

Ozone Therapy – A New Approach in Periodontal Management.

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Abstract: This review of literature is an attempt to summarize the uses of ozone therapy in periodontics. Gingival and periodontal diseases play a major role in dentistry. Bacteria is the main etiological factor. The use of ozone in dentistry has been proposed in dentistry because of its antimicrobial, disinfectant, biocompatibility and healing properties. The primary objective is to provide a general review about ozone therapy in periodontics. The secondary objective is to summarize the available in-vitro and in-vivo studies in Periodontics in which ozone has been used. This is useful for the future researchers in terms of what has been tried and what the potentials are for the clinical application of ozone in Periodontics.

Key words: Ozone, antimicrobial, immunostimulant, biosynthetic.

I. Introduction

Periodontitis is a destructive inflammatory disease of the supporting tissues of the teeth and is caused either by specific microorganisms or by a group of specific microorganisms, resulting in progressive destruction of periodontal ligament and alveolar bone with periodontal pocket formation, gingival recession, or both.[1]

Bacteria are the prime etiological agents in periodontal disease. To avoid elimination, bacteria need to adhere to either hard dental surfaces or epithelial surfaces. The oral biofilm formation and development, and the inside selection of specific microorganisms have been correlated with the most common oral pathologies, such as dental caries, periodontal disease and peri-implantitis.[2] The mechanical removal of the biofilm and adjunctive use of antibiotic disinfectants or various antibiotics have been the conventional methods for periodontal therapy.[3][4] Ozone therapy is one of the modern non-medication methods of treatment. Ozone is an unstable gas and it quickly gives up nascent Oxygen molecule to form Oxygen gas. Due to the property of releasing nascent Oxygen, it has been used in human medicine since long back to kill bacteria, fungi, to inactivate viruses and to control hemorrhages.[5]

II. History

The word ozone was first used by Schonbein in 1840. He subjected oxygen to electrical discharges and noted "the odour of electrical matter". Schonbein concluded that odour was due to a gas which he named ozone, from the Greek word ozein (odorant). However, it was not until 1932 that ozone was seriously studied by the scientific community, when ozonated water was used as a disinfectant by Dr. E. A. Fisch, [6] a Swiss dentist. Fisch had the first idea to use ozone as either a gas or ozonated water in his practice.

In 1856, just 16 years after its discovery, ozone was first used in a health care setting to disinfect operating rooms and sterilize surgical instruments.[7] By the end of the 19th century the use of ozone to disinfect drinking water of bacteria and viruses was well established in mainland Europe.[7][8]

At the time, ozone therapy was difficult and limited due to the lack of ozone-resistant materials, such as Nylon, Dacron, and Teflon, until 1950 when ozone-resistant materials were manufactured. At that time Joachim Hänsler, a German physicist and physician, joined another German physician, Hans Wolff, to develop the first ozone generator for medical use. Their design continues to be the basis for modern equipments.

III. Ozone therapy: chemistry and apparatus.

Ozone (O₃) is a triatomic molecule, consisting of three oxygen atoms. Its molecular weight is 47, 98 g/mol and thermodynamically highly instable compound that, dependent on system conditions like temperature and pressure, decompose to pure oxygen with a short half-life.[9] Ozone is an unstable gas that cannot be stored and should be used at once because it has a half-life of 40 min at 20 °C.[10] Ozone (O₃) is naturally produced by the photo dissociation of molecular oxygen (O₂) into activated oxygen atoms, which then react with further oxygen molecules. This transient radical anion rapidly becomes protonated, generating hydrogen trioxide (HO₃), which, in turn, decomposes to an even more powerful oxidant, the hydroxyl radical (OH). Ozone gas has a high oxidation potential and is 1.5 times greater than chloride when used as an antimicrobial agent against bacteria, viruses, fungi, and protozoa. It also has the capacity to stimulate blood circulation and the immune response. Such features justify the current interest in its application in medicine and dentistry.[11]

Ozone generators:

The first ozone generator for medical use was developed by German physicians named Joachim Hansler and Hans Wolff.

