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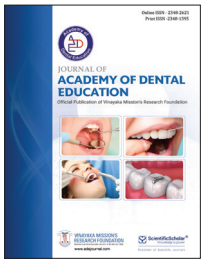
Journal of Academy of Dental Education



Review Article

Periodontal application of ozone therapy

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Received: 16 December 2022
Accepted: 13 October 2023
Published: 09 December 2023

DOI
10.25259/JADE_63_2022

Quick Response Code:

ABSTRACT

The prevalence of periodontium-related problems has been rising globally, impacting individuals across various age groups. Hence, it is crucial for the medical fraternity to address the treatment and subsequently prioritize prevention of the same. Periodontal infections involve the invasion by various bacterial inhabitants deep within the healthy pockets, leading to progressive recession with bone loss and tooth mobility, resulting in periodontitis. Therefore, effective decontamination of periodontal pockets is of paramount importance. Ozone, a natural constituent of the earth's atmosphere, has now revolutionized the field of medicine since its introduction. Due to its highly unstable and oxidizing form, its procurement and implementation of ozone were challenging initially. The recent advancement in technologies has made it possible to stabilize ozone, enabling comprehensive approaches to major ailments. This literature review intends to illustrate ozone therapy and its diversified application as an adjunct in surgical and nonsurgical periodontal therapies. Ozone therapy has proven its potentiality by promising faster tissue regeneration, aiding in wound healing to effectively decontaminate the pocket depths, resulting in a successful prognosis. The review explores diverse systems and products used for ozone generation across different modalities, with limitations of the same. Evidence provided in the literature will contribute to a better understanding of ozone therapy's role in improving periodontal health and guide future research in this field.

Keywords: Ozone therapy, Non-invasive, Tissue regeneration, Periodontal diseases

INTRODUCTION

Periodontal disease is a chronic inflammatory response of the periodontium surrounding teeth, leading to irreversible damage to the periodontal ligament with progressive destruction of alveolar bone in advanced stages. Periodontal-related diseases are the most common oral condition in the human population. The prevalence of periodontal diseases affects about 20–50% of the population globally.[1] This condition is considered one of the two core threats to the oral cavity, leading to tooth loss.[2] The percentage of affected adolescents in developing countries ranges from 35% to 70%, whereas in developed nations the affected ranges from 4% to 34%. The percentage of the affected adult population in developing countries ranges from 36 to 63%, with 14–47% of the affected adult population in developed countries. These diseases have shown an increased predilection for geriatric patients, with periodontal pockets of 6 mm or above in both developed and developing countries.[3] Due to the chronic nature of the disease, it becomes imperative to restrict its severity and prevalence through a comprehensive treatment planning and an effective prophylactic approach of the same. One such recent discovery involves, ozone therapy administered in either aqueous

or gaseous form. Being a potent oxidizing agent with high biocompatibility, this non-invasive treatment modality is been widely used in various fields of interest, including medicine, dentistry, and veterinary medicine.[4] The studies discussed below in this literature review will focus on the biological efficiency of ozone with inferences from various studies confirming the same, particularly in surgical and non-surgical procedures concerning the field of periodontology when used as a supplement.

HISTORY

The word "OZONE" took its origin from the Greek word *ozein* meaning "to smell." Ozone was originally discovered by a Dutch chemist, *Martinus van Marum, in 1785* while conducting electric sparking over water, when he noted a distinct smell, only to acknowledge later the smell being of ozone. A half-century later, it was *Christian Friedrich Schobein*, who theorized the presence of ozone.[5]

Ozone was first implicated in the medicinal field by Landler in 1870. However, it was in 1936 that it was taken under serious consideration by a Swiss dentist, Dr. E. A. Fisher,[6] where it was studied in the form of ozonated water and put into use during his daily practice. It was when one of his patients, Dr. E. Payr was getting treated for a gangrenous pulpite that and developed a great sense of interest in the local action of ozone during his treatment of the disease and later extended its application.

