883 ± 0.28825 »Day 14: 1.8117 ± 0.54421 »Day 21: 1.6475 ± 0.43944 »2 months of treatment: 1.5742 ± 0.40775 | SRP + Aqueous ozone: »Baseline: 2.5692±0.33619 »Day 14: 2.0367±0.42331 »Day 21: 1.8800±0.41613 »2 months of treatment: 1.5125±0.40672 SRP + distilled water: »Baseline: 2.3208±0.47116 »Day 14: 1.9917±0.59019 »Day 21: 1.8183±0.33739 »2 months of treatment: 1.6208±0.36828 | SRP + Aqueous ozone: »Baseline: 6.8333 ± 1.19342 »Day 14: 6.1667 ± 1.40346 »Day 21: 5.1667 ± 0.93744 »2 months of treatment: 4.5000 ± 0.79772 SRP + distilled water: »Baseline: 7.8333 ± 1.26730 »Day 14: 7.0833 ± 1.37895 »Day 21: 6.0833 ± 1.44338 »2 months of treatment: 5.1667 ± 1.02986 | ND | ND | ND | ND |

PD: Probing depth; BOP: bleeding on probing; CHX: Chlorhexidine; ND: Not described; NBW3: ozone nano-bubble water; M: Mesial; D: Distal; SRP: Scaling and root planning.

## Discussion

Studies about the use of ozone therapy in the field of periodontics are still scarce, therefore, the present systematic literature review selected only 11 articles after going through a few exclusion criteria (Kshitish and Laxman, 2010; Al Habashneh *et al*., 2015; Hayakumo *et al*., 2013; Katti and Chava, 2013; Pandya *et al*., 2016; Kaur *et al*., 2019; Seydanur *et al*., 2019; Tasdemir *et al*., 2019; Uraz *et al*., 2019; Vasthavi *et al*., 2020). Similar to the results by Moraschini *et al*. (2020) in a systematic review of twelve studies, we noticed that the association of ozone therapy with conventional non-surgical periodontal treatment, in addition to being scarce, is characterized as controversial and lacks effective results. However, due to the potential heterogeneity across the studies, the presence of confounding factors, and the short follow-up of some included researches, these results should not be considered definitive.

The comparison of studies referring to aqueous and gaseous ozone allows affirming that research on gas is the minority, considering its use is not as safe as water, and may cause some side effects such as epiphora, rhinitis, cough, headache, nausea, and vomiting, if inhaled through an open system (Seydanur *et al*., 2019; Tasdemir *et al*., 2019; Uraz *et al*., 2019). Thus, it can be said that aqueous ozone is safer for treating periodontal diseases than gaseous ozone.

This systematic review shows that when aqueous ozone is compared to 0.12% chlorhexidine or a placebo (saline solution or distilled water), similar results are found, demonstrating that aqueous ozone is so effective as CHX as adjuvant for periodontal treatment (Al Habashneh *et al*., 2015; Katti and Chava, 2013; Gupta and Depta, 2016; Vasthavi *et al*., 2020).

Some studies included in this research (Kshitish and Laxman, 2010; Kaur *et al*., 2019) showed that the aqueous ozone obtained satisfactory responses, when compared to chlorhexidine 0.12%. Katti and Chaya (2013) obtained satisfactory responses when compared with saline solution, regarding the following clinical parameters: biofilm index, gingival index, bleeding index, probing depth, level of clinical attachment. They also reported microbial properties against *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, and *Fusobacterium nucleatum*. Despite this, two studies (Al Habashneh *et al*., 2015; Vasthavi *et al*., 2020) showed similar effects between aqueous ozone and negative control (saline solution) groups. Thus, we cannot vehemently state that there was a superiority of aqueous ozone when compared to positive and negative controls. Thus, data from this systematic review should be analyzed with caution when extrapolated to the clinic. Furthermore, although gaseous ozone also showed clinical and microbial improvements, it had no additional positive effects on periodontal treatment (Seydanur *et al*., 2019; Tasdemir *et al*., 2019; Uraz *et al*., 2019; Leewananthawet *et al*., 2020).

