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REVIEW ARTICLE

Ozone therapy a frontier in Periodontics -A Review

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Abstract

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. Bacteria are the prime etiological agents in periodontal disease. The mechanical removal of the biofilm and adjunctive use of antibiotic disinfectants or various antibiotics have been the conventional methods for periodontal therapy. Ozone therapy is one of the modern non-medication methods of periodontal treatment. The objective is to provide a general review about ozone therapy in periodontics and to summarize uses and applications in Periodontics in which ozone has been used.

INTRODUCTION

A triatomic molecule with symbol O3 is ozone. The word ozone comes from the greek 'ozein' meaning adorant. It is continuously formed at an altitude of between 50000 to 100000 feet. Its molecular weight is 47,98 g/mol. It is a pale blue gas that condenses to a deep blue liquid. [1,2] Ozone is 1.6-fold denser and 10-fold more soluble in water (49 mL in 100 mL water at 0°C) than oxygen. Ozone is naturally produced by the photo dissociation of molecular oxygen(O2) into activated oxygen atoms, which then rea ct with further oxygen molecules. It is the fundamental form of oxygen that occurs naturally as a result of ultraviolet energy or lightning, causing a temporary recombination of oxygen atoms into groups of three.

Medical grade ozone is a mixture of pure O2 and O3 in the ratio of 0.1% to 5% of O3 and 95% to 99.5% of O2. Half life of O3 is 40 minutes at 20^{O} C. Ozone is an unstable gas and it quickly gives up nascent oxygen molecule. Because of this property , it has been used in human medicine.[3,4]

Evolution of Ozone therapy

Ozone therapy is one of the non surgical methods of periodontal treatment. It is being used for more than 100 years. Some of the advantages are simplicity of performance, good tolerance by patients, absence of side-effects or adverse reactions and high medical-social and economic efficiency. [5,6]

The ability of ozone to destroy toxic or noxious industrial impurities and to inactivate bacterial contaminants in sewage has made it an attractive alternative to chlorination. In 1901 Wiesbadecn, Germany became the first city to use ozonation for purification of its drinking water, followed by Zurich, Florence, Brussels, Marseille, Singapore and Moscow. The history of ozone's medical applications has nebulous and anecdotal beginnings.[7] Medical applications became widespread through out europe and america.

German chemist Christian Federick Schonbein is credited with the discovery of ozone in 1840. He first noticed the emergence of a pungent gas with an electric smell. In greek, he called it ozone. The first ozone generator was developed by Werner Von Siemens in Germany in 1857. The first report of ozone being used therapeutically to purify blood by C Lender in Germany in 1870.[3,4]

In 1932, ozonated water was used as a disinfectant by EA Fisch, a Swiss dentist. J. Hansler developed one of the first model of medical ozone generators. A. Wolff successfully treated putrescent wounds, suppurating bone fractures, fulminating inflammations and abscesses during the First World War, published his results in 1915. Erwin Payr, who presented his epoch-making publication, entitled "Ozone Treatment in Surgery" at the 59th Meeting of the German Surgical Society in 1935. This can be called the real beginning of ozone therapy.[5,6]

Following in his research the great number of publications by Payr and Aubourg, it was H. Wolff who subsequently introduced extracorporeal blood treatment into medical practice. Werkmeister developed local treatment methods in the form of "subatmospheric ozone gas application", Rokitansky presented the first comprehensive studies on the topical and systemic treatment of diabetic gangrene. Knoch then introduced rectal ozone insufflation into proctology. This is particularly applied in the case of rheumatism / arthritis and inflammatory diseases of the joints, for which Fahmy has developed a wide therapeutical concept. [7,8,9]

Biologic actions of ozone

There are several actions of ozone on human body, such as [10,11,12]

Antimicrobial 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. [10] Being a very strong oxidant it joins with biomolecules containing cysterine, cysteine, methionine, histidine all being part of bacterial cell membranes. Among cariogenic bacteria Streptococcus mutans and Streptococcus sobrinus are the most sensitive. Ozone easily acts on multi unsaturated fatty acids which occur in virus sheaths. Ozone reacts also with ascorbinians and tocopherols. [13]

