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Review Article

Review of ozone and its role in prosthodontics

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Abstract: Ozone is a triatomic molecule that has been indicated for the treatment of 260 different pathologies in medicine and dentistry. The ozone therapy has been proved to be more beneficial than various presently used conventional therapeutic modalities in dental treatment. It is widely used in dentistry for the last few years due to its unique properties including antimicrobial, immunostimulant, analgesic, antihypnotic and detoxicating effects. Because of its high oxidation potential, is effective against various microorganisms like bacteria, viruses, fungi, and protozoa which are necessary for plaque maintainence. Ozone has been established as a potent denture cleansing agent due to its anti-plaque properties.
Keywords: ozone, immuno stimulant, removable partial denture, denture cleanser, antihypnotic, microbial colonies

INTRODUCTION

Ozone (triatomic oxygen/ trioxygen) is a naturally occurring compound consisting of three oxygen atoms [1]. Ozone is the major contributor in self-cleansing mechanism of earth [2, 3]. Being heavier than air, it falls downwards to earth from high altitudes and combines with any pollutant that it comes in contact with. It is one of the most important gases in the stratosphere due to its ability to filter UV rays. This protective layer can be seen as the blue colored sky [4, 5].

HISTORY

Christian Friedrich Schonbein, a German chemist is considered to be the *father of ozone therapy*. In 1840, when he passed an electric discharge through water, a strange smell was produced, which he called Ozon, derived from the Greek word ozein (odor) [3].

During World War I, ozone gas was used for treating gaseous post-traumatic gangrene, infected wounds, burns and fistulas in German soldiers. Ozone therapy was accepted as an alternative medicine in the U.S.A. from 1880 until 1932. In dentistry, Dr. E.A. Fisch (1889-1966) was the first dentist to use ozonated water in his practice and introduced it to the German surgeon Dr. Erwin Payr (1871-1946) who used it in surgery and reported his results at the 59th Congress of the German Surgical Society in Berlin (1935). Earlier, the use of 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 Hansler, a German physicist joined Hans Wolff, another German physician, to develop the first ***ozone generator*** for medical use. Their design continues to be the basis for medical equipment.

OZONE PRODUCTION

Oxygen molecules in the air combine under the influence of ultraviolet radiation (from the sun) and electrical discharges (lightning) [6]. Intense physical stress on water (such as in areas of waterfalls and ocean waves crashing onto rocks) also results in production of ozone in nature. For medical use, highly specific gazettes known as *Ozone Generators* are used. Medical grade oxygen is made to flow through high voltage tubes with outputs ranging from 4000 V to 14000 V. Three different systems for generating ozone gas are:

Ultraviolet system: It produces low concentrations of ozone. It is used in esthetics, saunas and for air purification.

Corona Discharge system: It produces high concentrations of ozone. It is the *most common* system used in medicine. This system is easy to handle and it has a controlled ozone production rate.

Cold plasma system: used in air and water purification [7-9].
Two widely used ozone units in dentistry are: the heal ozone [10] and ozotop [6].

MECHANISM OF ACTION

Ozone therapy has a wide range of applications in treating various diseases owing to its unique properties including antimicrobial, immunostimulant, analgesic, antihypnotic, detoxicating, bioenergetic and biosynthetic actions.

Anti-microbial effects

Effect on bacteria, virus, fungus, protozoa

Bacteria

Ozone acts on bacterial cell membranes, by oxidation of their lipid and lipoprotein components. There is evidence for interaction with proteins as well [11, 12]. It renders the spores defective in germination, perhaps because of damage to the spore's inner membrane [13] Ozone at low concentration of 0.1 ppm, is sufficient to inactivate bacterial cells including their spores.

Virus

All viruses are susceptible to ozone; yet differ widely in their susceptibility.[14] Lipid-enveloped viruses are especially sensitive to ozone [15,16]. Analysis of viral components showed damage to polypeptide chains and envelope proteins impairing viral attachment capability, and breakage of viral RNA [14].

Fungal and protozoa

Ozone inhibits cell growth at certain stages, budding cells being the most sensitive [17].

Stimulation of Oxygen Metabolism

Ozone therapy causes an increase in the red blood cell glycolysis rate. This leads to the stimulation of 2,3-diphosphoglycerate leading to an increase in the amount of oxygen released to the tissues. Ozone activates the Krebs cycle by enhancing oxidative carboxylation of pyruvate, stimulating production of ATP. It also causes a significant reduction in NADH and helps to oxidize cytochrome C. There is stimulation of production of enzymes which act as free radical scavengers and cell-wall protectors: glutathione peroxidase, catalase and superoxide dismutase and prostacyclin (vasodilator) [18].

Effect on leukocytes

Ozone behaves as a weak cytokine such as tumor necrosis factor-α (TNF-α), interleukin-2, interleukin-6, interleukin-8, transforming growth factor-β [TGF-β]) inducer [19-22]. Ozone reacts with the unsaturated fatty acids of the lipid layer in cellular membranes, forming hydrogen peroxides (H_2O_2), one of the most significant cytokine inducers [23].