There are three different systems for generating ozone gas: [11]

- **Ultraviolet System:** produces low concentrations of ozone, used in esthetics, saunas, and for air purification.
- **Cold Plasma System:** used in air and water purification.
- **Corona Discharge System:** produces high concentrations of ozone. It is the most common system used in the medical/ dental field. It is easy to handle and it has a controlled ozone production rate.

Biological actions:

Anti microbial effect:

Ozone works destructively against bacteria, fungi and viruses. The antimicrobial effect of ozone is a result of its action on cells by damaging its cytoplasmic membrane due to ozonolysis of dual bonds and also ozone-induced modification of intracellular contents because of secondary oxidant effects. This action is selective to microbial cells but does not damage human body cells because of their major antioxidative ability.[12]

Immunostimulating effect:

Ozone influences cellular and humoral immune system. It stimulates proliferation of immunocompetent cells and synthesis of immunoglobulins. It also activates function of macrophages and increases sensitivity of microorganisms to phagocytosis. Ozone causes the synthesis of biologically active substances such as interleukins, leukotrienes, and prostaglandins which is beneficial in reducing inflammation and wound healing. Ozone in high concentrations causes immunodepressive effect whereas in its low concentration immunostimulating effect. [13]

Antihypoxic effect:

Ozone improves the transportation of oxygen in blood, which results in change of cellular metabolism-activation of aerobic processes (glycolysis, Krebs cycle, β -oxidation of fatty acids) and use of energetic resources. Ozone improves the metabolism of inflamed tissues by increasing their oxygenation and reducing total inflammatory processes. [14]

Biosynthetic effect:

It activates mechanisms of protein synthesis increases amount of ribosomes and mitochondria in the cells. These changes on the cellular level explain elevation of functional activity and regeneration potential of tissues and organs.[15]

Goals of ozone therapy:[16]

1. Elimination of pathogens.
2. Restoration of proper oxygen metabolism.
3. Induction of a friendly ecologic environment.
4. Increased circulation.
5. Immune activation.
6. Simulation of the humoral anti-oxidant system.

Appliances producing ozone for dental use:[17]

1. HealOzone by KaVo is air-

It is air based and the application of the gas takes place in a closed circuit. Its surplus is sucked out and neutralized by manganese ions. The concentration of ozone in the cap adjacent to the tissue amounts to 2100 ppm. Perfect air tightness of the cap is necessary for the application of ozone. Therefore, the application is only possible on the surfaces where such air tightness can be provided.

2. OzonyTron by MYMED Gmb H. –

Oxygen activation generator uses the power of high frequency and voltage. Activated oxygen (ozone) concentration can be adjusted in 5 levels via current strength. Inside the glass probe, which is formed by a double glass camera, is a noble gasses mixture that is conducting and emitting electromagnetic energy. When the tip of the probe gets in contact with the body it emits energy around the treated area and splits environmental diatomic oxygen in singular atomic oxygen and ozone. The concentration of ozone in the operation field is 10 to 100 µg/ml (becomes a fungi, virus, and bactericide at the intensity of 1–5 µg/ml). There is no closed circuit here, therefore, ozone can be applied to the places that are difficult to reach, e.g. gingival pockets or root canals.

3. Product photo (Prozone) by W&H –

It is characterized by its ease of use and safety of application (preset tissue-compatible dosages in the indication areas of periodontitis and endodontitis). Prozone ensures a hygienic procedure during the gassing of the pockets due to its exchangeable plastic attachments (Perio tips or Endo tips).

IV. Routes of Administration

Gaseous ozone - Ozone can be used in gaseous form via an open system or via a sealing suction system to avoid inhalation and its adverse effects.

Ozonated water - Ozonated water has been shown to be very effective against bacteria, fungi and viruses.