Immunostimulating Effect- Ozone influences cellular and humoral immune system. It stimulates proliferation of immunocompetent cells and synthesis of immunoglobulins.[10,14] Ozone causes the synthesis of biologically active substances such as interleukins, leukotrienes and prostaglandins which is beneficial in reducing inflammation and wound healing.[10] Ozone in high concentration causes immunodepressive effect whereas in its low concentration immunostimulating effect. [13]

Antihypoxic effect- Ozone brings about the rise of pO2 in tissues and improves transportation of oxygen in blood, which results in change of cellular metabolism – activation of aerobic processes and use of energetic resources.[10] This in consequence reduces blood cell rolling and enables blood flow in capillary vessels. By increasing the concentration of 2,3 Diphosphoglycerate (2,3-DPG), ozone changes the configuration of erythrocytes, which enables them to return oxygen in the inflamed tissue. [13]

Biosynthetic Effect- It activates mechanisms of protein synthesis, increases amount of ribosomes and mitochondria in cells. These changes on the cellular level explain elevation of functional activity and regeneration potential of tissues and organs. [10]

Ozone causes secretion of vasodilators such as NO, which is responsible for dilatation of arterioles and venules. [10] It also activates angiogenesis. [13] Ozone, when acting on the organic substance of mineralized tooth tissues intensifies their remineralization potential. At the same time, it is capable of "opening" dentinal tubules, which enables the diffusion of calcium and phosphorus ions to the deeper layers of carious cavities. [15] A high concentration of ozone kills bacteria very quickly and is thousand times more powerful than other bacterial killing agents. Evidence-based research has shown that at this concentration, ozone effectively kills bacteria, fungi, viruses and parasites. [16] As an antimicrobial agent, it is a powerful oxidizer at a dramatically lower concentration than chlorine with none of the toxic side effects. One molecule of ozone is equal to between 3,000 to 10,000 molecules of chlorine and it kills pathogenic organisms 3,500 times faster. [16] Studies have revealed that it only takes 10 sec to kill 99 % of bacteria, fungi and viruses. [17] It can oxidize many organic compounds and it is a powerful germicide. [18] Some of the other effects are circulatory enhancement, disruption of tumor metabolism and stimulation of oxygen metabolism. [19,20]

APPLICATIONS IN PERIODONTAL THERAPY

Gingivitis and periodontitis are characterized by a local hypoxia of tissues and also by various microbic florae that may contain over 500 species. Accumulations of bacterial plaque in the gingival crevice area in an increased amount causes changes in the oral cavity ecology leading to both gingivitis and periodontitis. Dental biofilm makes it difficult for antibiotics in targeting putative periodontal pathogens. Higher concentrations of antibiotics are required to kill these organisms which are inevitably associated with toxic adverse effect on the host microbial flora. The application of ozone therapy in periodontics showed promising results. Both gaseous and aqueous ozone are used as a substitute to mechanical debridement. Ozone can be used to help treat periodontal disease by using ozonated water flushed below

the gum line and/or ozone gas infiltrated into the gum tissue and supporting tissues. Ozonated water (4mg/l) strongly inhibited the formation of dental plaque and reduced the number of sub gingival pathogens both gram positive and gram negative organisms.

The main use of ozone in dentistry is relays on its antimicrobial properties. It is proved to be effective against both Gram positive and Gram negative bacteria, viruses and fungi. [21]

It has been reported by many authors and supported that ozone has an antimicrobicidal effect. Ozone may be effective as it is known to kill microorganisms by rupturing their cell walls and cytoplasmic membranes. This involves chemical modification and fragmentation of mono unsaturated and poly- unsaturated fatty acids in the cell wall. When the membrane is damaged, its permeability increases and ozone molecules can readily enter the cells. [22,23]It is known that specific bacteria are implicated as causative factors that can lead to the development of periodontitis and that oral microbial plaque consists of different types of bacteria that live on host surfaces. Current treatment of periodontitis is based on disinfecting the supragingival and subgingival tissues in order to re-establish a microorganism-free environment. This fact renders ozone application reasonable and justifiable treatment option. It has been shown in-vitro that ozone is bactericidal against periodontopathic microorganisms [19]. Ozone nano-bubble water has been also studied and shown to have potential as an adjunct to periodontal treatment. [20]Ozone has been reported to accelerate the healing of soft tissue conditions, i.e. aphthous ulcers, herpes labialis, Acute necrotizing ulcerative gingivitis (ANUG) and other gum infections.