Platelets

H_2O_2 generated by blood ozonation activate phospholipase C, phospholipase A2, cyclo-oxygenases and lipoxygenases, and thromboxane synthetase, allowing a step increase of intracellular calcium, release of prostaglandin E2, prostaglandin F2a, and thromboxane A2 with irreversible platelet aggregation [24-26].

Activation of immune system

Ozone administered at a concentration of between 30 and 55 lg/cc causes the greatest increase in the production of interferon and the greatest output of tumor necrosis factor and interleukin-2 that launches an entire cascade of subsequent immunological reactions.[27]

Mechanism of action of O_3 on the human lungs

Ozone exposure induces a significant mean reduction in vital capacity. It significantly increases mean airway resistance and specific airway resistance but does not change dynamic or static pulmonary compliance or viscous or elastic work. It also significantly reduces maximal transpulmonary pressure. And further more significantly increases respiratory rate and decreases tidal volume [27].

USES OF OZONE IN PROSTHODONTICS

Ozone is widely used in dentistry for the last few years due to its unique properties including antimicrobial, immunostimulant, analgesic, antihypnotic and detoxicating effects. Ozone has high oxidizing potential which acts on microorganisms to inhibit or kill their growth, necessary for plaque maintainence. Ozone is used in dentistry in gaseous, ozonated water and as ozonated oils. Ozone was shown to be biocompatible and is used in all aspects of dentistry. It has been shown to stimulate remineralization of recent caries-affected teeth and is used as a preventive therapy in caries, root caries, and intracanal irrigants in endodontic treatment. It has been used in treatment of alveolitis, avascular osteonecrosis of the jaw, and herpes virus infection. It also inhibits plaque formation and can be used as an adjuvant in periodontal surgical and maintenance phase. Ozone has also been used in dental unit water line to disinfect water. Advantage of ozone therapy is it is an atraumatic, biologically based treatment. While laboratory studies suggest a promising potential of ozone in dentistry, less number of clinical studies were documented.

Removable partial dentures should be designed primarily to preserve the retaining teeth (De Van, 1952). However, similar to many restorative procedures which encroach upon the periodontal tissues (Review—Leon, 1977), partial dentures may have a deleterious effect upon the very structures they are designed to preserve (Carlsson, Hedgegard & Koivuman, 1965;

Rantanen *et al.*, 1971). Thus plaque control by the patient has been stated to be a major factor in determining the long term effects of partial dentures on the periodontal tissues.

Stomatitis-inducing denture plaque had a complex, mainly Gram-positive, bacterial flora similar to that found in cases of healthy mucosa except for the proportions of various Gram-positive rods and Gram-negative cocci. In stomatitis, *Actinomyces* species made up a smaller proportion than in healthy. The proportions of *Lactobacillus, Propionibacterium,* and *Araclinia* species were higher in stomatitis. *Propionibacterium* species were part of the predominant flora. Dental plaque is developed by microbial adherence, aggregation and growth in the absence of adequate denture hygiene. The nutrients for growth are derived from saliva, oral mucosa, and diet. Food retention under dentures and sugar consumption causes low plaque pH values for extended periods [28, 29]. The high proportions of lactobacilli and *S. mutans* in some samples probably reflect such high-sugar, low-pH conditions [30]. Frequent sugar intake is favorable for yeast colonization and pathogenicity,[31] and in fact denture-induced stomatitis has been found to be initiated and aggravated by sucrose rinses [32]. In spite of the lack of correlation between stomatitis and yeast quantities in some studies,[33,34] yeasts must, still be considered important opportunistic pathogens in denture- induced stomatitis [35-40]. In *Candida albicans* and to less extent in other yeast species, several virulence factors have been dernonstrated in *vitro,* notably phospholipase[41], and acidic proteinases capable of degrading keratin [42, 43], collagen[44], serum albumin[45], saliva proteins[46], immunoglobulins Gl, Al and A2, and alpha- 2-macroglobulin [47, 48] C. *albicans* produces large quantities of acetic and pyruvic acid. Yeasts adhere well to denture base materials [49, 50] *in vitro,* although adherence varies with strain and environmental conditions, being promoted by sugars [50, 51].

Denture stomatitis is routinely encountered in clinical practice which is a manifestation of plaque accumulation on the surface of the denture and hence effective denture plaque control should be initiated to prevent such outcomes. One successful method to do so is the use of ozone as denture cleaner.