Ozonized oil - In addition to gaseous and aqueous form, oils that are ozonized also seems extremely convenient. Though gaseous ozone was shown to have more effective microbicidal properties than aqueous form, due to its toxic effects if inhaled, ozonated water is the most preferred form for use in dentistry. Therefore a safe system for applying gaseous ozone into the periodontal pocket that avoids inhalation still needs to be developed. [18]

V. Ozone therapy in periodontics:

Periodontal disease is a multifactorial disease process. The role of micro organisms and host response in the etiology of periodontal disease is well established. Ozonated water (4 mg/l) was found effective for killing gram-positive and gram-negative oral microorganisms and oral *Candida albicans* in pure culture as well as bacteria in plaque biofilm and therefore might be useful as a mouth rinse to control oral infectious microorganisms in dental plaque. Thanomsub et al. 2002 tested the effects of ozone treatment on cell growth and ultra-structural changes in bacteria (*Escherichia coli*, *Salmonella* sp., *Staphylococcus aureus* and *Bacillus subtilis*). It was discovered that ozone at 0.167 mg/min/l can be used to sterilize water, which is contaminated with up to 105 cfu/ml bacteria within 30 min. Destroying of bacterial cell membrane was observed, subsequently producing intercellular leakage and eventually causing cell lysis. Nevertheless, these ozone concentrations have no significant effect on the cell viability in bacterial cultures at higher concentrations of 106 and 107 cfu/ml. [19] Ebensberger et al. in 2002 evaluated the effect of irrigation with ozonated water on the proliferation of cells in the periodontal ligament adhering to the root surfaces of 23 freshly extracted completely erupted third molars. The teeth were randomly treated by intensive irrigation with ozonated water for 2 min or irrigation with a sterile isotonic saline solution, serving as a control group. The periodontal cells of these teeth were studied immunohistochemically to mark proliferating cell nuclear antigen. It was observed that the labeling index (the number of positive cells compared to the total number of cells suggesting enhancement of metabolism) was higher among the teeth irrigated with ozone (7.8% vs. 6.6%); however, the difference was not statistically significant ($P = 0.24$). They concluded that the 2 min irrigation of the avulsed teeth with non-isotonic ozonated water might lead not only to a mechanical cleansing, but also decontaminate the root surface, with no negative effect on periodontal cells remaining on the tooth surface. [20] Nagayoshi et al. 2004 tested the efficacy of ozonated water on survival and permeability of oral microorganisms. Gram negative bacteria, such as *Porphyromonas endodontalis* and *Porphyromonas gingivalis* substantially more sensitive to ozonated water than gram positive oral streptococci and *C. albicans* in pure culture. Furthermore ozonated water had strong bactericidal activity against bacteria in plaque biofilm. In addition, ozonated water inhibited the accumulation of experimental dental plaque in vitro. [21] Ramzy et al. in 2005 irrigated the periodontal pockets by ozonized water in 22 patients suffering from aggressive periodontitis. Periodontal pockets were irrigated with 150 ml of ozonized water over 5-10 min once weekly for a clinical 4 weeks study using a blunt tipped sterile plastic syringe. High significant improvement regarding pocket depth plaque index gingival index and bacterial count was recorded related to quadrants treated by scaling and root planing together with ozone application. They also reported significant reduction in bacterial count in sites treated with ozonized water. [22]

Huth et al. in 2006, in their study declared that the aqueous form of ozone, as a potential antiseptic agent, showed less cytotoxicity than gaseous ozone or established anti microbials (chlorhexidine digluconate [CHX]: 2%, 0.2%; sodium hypochlorite 5.25%, 2.25%; hydrogen peroxide-H₂O₂ 3%) under most conditions.

Therefore, aqueous ozone fulfills optimal cell biological characteristics in terms of biocompatibility for oral application. [23]

Muller et al. in 2007 compared the influence of ozone gas with photodynamic therapy (PDT) and known antiseptic agents (2% chlorhexidine, 0.5 and 5% hypochlorate solutions) on a multispecies oral biofilm in vitro. *Actinomyces naeslundii*, *Veillonella dispar*, *Fusobacterium nucleatum*, *Streptococcus sobrinus*, *Streptococcus oralis* *Ibicans* were studied. Gasiform ozone was produced by vacuum ozone delivery system Kavo Healozone. They concluded that the matrix-embedded microbial populations in biofilm are well protected towards antimicrobial agents. Only 5% hypochlorate solution was able to eliminate all bacteria effectively. Usage of gasiform ozone or PDT was not able to reduce bacteria in the biofilm. [24]

