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Efficacy of Ozone as an Adjunctive Anti-microbial in the Non-surgical Treatment of Chronic and Aggressive Periodontitis: A Systematic Review Protocol

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Abstract This is a protocol for a review so there is no abstract. The main objective of this review is to compute a summary effect for the adjunctive use of ozone with scaling and root planning (SRP) in the treatment of these diseases. This review will also seek to explore possible heterogeneity that may be present due to different ozone forms used during treatment.

Keywords: *periodontal diseases, ozone therapy, scaling and root planning, clinical attachment level, probing pocket depth, plaque index, bleeding on probing, gingival index, adjunct, aggressive periodontitis, chronic periodontitis*

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1. Background

1.1. Description of Condition: Epidemiology and Classification

Periodontal diseases (PD) are one of the most prevalent oral health problems in the world. It is the major cause of tooth mortality in the adult population. A recent report [1] indicates that almost half of all adults aged 30 years and older have some form of periodontal disease. The incidence of periodontal disease is said to increase with age; 70.1% of adults 65 years and older have periodontal disease. It is more common in males than females (56.4% vs 38.4%), those living below the federal poverty level (65.4%), those with less than a high school education (66.9%), and current smokers (64.2%). The two major subdivisions of PD are gingivitis -when the disease is confined to the gingival tissues; and periodontitis-which occurs when the gingiva and other supporting periodontal tissues are affected by the inflammatory process. This review however will focus on chronic and aggressive PD subtypes.

Chronic PD is an inflammatory disorder that leads to periodontal tissue damage and bone loss as a result of complex interactions between pathogenic bacteria and the host's immunity. It refers to progression of the disease over time without treatment and does not suggest that the disease is "untreatable". It is classified based on the severity of loss of clinical attachment [2] as; slight: 1-2 mm clinical attachment loss (CAL); moderate: 3-4 mm CAL and severe: > 5 mm CAL. Radiographically, it is associated with varying degree of bone loss. Aggressive periodontitis on the other hand is distinguished from chronic periodontitis by the age of onset, rapid rate of destruction, composition of the sub-gingival microflora, alteration in the host immune response, familial aggregation of diseased individuals, and a strong racial influence [3]. Although they are treated as different disease entities, they share many clinical features- they are both complex infections that occur in susceptible hosts and are caused by biofilms with indigenous oral microbiota on tooth surfaces [4]. Host response to the biofilms is primarily responsible for the loss of periodontal attachment and alveolar bone supporting the teeth [5]. If left untreated, the eventual outcome of these diseases is tooth loss. Both disease entities are not only known to cause psychological discomfort, functional limitation and physical pain among patients; they have also been associated with several systemic conditions such as cardiovascular diseases and diabetes [6].

1.2. Description of Intervention: Ozone and SRP

The aim of traditional periodontal therapy is to reduce the accumulation of dental biofilm and eliminate pathological bacteria occupying the periodontal pockets. The desired outcomes in these patients include reduction of clinical signs of inflammation, reduction of probing pocket depth and gain in clinical attachment level around affected tooth/teeth. Scaling and root planning procedure (SRP) which is a component of the initial periodontal

therapy (hygiene) phase constitutes the most important part of treatment for periodontitis. However, there are limitations to this mechanical procedure due to varying depth of periodontal pockets and other hard-to-reach regions in the mouth [7] making the elimination of causative microbes with SRP alone hardly sufficient. Ozone is a chemical compound consisting of three oxygen atoms (O_3-triatomic oxygen), a higher energetic form than normal atmospheric oxygen (O_2). Molecular weight of ozone is 41.98 g/mol. Although it is an unstable gas that quickly gives up nascent oxygen molecule to form oxygen gas, it is also a powerful oxidizer. Due to the property of releasing nascent oxygen, it has been used in human medicine for a long time to kill bacteria, fungi, inactivate viruses and to control hemorrhages [8]. Recently, ozone has been proposed as an alternative oral antiseptic in dentistry. In contrast with traditional medicines and modalities such as antibiotics and disinfectants, ozone therapy is quite inexpensive, predictable and conservative. The anti-microbial action is selective to microbial cells and does not damage human body cells because of their major anti-oxidative ability [9]. Several in-vitro studies confirm its bactericidal effect against periodontal bacteria, noting that when the concentration of ozone in a medium is increased and the reaction time extended, its antimicrobial effect also increases [10]. Ozone therapy has been proposed to be more beneficial than present conventional therapeutic modalities because treating patients with ozone lessens treatment time and eradicates the bacteria count more specifically [11]. It is completely painless with minimal other adverse effects and thus increases the acceptability of the treatment to patients. Based on its medium of delivery, it is stated that ozone concentration varies between 1 and 100 µg/ml (0.05-5%) [12]. It is said to be part of the evolving trend in minimally invasive dentistry (MI) because the possibility of its wide therapeutic use is associated with current trends in dentistry that place major emphasis on prevention.