As for the use of CHX, it is known to be a gold-standard antimicrobial for biofilm control, and presents a broad antiseptic spectrum and substantivity (Kshitish and Laxman, 2010; Soorgani *et al*., 2019; Badar *et al*., 2020). However, when using CHX as a mouthwash of continuous use, some damage may occur to the patient, such as unpleasant taste, burning, and tooth staining; unlike aqueous ozone, which can be used as a mouthwash without causing damage. Ozonated water can be useful for CLX, as it had similar results (Kaur *et al*., 2019, Kshitish and Laxman, 2010) and as an advantage, ozonized water does not have side effects like CLX (Kumar *et al*., 2014; Pandya *et al*., 2016, Badar *et al*., 2020, Nicolini *et al*., 2020).

Regarding the assessment of the internal methodological risk of bias, six studies were considered as "low" risk of bias (Al Habashneh *et al*., 2015; Hayakumo *et al*., 2013; Seydanur *et al*., 2019; Tasdemir *et al*., 2019; Uraz *et al*., 2019; Vasthavi *et al*., 2020), one study was considered a "high" risk of bias (Katti and Chava, 2013), three studies were considered "uncertain" risk of bias (Kshitish and Laxman, 2010; Issac *et al*., 2015; Pandya *et al*., 2016), and one study was considered as "low" and "uncertain" risk of bias (Kaur *et al*., 2019). Only one study was considered as "high" risk of bias, for not blinding participants, professionals, and outcome evaluators; because it was incomplete, which may affect the outcome; and because not all predetermined primary outcomes were reported (Katti and Chava, 2013). The other studies were classified as a low or uncertain risk of bias, with the majority representing a low risk (Kshitish and Laxman, 2010; Al Habashneh *et al*., 2015; Hayakumo *et al*., 2013; Pandya *et al*., 2016; Kaur *et al*., 2019; Seydanur *et al*., 2019; Tasdemir *et al*., 2019; Uraz *et al*., 2019; Vasthavi *et al*., 2020). Thus, despite the researched topic being little explored in the literature, it can be considered that, as a whole, the systematic review carried out presents reliability in relation to the selected studies.

Some of the clinical parameters analyzed improved with the use of ozone. Its action is effective in reducing the levels of biofilm and gingival bleeding, inhibiting the loss of clinical attachment, and minimizing inflammation (Kshitish and Laxman, 2010; Huth *et al*., 2010; Katti and Chava, 2013; Kaur *et al*., 2019). However, as the number of studies with such claims is small, they cannot be transferred to daily clinical activity. It is therefore suggested, based on the present systematic review, that more studies, preferably clinical ones, be performed on the effectiveness of aqueous or gaseous ozone therapy combined with conventional periodontal therapies.

It must also be remembered that, in addition to aqueous ozone not showing additional effectiveness compared to conventional periodontal treatment, aqueous ozone has a half-life of only 20 minutes. So, it degrades rapidly in oxygen and should be used in the first 5 to 10 minutes to guarantee its power, being therefore impossible to produce a medicine that is applied in periodontal treatments (Gupta and Deepa, 2016). Therefore, researches have been developed aiming to overcome this disadvantage. The ozone nano-bubble water generation technology (NBW3) is an example, which has an antimicrobial effect for more than six months in case there is no influence of ultraviolet rays (Hayakumo *et al*., 2013).

The limitations of this study include the small number of participants involved in the research, the short follow-up time, thus indicating the need of further researches to explore the subject hereby discussed and perhaps increase the time of treatment supervision. It is also worth noting that ozone therapy is recent and requires further clinical studies, emphasizing randomized clinical trials.

## Conclusion

No efficacy was observed using ozone in the gas form. However, in some studies the use of aqueous ozone has similar effects to CHX, without side effects as tongue and dental staining and changes in the taste. Further studies are needed.