Ozone may be considered as an adjunctive to conventional treatment strategy due to its powerful ability to inactivate microorganisms. Ebensberger et al [24] 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. 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.

Nagayoshi et al [22] examined the effect of ozonated water on oral microorganisms and dental plaque. They confirm that ozonated water was highly effective in killing of both gram positive and gram negative micro-organisms. Depending on the dosage, the oral microbes were inactivated after 10 seconds. Gram negative anaerobes, such as Porphyromonas endodontalis and Porphyromonas gingivalis were substantially more sensitive to ozonated water than gram positive oral streptococci and Candida 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.

Ramzy et al [25] irrigated the periodontal pockets by ozonized water in 22 patients suffering from aggressive periodontitis (age range from 13 to 25 years). High significant improvement regarding pocket depth, plaque index, gingival index and bacterial count was recorded related to quadrants treated by scaling and root planning together with ozone application. They also reported significant reduction in bacterial count in sites treated with ozonized water.

Huth et al in a study declared that the aqueous form of ozone, as a potential antiseptic agent, showed less cytotoxicity than gaseous ozone or established antimicrobials (chlorhexidine digluconate CHX 2%, 0.2%; sodium hypochlorite-NaOCl 5.25%, 2.25%; hydrogen peroxide-H2O2 3%) under most conditions. Therefore, aqueous ozone fulfils optimal cell biological characteristics in terms of biocompatibility for oral application. [26]

Huth et al examined the effect of ozone on the influence on the host immune response. These researchers chose the NF-kappaB system, a paradigm for inflammation-associated signalling/transcription. The Huth 2007 study establishes a condition under which aqueous ozone exerts inhibitory effects on the NF-kappaB system, suggesting that it has an anti-inflammatory capacity.[27] Muller et al 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. 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 significantly or completely eliminate bacteria in the biofilm.[28]

Kronusova used ozone in prevention of dental caries in fissures of the first permanent molars in children, application of ozone in prepared cavity, after tooth extraction, in case of postextractional complications, in patients with chronic gingivitis, periodontitis and periodontal abscesses, herpes labialis, purulent periodontitis, dentition difficilis, etc. Almost all patients with gingivitis showed subjective and objective improvement of their status, as well as patients with periodontal abscess, where no exudation was observed. Application of ozone after tooth extraction was found also quite useful – only 10 % of patients suffered from such complication as alveolitis sicca, but even in these cases the clinical course was shorter and more moderate. [29]

The influence of ozonized water on the epithelial wound healing process in the oral cavity was observed by Filippi. [30] It was found that ozonized water applied on the daily basis can accelerate the healing rate in oral mucosa. The comparison with wounds without treatment shows that daily treatment with ozonized water accelerates the physiological healing rate.

Kshitish and Laxman conducted a randomized, double-blind, crossover split-mouth study on 16 patients suffering from generalized chronic periodontitis. By using O3 and chlorhexidine, there was no antibacterial effect on Porphyromonas gingivalis (Pg) and Tannerella forsythensis. The antifungal effect of ozone from baseline (37%) to 7th day (12.5%) was pronounced during the study period, unlike CHX, which did not demonstrate any antifungal effect. No antiviral property of ozone was observed. The antiviral 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. [31]

While testing the efficacy of ozone therapy on oral micorganisms, it was found that gram negative anaerobes like Porphyromonas endodontalis and Porphyromonas gingivalis were more sensitive to ozonated water than gram positive oral streptococci and Candida albicans.[22]However, in another study that compared ozone therapy (both aqueous and gaseous) and chlorhexidine, it was found that none of the agents were able to substantially reduce the A. actinomycetemcomitans count on biofilm cultures.[26]