Review Justification: Shortcomings of current disinfectants used as adjunctive in the treatment of chronic and aggressive periodontitis and available evidence.

Sub-gingival irrigation [13] with various antiseptic agents such as povidone-iodine, chlorhexidine, hydrogen peroxide and use of local and systemic anti-biotics such as metronidazole has been performed in conjunction with SRP. The use of these agents with SRP has produced significant clinical benefits relative to conventional mechanical root debridement alone. However, these existing antiseptic agents have several shortcomings, e.g., the prolonged use of chlorhexidine is associated with mucosal desquamation, tooth staining, and altered taste sensation. Also, an increasing number of immediate type allergies to this agent such as anaphylactic shock have been reported. Povidone-iodine use is contra-indicated in individuals who are allergic to iodine, suffering from thyroid dysfunction, or are pregnant or nursing. Sodium hypochloride (NaOCl) or hydrogen peroxide (H2O2) may result in hemorrhage, edema, and skin ulceration in oral tissues [14]. The increased use of antibiotics is known to present the risk of developing resistant microbial species [15].

Clinical controlled studies carried out in humans although limited in number have produced conflicting results on the efficacy of ozone use. This divergence of study results may be related to clinical and methodological differences such as difference in patient demographics, method of ozone delivery, frequency, and duration of application etc. An extensive search of several databases such as the Cochrane Library and MEDLINE yielded no systematic review on the efficacy of ozone use as an adjunctive hence this review.

2. Method

2.1. Eligibility Criteria

Type of studies: This review will consider randomized controlled clinical trials (parallel group design and within participant design)

2.2. Inclusion Criteria

2.2.1. Type of Participants

This review will consider studies with participants aged 18 and older with a diagnosis of chronic and aggressive PD. Diagnosis of these diseases will be based on the severity [2] of the loss of clinical attachment; slight (1-2mm CAL), moderate (3-4mm CAL) and severe (>5mm CAL) examined using a standardized periodontal probe. For aggressive PD, part of the diagnostic criteria will include radiographic evidence of bone loss which should be bilaterally symmetric, rapid and severe around the permanent first molar and incisor regions if localized; and around most teeth if generalized as well.

2.2.2. Type of Intervention

This review will include studies that evaluates the use of ozone in various forms (ozone gas, irrigation with ozonated water, and use of ozonized oil/gel) with SRP. Therapeutic methods of administration of intra-oral ozone include: irrigation with ozonated water, insufflation of periodontal pockets with gas and topical application of ozonated oil.

2.2.3. Comparator

Conventional non-surgical periodontal treatment also known as scaling and root planning (SRP) alone.

2.2.4. Type of Treatment Outcome Measures

Primary outcomes of interest are gain in clinical attachment level (CAL) [16] and reduction in probing pocket depth (PPD) [16] both measured in millimeters(mm) at study sites. PPD is measured from the base of the periodontal pocket to the gingival margin and CAL is assessed by measuring the distance between the cemento-enamel junction and the bottom of the pocket. Secondary outcomes of interest are changes at study sites in the following: plaque index (PI) [17], gingival index (GI) [18] and bleeding on probing (BOP) [19] scores. All parameters will be presented on a continuous scale using standardized indices and instruments. Measurements will be carried out at multiple time points; baseline and one, two, three or six months after intervention. For this review, end points will vary between individual studies. To capture the effect of ozone on a longer-term basis, the last measurements recorded at the end of individual studies will be recorded and used for the quantitative analysis.