## References


Akobeng AK. Principles of evidence based medicine. *Arch Dis Child*. 2005;**90**:837-40.

Al Habashneh R, Alsalman W, Khader Y. Ozone as an adjunct to conventional nonsurgical therapy in chronic periodontitis: a randomized controlled clinical trial. *J Periodont Res*. 2015;**50**:37-43.

Badar SB, Zafar K, Ghafoor R, Khan FR. Comparative evaluation of chlorhexidine, metronidazole and combination gels on gingivitis: A randomized clinical trial. *Int J Surg Protoc.* 2019; **14**:30-33.

Bartold PM. Lifestyle and periodontitis: The emergence of personalized periodontics. *Periodontol 2000*. 2018; **78**:7-11.

Carinci F, Palmieri A, Girardi A, Cura F, Lauritano D. Aquolab® ozone-therapy is an efficient adjuvant in the treatment of chronic periodontitis: A case-control study. *J Orofac Sci*. 2015;**7**:27-32.

Gupta S, Deepa D. Applications of ozone therapy in dentistry. *J Oral Res Rev*. 2016; **8** :86-91.

Gupta G, Mansi B. Ozone therapy in periodontics. *J Med Life*. 2012;**5**:59-67.

Hayakumo S, Arakawa S, Mano Y, *et al*. Clinical and microbiological effects of ozone nano-bubble water irrigation as an adjunct to mechanical subgingival debridement in periodontitis patients in a randomized controlled trial. *Clin Oral Invest*. 2013;**17**:379-388.

Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JAC, Cochrane Bias Methods Group, Cochrane Statistical Methods Group. The Cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ.* 2011; **343**:1-9.

Hooijmans CR, Rovers MM, Vries RBM, *et al*. SYRCLE's risk of bias tool for animal studies. *BMC Med Res Methodol.* 2014; **43**:1-9.

Huth KC, Quirling M, Lenzke S, Paschos E, Kamereck K, Brand K, Hickel R, Ilie N. Effectiveness of ozone against periodontal pathogenic microorganisms. *Eur J Oral Sci.* 2011;**119**: 204-210.

Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, Ioannidis JP, *et al*. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. *Ann Intern Med.* 2015;**162**:777-784.

Issac AV, Mathew JJ, Ambooken M, Kachappilly AJ, Ajithkumar PK, Johny T, Vk L, Samuel A. Management of chronic periodontitis using subgingival irrigation of ozonized water: A clinical and microbiological study. *J Clin Diagn Res.* 2015;**9**:29-33.

Katti SS, Chava VK. Effect of ozonised water on Chronic periodontitis - A clinical study. *J Int Oral Health*. 2013; **5** :79-84.

Kaur A, Bhavikatti SK, Das SS, Khanna S, Jain M, Kaur A. Efficacy of ozonised water and 0.2% chlorhexidine gluconate in the management of chronic periodontitis when used as an irrigant in conjugation with phase I therapy. *J Contemp Dent Pract*. 2019; **20**:318-323.

Kshitish D, Laxman VK. The use of ozonated water and 0.2% chlorhexidine in the treatment of periodontitis patients: A clinical and microbiologic study. *Ind J Dent Res.* 2010;**21**(3):341-348.

Kumar A, Bhagawati S, Tyagi P, Kumar P. Current interpretations and scientific rationale of the ozone usage in dentistry: A systematic review of literature. *Eur J Gen Dent*. 2014;**3**(3):175-180.

Leewananthawet A, Arakawa S, Okano T, Daitoku Kinoshita R, Ashida H, Izumi Y, Suzuki T. Ozone ultrafine bubble water induces the cellular signaling involved in oxidative stress responses in human periodontal ligament fibroblasts. *Sci Technol Adv Mater.* 2019; **20**:589-598.

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med.* 2009; **7**:1-34.

Moher D, Liberati A, Tetzlaff J, Altman DG, Prisma Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009; **7**:2-9.