In 1957, Joachim Hänsler and Hans Wolff, German physicists, developed the first ozone generator for medical usage, which now continues to be a basis for modern medical-grade ozone generators.[7]

BIOLOGICAL ACTION UNDERTAKEN BY THE OZONE ADMINISTRATION

This non-invasive treatment modality is now used as an adjunctive or preventive treatment, resulting in successful prognoses in the field of medicine, which is now gaining popularity. Ozone therapy is well known for its antibacterial activity along with its anti-hypoxic effect and has proven its efficacy in immune stimulatory activity as well. The following are the biological actions undertaken by the ozone administration:

Antimicrobial action

Ozone is proven to be highly effective in the destruction of microorganisms such as bacteria, viruses, and fungi. The ozone directly acts on the cell membranes in these cases. In bacteria, it acts directly on the cytoplasmic membrane by ozonolysis of the dual bond duality with the ability to modify the intercellular contents through oxidation of the proteins in various organelles within the bacteria. This act is non-specific and selective in nature, where Gram-positive shows more sensitivity to ozone than Gram-negative. The potency of action increases in the presence of a liquid medium with an acidic pH. This action is selective to microbial cells but does not damage the body cells because of their major anti-oxidative ability.[8] Ozone has shown to be competent toward the viral sheaths, where it acts on the multi-unsaturated fatty acids chains of the lipid sheath and disintegrates the viral sheath.[9]

Immune stimulating action

Various studies concluded the immune stimulating effect influences both the humoral and the cell-mediated immune systems.[8] The ozone functions by activating the macrophages, stimulating the release of certain chemical mediators such as cytokine, setting in action a cascade of biochemical reactions, and resulting in the production of various anti-inflammatory mediators such as leukotrienes, interleukins, and prostaglandins. Thus decreasing the inflammation and aiding in effective wound healing.[8] In high concentrations, ozone acts by depressing immune activity, whereas in cases of low concentration, it increases immune activity.[9]

Anti-hypoxic action

Ozone has been shown to elevate the pO_2 levels in tissues and improve oxygen transportation throughout. In repetitive low doses, it protects the calls against oxygen free radicals by activating various enzymes such as superoxide dismutases, catalases, dehydrogenases, and glutathione. It also prevents the aggravation of erythrocytes and increases the contact surface area for the attachment of oxygen, for better transportation.[8] Ozone also improves the metabolism of inflamed tissues by reducing local inflammation and potentiating the oxidation process.

Biosynthetic action

By influencing the biochemical processes within the cells, it stimulates protein synthesis and thus increases the amount of ribosomes and mitochondria within. At the cellular level, this explains the regenerative potentiality of the tissues and organs post-ozone therapy.[8] It also aids in the activation of angiogenesis.[9]

GENERATION OF OZONE

Medical grade ozone is used in the ratio of 0.05–5% of O_3 and 95–99.95% of O_2. Due to the unstable nature of ozone, it is to be manufactured freshly before the

treatment. The three systems used for the generation are as follows: [10]

Ultraviolet system

Ozone is created by the photolysis of the O_2 molecule by ultraviolet light in the range of 160–240 nm, producing a low concentration of ozone, commonly implicated in air purification or esthetic treatment modalities.

Corona discharge system

The system results in the cleavage of the oxygen molecule as two oxygen radicals, thus producing a high concentration of ozone. This is the most common form of ozone generator. Used in the medical/dental field.

Cold plasma system

This utilizes oxygen as the input source and is used to produce ozone in the concentration of 5–7%. Used in air and water purification systems widely.

MANUFACTURE OF OZONE IN DENTISTRY

The table 1 mentioned below has stated the various manufacturing industries responsible for medical grade ozone producing devices, with a holistic overview of the same.