2.3. Information Sources

The following databases will be searched for relevant studies: Cochrane Central Register of Controlled Trials (from 1992), MEDLINE via OVID (from 1946), CINAHL via EBSCO (Cumulative Index to Nursing and Allied Health Literature, from 1981), SCOPUS via Elsevier (from 1960) and Web of Science (from 1980). An initial search of PUBMED will be performed to identify relevant keywords. For the second stage search, all identified keywords and index terms will be searched for across all included databases listed above. Electronic versions of the following journals will also searched: Journal of Dentistry, Journal of Dental Research, Journal of Periodontology, Journal of Clinical Periodontology, Journal of Periodontal Research, Journal of the American Dental Association, Journal of Clinical Dentistry and Clinical Oral Investigations. In a third search, the reference lists of all identified articles and grey literature sites such as opengrey.eu and Google Scholar will be searched for additional studies. Only studies published in English will be reviewed. Keywords to be in MEDLINE and Google Scholar are listed below;

Periodontitis or chronic periodontitis
Chronic Periodontitis/ Clinical attachment loss/aggressive periodontitis
Early onset periodontitis/rapidly progressive periodontitis/juvenile periodontitis
Periodontal Pocket/Chronic Periodontitis
Ozone or ozonotherapy
Ozonated water
Ozonized water or ozone
Gaseous ozone or ozone gas
Ozone oil or ozonized oil
Non-surgical periodontal treatment or dental scaling
Non-surgical periodontal therapy or scaling or root planing
Adjunct periodontal therapy or initial non-surgical periodontal therapy
Non-surgical periodontal treatment or dental scaling or root planning
Tooth loss/ clinical attachment loss/tooth mortality

2.4. Selection of Studies

Efforts will be made to identify and deal with duplicate reports of the same studies by following the search and selection strategy outlined in the Cochrane Handbook for Systematic Reviews of Interventions [20]. Studies will be compared by authors' names, date of study, location and name of institution and journal of publication to remove duplicate articles. The process for study selection will include: merging search results in Endnote, screening of title and abstracts to identify and remove irrelevant studies, retrieval and a full review of potential studies.

2.5. Quality Assessment

Studies meeting the inclusion criteria will be assessed for their methodological quality using the Revman Cochrane appraisal template. Study assessment will be performed independently by two reviewers, and any disagreement will be settled by discussion with a third review author. The presence of the following features will be used to assess for selection bias, performance bias, detection bias and attrition bias respectively;
- allocation concealment and random sequencing between treatment and control group for selection bias,
- Blinding of investigators and outcome assessors for performance and detection bias respectively
- Use of intent to treat analysis for attrition bias.

Other bias due to group difference at baseline, difference in group treatment and reliability of outcomes will also be assessed. A decision rule of 4 low-risk scores out of a possible score of 7 will be the basis for study inclusion in the review.

2.6. Data Extraction

Data will be extracted using the Cochrane data extraction tool for RCTs [20]. The following information will be considered; study characteristics, population and setting, methods, participants, intervention, outcome, and results. Specifically, the following will be extracted for each paper:

Patients demographics
Setting of program
Study design
Method of subject recruitment
Forms of intervention (ozonated water, ozone gas and ozonated oil)
Length of intervention
Outcome description
Statistical method used
Conclusion of study authors.

3. Data Analysis

Statistical analysis/meta-analysis will be carried out using the Comprehensive Meta-Analysis (CMA) software program version 3. The unit of analysis for this review will include all individual studies that meets the inclusion criteria. A meta-analysis on each outcome variable will be performed on studies with similar intervention comparators to calculate the mean treatment effect across these studies. Results will be expressed as a standardized mean difference to assess the magnitude of the effect between the two groups with 95% confidence intervals (CI). The summary effect sizes will be presented on a forest plot to aid interpretation. A random effects model will be used in this analysis because it allows for between-study variability.

Assessment of heterogeneity will be performed in three stages[21]; visual inspection of the meta-view/forest plot of each pooled outcome, the statistical significance of the Q test and the I^2 test that indicates the magnitude of the heterogeneity. It is expected that homogeneous studies will have similar direction and magnitude of effect. This will be represented by rectangular symbols at similar positions on the X-axis when viewing the forest plot. Bias across studies: Visual examination of the funnel plot will be used to assess publication bias/selective reporting of the primary outcome measures.