Ozonated water is a powerful antimicrobial agent against bacteria, fungi, protozoa, and viruses. ozone, in the gaseous or aqueous phase, can kill bacteria, fungi, and viruses [52,53]. The efficacy of disinfectants is usually evaluated on the basis of a decrease in cultivable microorganisms, as tested in this study [54]. Ozonated water (0.5–4 mg/l) was highly effective in killing both gram positive and gram-negative oral microorganisms. Among them, the gram-negative bacteria, such as the endodontopathic bacterium P. endodontalis and the periodontopathic bacterium P. gingivalis, were substantially more sensitive to ozonated water than the gram-positive oral streptococci and C. albicans in pure culture (that ozonated water might be especially useful for killing oral infectious microorganisms [55]. The advantages of ozone in the aqueous phase are its potency, ease of handling, lack of mutagenicity, rapid microbicidal effects, and suitability for use as a soaking solution for medical and dental instruments [56]. Scanning electron microscopic analysis revealed absence of viable C. albicans cells remained on resin plates treated with flowing ozonated water or after immersion in ozonated water with ultra-sonication. C. albicans is detached from the resin plate through functional and structural disorders in the cytoplasmic membranes. Neo Ozone Water-S apparatus is able to supply a large enough dose of ozonated water in a continual flow and should be useful for cleaning and disinfecting C. albicans adhering denture plates. Nagayoshi et al. tested the efficacy of ozonated water on survival and permeability of oral micro-organisms and dental plaque found that ozonated water had a rapid antimicrobial effect on oral microorganisms in pure culture, and that an ozone concentration of 2–4 mg/l was needed to kill the cells. The results of this study showed that there were no significant differences in microbicidal activity between ozonated water and povidone iodine in pure cultures of S. mutans and C. albicans. He also found that ozonated water with antiplaque activity might be effective as a disinfectant solution for dental instruments and removable dentures. Through functional and structural disorder in the cytoplasmic membrane. Although rapid degradation is one of the major environmental advantages of ozonated water, this also produces a rapid decrease in microbicidal activity [57] Addy & Wright [58] compared the antimicrobial activities of two antiseptic mouthwashes, 1% povidone iodine and 0.2% chlorhexidine gluconate, and suggested that the lack of prolonged action of povidone iodine in the oral cavity may be related to its reported lack of antiplaque activity.

Membrane permeability is a key element to cell viability, and the changes in permeability involve the loss of several vital processes linked to the cytoplasmic membrane [59, 60]. It is generally accepted that oxidation due to ozone induces the destruction of cell walls and cytoplasmic membranes of microorganisms, and that differences in the sensitivity to ozonated water are probably due to differences in the structure of the cell walls of microorganisms [61]. After the membrane is damaged by oxidation, the permeability of the membrane increases, and ozone molecules can readily enter the cells [62]. A scanning electron microscopic analysis revealed some holes in the membrane when S. mutans cells were treated with ozonated water. Ozonated water had strong bactericidal activity against bacteria in plaque biofilm. In addition, ozonated water inhibited the accumulation of experimental dental plaque in vitro [63]. The use of

ozone as denture cleaner is effective against methicillin-resistant S. aureus and viruses [68]. There is also some evidence on the effectiveness of aqueous ozone application in adjunct to amino alcohol for decontamination of the implant surfaces.[57] Huth *et al.;* [64] in their 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 [64]. Patients suffering from peri implantitis were investigated by Karapetian *et al.;* [65]. They compared the effectiveness of conventional, surgical and ozone therapy methods to cure peri implantitis. They reported that the main challenge seems to be the decontamination of the implant surface, its surrounding tissue and the prevention of recolonization with periodontal pathogenic bacteria. And the most effective bacterial reduction was recorded in the ozone-treated patient group [66].

WHY OZONE BETTER THAN OTHER???

Ozone can be applied for cleaning the surface of removable partial denture alloys with little impact on the quality of alloy in terms of reflectance, surface roughness, and weight [67]. Direct exposure to gaseous ozone was a more effective microbicide compared with ozonated water. Therefore gaseous ozone can be clinically useful for disinfection of removable prosthesis. (Oizumi M *et al*., 1998) Acid-electrolyzed water also has a powerful sterilizing effect, and it has been used for debriding periodontal pockets and for cleaning several dental appliances. Acid-electrolyzed water caused significant changes not only in the Au-Cu-Ag-Pd alloy, but also in the Au-Ag-Pt alloy after only 1 day. The oxidation of the Au-Cu-Ag-Pd alloy with acid-electrolyzed water was the most significant finding of all the tests. The increase in the weight was probably due to oxides formed by the acid-electrolyzed water treatment, which built up on the surface of the Au-Cu-Ag-Pd alloy. The use of acid-electrolyzed water for intraoral cleaning in a patient with prostheses made of this alloy would eventually because accelerated oxidation. Ozone itself quickly decomposes into oxygen with a half-life of 12 minutes at pH 7. Thus, there is no possibility of significant concentrations of ozone remaining on the denture after cleaning. Cleaning dentures with ozone is safer than cleaning with some denture cleaners or acid-electrolyzed water where there is a possibility of acids or alkalis remaining and being ingested [67].

CONCLUSION

Use of ozone in dentistry has started new era of refinement in various aspects. Due to its multifunctional properties, it has been widely used since recent few years. In some way, it is better than conventional procedures, treating patients with ozone therapy lessens the treatment time with an immense deal of variation and it eradicates the bacterial count more specifically but on other hand, more interventional studies should be conducted safe and well defined parameters to determine the precise indications and guidelines for routine use of ozone in the treatment of various dental pathologies. More number of randomized, controlled trials needs to be conducted to determine the precise indications and guidelines to treat various dental pathologies with this promising medical agent.

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