SAFETY PRECAUTIONS AND GUIDELINES FOR HANDLING

Ozone, when administered in its gaseous form, without any proper administration specification, can source ozone

Table 1: Manufacture of ozone in dentistry.

Product	System used	Form	Advantages	Disadvantages
Ozonette DENT (Sold by Sedecal)[11]	Corona discharge system	Gaseous form	1. Handheld syringe application. 2. Ozone flow rate and concentration can be adjusted with uniform distribution. 3. AOD 4. Ozone is removed by the double independent circuit with two internal catalysts. 5. Compatible with O2 cylinder.	1. Uneconomical.
Ozonytron-XPO (MIO Int. OZONYTRON GmbH)[12]	Cold plasma system	Gaseous form	1. Application through – Plasma electrode/nozzle/mouth tray 2. Can be used in various treatment modalities (disinfection of cavities, root canals, gingival pockets) along with in office/internal bleaching with different applicators provided. 3. Mouth Tray, encloses the targeted area from the oral cavity, preventing inhalation of ozone plasma.	1. Chances of leakage with plasma electrode; thus be used with saliva ejector. 2. Plasma is directly generated at the treatment site, creating microcurrent. Thus contraindicated in • Epileptic patient • Cardiac pacemaker • Hypersensitivity to electric impulses.
Ozonsan cytozon (Hansler Medical)[13]	Normobaric infusion therapy (ozonized water)	Aqueous form	1. Application through handpick or water outlet tap. 2. Additional bayonet connection allows multiple connections of devices such as ultrasonic devices or piezosurgery 3. Ease of handling 4. Safe handling 5. Painless treatment modality.	1. Less effective when compared to gaseous ozone.
OxActiv (ozonated olive oil gel)[14]	Infused ozone in gel based product	Aqueous gel	1. Ease of application 2. Safe handling 3. Cost-effective 4. Ease of availability.	1. Least effective when compared to all the other modalities discussed above.

AOD: Automatic overpressure detection. Manufacture of ozone in dentistry

toxicity via inhalation. Has been known to show the following side effects mentioned below:[10]

1. Epiphora
2. Upper respiratory tract irritation
3. Rhinitis
4. Cough
5. Headache
6. Occasional nausea.

Adversities caused either by leakage or unmoderated gaseous doses can potentially result in ozone intoxication. The following must be performed, immediately:[10]

1. The patient must be placed in a supine position
2. Inhalation of humid oxygen
3. Administration of ascorbic acid, Vitamin E, and N-acetylcysteine [Figure 1].

EVIDENCE OF OZONE APPLICATION IN PERIODONTOLOGY

The table 2 mentioned below is an assemblage of various studies conducted regarding the application of ozone therapy and its results in applied periodontolgy with Inferences of the same.

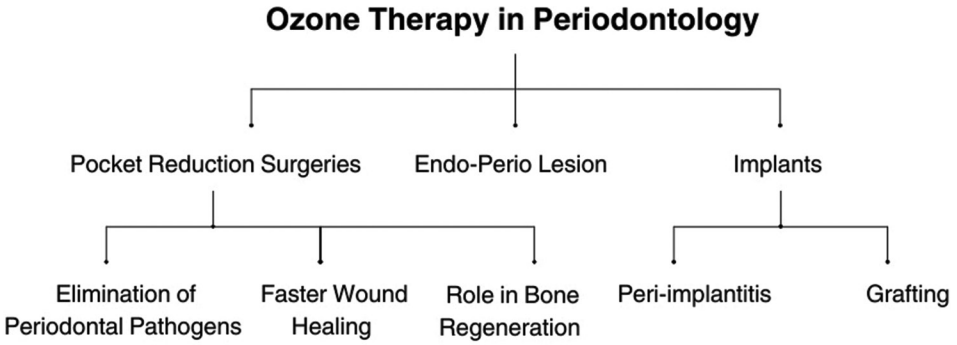

Figure 1: Ozone therapy in periodontology.