The use of ozonized solutions for complex treatment of inflammatory diseases of paradontium was studied by Sorokina and Zaslavskaja, 1997.[32] Ozone was found to have a potent antibacterial effect explained by the fact that it causes disruption of the envelope integrity through peroxidation of phospholipeds (Unsal et al., 1995 and Agapov et al., 2001).[33] Agapov et al., (2001) also explained that ozone can cause stimulation of body's own defenses. [34]

Ozone was found to considerably inactivate microorganisms causing periodontitis and antifungal effect was observed when compared to chlorhexidine, but did not show any antiviral effect. [24,31] The study of effect of ozonated water on proliferation of cells in periodontal ligament has resulted in the decontamination of root surface, without negative effect on the remaining periodontal cells on root surface [31]. And also there is reduction in the plaque index, gingival index and bleeding index by using ozone irrigation when compared to chlorhexidine [24].

Thanomsub et al. 2002 tested the effects of ozone treatment on cell growth and ultrastructural changes in bacteria (Escherichia coli, Salmonella sp., Staphylococcus aureus and Bacillus subtilis). Destroying of bacterial cell membrane was observed, subsequently producing intercellular leakage and eventually causing cell lysis.[35] 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. [36]

Dodwad et al. in 2011 compared the effect of oral irrigation with ozonated water, 0.2% Chlorhexidine and 10% Povidone iodine in patients with chronic periodontitis. The study concluded that local ozone application can serve as potent atraumatic, antimicrobial agent to treat periodontal disease nonsurgically both for home care and professional practice. It may also serve as good tool during supportive periodontal therapy.[37]

In a study gaseous Ozone showed selective efficacy to reduce adherent bacteria on Titanium and Zirconia without affecting adhesion and proliferation of osteoblastic cells. Porphyromonas gingivalis was eliminated by Ozone from all surfaces with in 24 sec to below the detection limit (99.94%), while Streptococcus sanguis was more resistant and showed the highest reduction on zirconia substrates (90%) [38].

The use of ozone around implants is supported by published research showing that ozone not only effectively sterilizes the surfaces of both the implant and bone, but also switches on the reparative mechanisms allowing tissue regeneration around implant surfaces.[39] According to Matsumura et al [40,41] ozone does not have a major impact on stimulation of gingival cells for osteoblastic activity in the regeneration of the periodontium around implants.

Peri-implantitis

Ozone can play an important role and be used as gas or in aqueous form. An appropriate length of PVC or silicone cap can be cut to cover the abutment fully. It should properly seal the gingival borders around the implant. For the prevention of periimplantitis an adequate and steady plaque control regimen must be ensured. Ozone, a powerful antimicrobial kills the microorganisms causing periimplantitis. In addition ozone shows a positive wound healing effect due to the increase of tissue circulation. Gasiform ozone or ozonized water shows an increased healing compared to wound healing without ozone therapy. (Karapetian VE et al., 2007).[42] A study by Hauser et al. investigated the use of gaseous ozone on bacteria adhering to implant surfaces and showed a selective reducation in bacteria, concluding that gaseous ozone may have a role in treatment of peri-implantitis [43]

Conclusions-

Ozone therapy is quite inexpensive, predictable and conservative. The ozone therapy has been more beneficial than present conventional therapeutic modalities. This state of the art technology allows us to take a minimally invasive and conservative approach to dental treatment. The elucidation of molecular mechanisms of ozone further benefits practical application in dentistry. Treating patients with ozone therapy reduces the treatment time with a great deal of difference and it eliminates the bacterial count more precisely. The treatment is completely painless and increases the patients' acceptability and compliance with minimal adverse effects. Scientific support demonstrated by various studies shows

Ozone therapy as a potential therapy in field of medicine and dentistry. Ozone offers a simple adjunctive therapy for managing periodontal disease alongside convention methods. Further research is indicated.

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