Moraschini V, Kischinhevsky ICC, Calasans-Maia MD, Shibli JA, Sartoretto SC, Figueredo CM, Granjeiro JM. Ineffectiveness of ozone therapy in nonsurgical periodontal treatment: a systematic review and metaanalysis of randomized clinical trials. *Clin Oral Investig*. 2020; **24**(6):1877-1888.

Naik SV, KR, Kohli S, Zohabhasan S, Bhatia, S. Ozone-a biological therapy in dentistry- reality or myth? *Open Dent J.* 2016;**10**(1):196-206.

Nicolini AC, Rotta IS, Langa GPJ, Friedrich SA, Arroyo-Bonilla DA, Wagner MC, Weidlich P, Rösing CK, Cavagni J. Efficacy of ozonated water mouthwash on early plaque formation and gingival inflammation: a randomized controlled crossover clinical trial. *Clin Oral Invest.* 2020:1-8.

Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev.* 2016;**5**(210):1-10.

Pandya DJ, Manohar B, Mathur LK, Shankarapillai R. Comparative evaluation of two subgingival irrigating solutions in the management of periodontal disease: A clinicomicrobial study. *J Indian Soc Periodonto.* 2016;**20**(6):597-692.

Saini R. Ozone therapy in dentistry: A strategic review. *J Nat Sc Biol Med.* 2011;**2**(2):151-153.

Seydanur-Dengizek E, Serkan D, Abubekir E, Aysun Bay K, Onder O, Arife C. Evaluating clinical and laboratory effects of ozone in non-surgical periodontal treatment: a randomized controlled trial. *J Appl Oral Sci.* 2019; **27**:1-8.

Smiley CJ, Tracy SL, Abt E, Michalowicz BS, John MT, Gunsolley J, Cobb CM, Rossmann J, Harrel SK, Forrest JL, Hujoel PP, Noraian KW, Greenwell H, Frantsve-Hawley J, Estrich C, Hanson N. Systematic review and meta-analysis on the nonsurgical treatment of chornuc periodontitis by means of scaling and root planing with or without adjuncts. *J Am Dent Assoc*. 2015: **46**(7): 508-524.

Soorgani N, Agrawal R, Khashu H, *et al*. Efficacy of ozone therapy as an adjunct to scaling and root planing: A clinical and microbiological study. *Int J Prev Clin Dent*. 2019;**6**:14-16.

Srikanth A, Sathish M, Sri Harsha AV. Application of ozone in the treatment of periodontal disease. *J Pharm Bioallied Sci.* 2013;**5**(1):89-94.

Stone PW. Popping the (PICO) question in research and evidence-based practice. *Appl Nurs Res*. 2002;**15**:197-198.

Suh Y, Patel S, Re K, Gandhi J, *et al*. Clinical utility of ozone therapy in dental and oral medicine. *Med Gas Res.* 2019; **9**:163-167.

Tasdemir Z, Oskaybas MN, Alkan AB and Cakmak O. The effects of ozone therapy on periodontal therapy: A randomized placebo-controlled clinical trial. *Oral Dis.* 2019;**25**(4):1195-1202.

Uraz A, Karaduman B, Isler SÇ and Gönen S. Ozone application as adjunctive therapy in chronic periodontitis: Clinical, microbiological and biochemical aspects. *J Dent Sci.* 2019;**1**(1):1-11.

Vasthavi C, Babu HM, Rangaraju VM, *et al*. Evaluation of ozone as an adjunct to scaling and root planing in the treatment of chronic periodontitis: A randomized clinico-microbial study. *J Indian Soc Periodontol.* 2020;**24**(1):42-46.

Vettore MV, Marques RAA and Peres MA. Social inequalities and periodontal disease: multilevel approach in SBBrasil 2010 survey. *Rev Saúde Pública*. 2013;**47**(3):29-39.

Yan Y, Zhan Y, Wang X and Hou J. Clinical evaluation of ultrasonic subgingival debridement versus ultrasonic subgingival scaling combined with manual root planing in the treatment of periodontitis: study protocol for a randomized controlled trial. *Trials.* 2020;**21**(1):1-7.

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