Karapetian et al. in a study of peri-implantitis, treatment with conventional, surgical and ozone therapy methods was investigated and it was found that the most effective bacteria reduction was in the ozone-treated group. [25]

Brauner has demonstrated that the combination of professional tooth cleaning and daily rinsing of the mouth with ozone water can improve clinical findings in cases of gingivitis and periodontitis. Plaque indices and a tendency to bleed, however, quickly return if the professional measures are interrupted. Rinsing the mouth with ozone water without any mechanical procedures for plaque reduction were unsuccessful. [26]

Kshitish and Laxman in 2010 conducted a randomized, double-blind, crossover split-mouth study on 16 patients suffering from generalized chronic periodontitis. The study period of 18 days was divided into two time-intervals, i.e., baseline (0 days) to the 7 th day, with a wash out period of 4 days followed by a second time-interval of 7 days. Subgingival irrigation of each half of the mouth with either ozone or chlorhexidine was done at different time intervals. They observed a higher percentage of reduction in plaque index (12%), gingival index (29%), and bleeding index (26%) using ozone irrigation as compared to chlorhexidine. The percentile reduction of *Aggregatibacter actinomycetemcomitans*(Aa.) (25%) using ozone was appreciable as compared to no change in Aa occurrence using chlorhexidine. By using O 3 and chlorhexidine, there was no anti-bacterial effect on *Porphyromonas gingivalis* (Pg) and *Tannerella forsythensis*. The anti-fungal effect of ozone from baseline (37%) to 7 th day (12.5%) was pronounced during the study period, unlike CHX, which did not demonstrate any anti-fungal effect. No anti-viral property of ozone was observed. The anti-viral efficacy of chlorhexidine was better than that of ozone. They concluded that despite the substantivity of chlorhexidine, the single irrigation of ozone is quite effective to inactivate microorganisms. [27]

Huth, et al. in 2011 compared the effectiveness of ozone with that of the established antiseptic CHX, against periodontal microorganisms. There were no significant differences in the effectiveness of aqueous ozone (20 µg ml [-1]) or gaseous ozone (≥4 g [-3]) compared with 2% CHX but they were more effective than 0.2% CHX. Therefore, high-concentrated gaseous and aqueous ozone merit further investigation as antiseptics in periodontitis therapy. [28]

VI. Contraindications for ozone therapy:

The following are contraindications of ozone therapy

1. Pregnancy
2. Glucose- 6- phosphatase dehydrogenase deficiency (favism)
3. Hyper thyroidism
4. Severe anemia
5. Severe myasthenia
6. Active hemorrhage

VII. Ozone toxicity:

Overwhelming evidence shows that the bronchial-pulmonary system is very sensitive to ozone and this gas should never be inhaled. [32] The respiratory tract lining fluid is constituted by a very thin, watery film containing a minimal amount of antioxidants that makes mucosal cells extremely vulnerable to oxidation. Pulmonary embolism, which occurred during direct intravenous administration of O 2 /O 3 , an application prohibited by the European Society of Ozone therapy since 1983. [29] Known side effects are epiphora and upper respiratory irritation, rhinitis, cough, headache, occasional nausea, and vomiting.

VIII. Conclusion:

In contrast with traditional medicines and modalities such as antibiotics and disinfectants, ozone therapy is quite inexpensive, predictable and conservative. The ozone therapy has been more beneficial than present conventional therapeutic modalities. Treating patients with ozone therapy lessens the treatment time with an immense deal of variation and it eradicates the bacterial count more specifically. The treatment is

completely painless and increases the patients' acceptability and compliance with minimal adverse effects. Although more clinical research has to be done to standardize indications and treatment procedures of ozone therapy, still many different approaches are so promising, or already established, that hopefully the use of ozone therapy becomes a standard treatment for disinfection of an operation sites in dentistry.

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