Table 2: Evidence of ozone application in periodontology.

Author and year of publication	Use of ozone	Inference of the study conducted
Huth *et al.* 2007[15]	As an antiseptic agent. As a pre-surgical mouth rinse.	The study confirmed the aqueous form of ozone as a potential antiseptic agent with low cytotoxicity for oral application.
Filippi[16]	As an irrigant post-surgical procedures for swift healing of the wound.	The study concluded an accelerated wound healing in the oral mucosa within the first 48 h with ozone water.
Nagayoshi *et al.* 2004[17]	As an irrigant peri dental procedure. As a mouth rinse	The study concluded the bactericidal effect of ozonated water over oral biofilm with a predilection for Gram-negative bacteria *in vitro*.
Hems *et al.* 2005[18]	As an irrigating agent.	Tested the efficacy of aqueous and gaseous forms of ozone against *Enterococcus faecalis* in biofilm.
Kshitish and Laxman 2010[19]	As an irrigating agent, to reduce pocket depth. As mouth rinse.	The study interpreted a higher percentage in reduction of plaque index, gingival index, and bleeding index with the use of ozonated water in comparison with CHX, with percentile reduction in aggregatibacter actinomycetemcomitans (Aa) in patients of chronic generalized periodontitis.
Ramzy *et al.* 2005[20]	As an irrigant during the treatment of aggressive periodontitis	The study conducted in patients suffering from aggressive periodontitis was irrigated once weekly with 150 mL of ozonated water, concluding a significant reduction of bacterial count in periodontal pockets.
Hauser–Gerspach *et al.* 2012[21]	As a sterilizing agent prior to implant placement in the oral cavity, reducing chances of peri-implantitis.	The study concluded the antimicrobial efficacy of gaseous ozone against bacteria adherent over titanium and zirconia dental implants, without affecting the adhesion and proliferation of the osteoblastic cells.
Ebensberger *et al.* 2002[22]	As a cleaning agent and for root surface decontamination for an avulsed tooth reimplantation.	The study concluded the 2-min irrigation with isotonic ozonated water decontaminated the root surface with on deteriorating effect over the periodontal cells viable over the root surface, along with mechanical cleaning.

Evidence of ozone application in periodontology

CONTRAINDICATIONS OF OZONE THERAPY IN PERIODONTOLOGY

The following mentioned below are some of the contraindications, during the administration of ozone therapy:[10]

- Pregnancy, particularly the early phase, excludes any mutagenic risk, although it is unlikely[23]
- Glucose-6-phosphate-dehydrogenase deficiency (G-6-PD) (favism): The enzyme G-6-PD is crucial for eliminating equivalents able to abolish excessive oxidation and intensive hemolysis. Deficiency of the same, results in hemolytic disease known as favism. On exposure to ozone, it is associated with the precipitation of acute hemolysis in such cases[24]
- Hyperthyroidism: The sensitivity of the lung to damage due to ozone therapy may be highly dependent on an individual's thyroid hormone status. The chances of aggravation of the lung toxicity in patients with a hyperthyroid state are more likely[25]
- Severe anemia
- Severe myasthenia gravis
- Active hemorrhage
- Acute alcohol intoxication
- Recent myocardial infarction.

CONCLUSION

Ozone has wide application in both medical and dental fields due to its various benefactors aiding in faster healing processes and disinfection has proven to be an efficient adjunct to conventional surgical procedures. Due to its simplicity of usage, it has no side effects and has been shown to have good tolerance among patients and economic efficiency thus becoming a popular modality. In periodontology, this modality is used effectively in the treatment of peri-implantitis, disinfection of periodontal pockets, regeneration of bone, and speeding the process of wound healing post surgeries.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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How to cite this article: Tyagi A, Khattri S. Periodontal application of ozone therapy. J Academy Dent Educ. 2023;9:80-5. doi: 10.25259/JADE_63_2022