3.1. Sub-group Analysis

One of the objectives of this review is to explore the variability in the efficacy of various forms of ozone used with SRP versus SRP alone. Sub-group analysis will be

carried out to investigate heterogeneity based on ozone form (water, aqueous or gas) and its influence on the effect size of the dependent variables.

Conflicts of Interest

None.

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References

[1] Eke PI, Dye B, Wei L, Thornton-Evans G, Genco R (2012). Prevalence of Periodontitis in Adults in the United States: 2009 and 2010. J Dent Res: 1-7.

[2] 1999 International Workshop for a Classification of Periodontal Diseases and Conditions.

[3] Joshipura V, Yadalam U, Brahmavar B. (2015). Aggressive periodontitis: A review. J Int Clin Dent Res Organ 7(1) :11-17.

[4] Armitage GC (2000). Comparison of the microbiological features of chronic and aggressive periodontitis. Periodontol; 53: 70-88.

[5] Schenkein HA (2006). Host responses in maintaining periodontal health and determining periodontal disease. Periodontol 2000; 40: 77-93 2006.

[6] Otomo-Corgel J, Pucher JJ, Rethman MP, Reynolds MA. (2012). State of the Science: Chronic periodontitis and systemic health. J Evid Base Dent Pract, 12(3): 20-28.

[7] Skurska A, Pietruska MD, Paniczko-Drężek A, Dolińska E, Zelazowska-Rutkowska B, Zak J, Pietruski J, Milewski R, Wysocka J (2010). Evaluation of the influence of ozonotherapy on the clinical parameters and MMP levels in patients with chronic and aggressive periodontitis. Adv Med Sci; 55(2):297-307.

[8] Srikanth, A., Sathish, M., & Sri Harsha, A. V. (2013). Application of ozone in the treatment of periodontal disease. Journal of Pharmacy & Bioallied Sciences; 5(Suppl 1), S89-S94.

[9] Tatsuya F, Kazuya M, Yoshimasa M , Shin-ichi F, Gotaro S, Yasuhiro I, Akihiko S, Pao-Li W (2014). Antimicrobial Effects of Ozone Gel Against Periodontal Bacteria. Journal of Hard Tissue Biology; 23(4) 445-448.

[10] Gupta G, Mansi B (2012). Ozone therapy in periodontics. Journal of Medicine and Life; 5(1): 59-67.

[11] Saini, R. (2011) Ozone therapy in dentistry: A strategic review. Journal of Natural Science, Biology, and Medicine; 2(2), 151–153.

[12] Maiya A (2011). Application of ozone in dentistry. Int J Clin Dent Sci; 2: 23-7.

[13] Hayakumo, S., Arakawa, S., Mano, Y. and Izumi, Y (2013). Clinical and microbiological effects of ozone nanobubble water irrigation as an adjunct to mechanical subgingival debridement in periodontitis patients in a randomized controlled trial. Clinical Oral Investigations; 17: 379-388.

[14] Huth KC, Jakob FM, Saugel B, Cappello C, Paschos E, Hollweck R, Hickel R, Brand K (2006). Effect of ozone on oral cells compared with established antimicrobials. Eur J Oral Sci; 114: 435-440.

[15] Yilmaz S, Algan S, Gursoy H, Noyan U, Kuru B. E, Kadir, T (2013). Evaluation of the clinical and antimicrobial effects of the Er:YAG laser or topical gaseous ozone as adjuncts to initial periodontal therapy. Photomed Laser Surg; 31(6): 293-298 2013.

[16] Ramfjord SP (1967). The periodontal disease index (PDI). J Periodontol; 6: 602-610.

[17] Silness J, Loe H (1964). Periodontal disease in pregnancy 2. Correlation between oral hygiene and periodontal condition. Acta Odontol Scand; 22: 121-135.

[18] Loe H, Silness J (1963). Periodontal disease in pregnancy. Prevalence and severity. Acta Odontol Scand; 21:533-51.

[19] Ainamo J, Bay I (1975). Problems and proposals for recording gingivitis and plaque. Int Dent J; 4: 229-35.

[20] Higgins JPT, Green S (2011). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. Available from www.cochrane-handbook.org.

[21] Whitehead A (2003). Meta-analysis of Controlled Trials. Published by John Wiley& Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex PO19 8SQ, England.