

Ozone Therapy- Boon to Dentistry and Medicine

Abstract

Ozone therapy has successfully being used in the medical field for treatment of various diseases for more than 100 years. The versatility of ozone therapy, its unique properties, noninvasive nature, absence of side effects or adverse reactions were responsible for its wide spread use. 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. Advantage of ozone therapy is that 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. 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. This review of literature is an attempt to summarize its therapeutic potential in dentistry and its possible clinical application in future.

Key Words

Ozone; ozone therapy; application in dentistry; contraindications of ozone

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INTRODUCTION

The word ozone originates from the Greek word ozein, which means odor and was first used by German chemist Christian Friedrich Schonbein, father of ozone therapy in 1840. Ozone is a natural gaseous molecule made up of three oxygen atoms. Ozone therapy can be defined as a versatile bio-oxidative therapy in which oxygen/ozone is administered via gas or dissolved in water or oil base to obtain therapeutic benefits.^[1,2] Introduction of oxygen/ozone therapy has truly revolutionized dentistry. This newer concept addresses the multifactorial infective states within the oral cavity in an effective, safe, non-toxic manner. In the last decade a number of therapeutic protocols have been developed to address common dental infections associated with periodontal disease, root canal therapy and caries. This article discusses the concepts & implementation of oxygen/ozone therapy in dentistry. The first application of ozone in medical field seems to have been for treating gaseous, post-traumatic gangrene in German soldiers during the 1st world war.^[3] However a big

step forward was the invention of a reliable ozoniser for medical use by the physicist Joachim Hansler (1908-1981). The idea to use ozone in medicine developed slowly during the last century and it was stimulated by the lack of antibiotics and the disinfectant properties of ozone. Ozone, which is used for medical purposes, is a gas mixture comprised of 95 to 99.95% oxygen and 0.05 to 5% pure ozone. Due to proven therapeutic advantages of ozone, many fields in dentistry could benefit from ozone therapy. The first dentist who used ozone was Edward Fisch in 1950 for treating Austrian surgeon Ernst Payr for a gangrenous pulpitis and thereby inspired him to begin a line of investigations dedicated to ozone use in health care.^[4]

OZONE GENERATION

The first ozone generator for medical use was developed by German physicians named Joachim Hansler and Hans Wolff. Their design continues to be the basis for modern equipment. Medical grade ozone is a mixture of pure oxygen and pure ozone in the ratio of 0.05% to 5% of O₃ and 95% to

99.95% of O₂. Due to the instability of the O₃ molecule, medical grade ozone must be prepared immediately before use. After preparation with in less than an hour, only half of the mixture is still ozone while the other half is transformed into oxygen. As a result, it is impossible to store ozone over long periods of time. In order to control the decomposition of O₃ into oxygen it can be associated with a vehicle with aqueous properties to promote the conversion more quickly or with a vehicle with more viscous properties to retard the conversion.^[4] There are 3 different systems of generating Ozone gas.^[5,6]

1. Ultra violet system produces low concentrations of Ozone used in esthetics, saunas, air purification.
2. Cold plasma system used in air and water purification.
3. Corona discharge system produces high concentration of Ozone.

4. 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. Commercially available ozone generator: Cur Ozone USA Inc. (Ontario, Canada) developed the Heal Ozone, which is now distributed by KaVo Dental (KaVo, Biberach, Germany), for use in dentistry.^[4]



Fig. 1: Ozonytron X

MODES OF OZONE ADMINISTRATION

The route of Ozone administration is topical or loco regional in gaseous or aqueous form or as Ozonated olive or sunflower oil. Irrigation is utilized for stomatitis, herpetic lesions and periodontal infections. Insufflation is used for decay, periodontal infections and endodontic treatment.^[7,8]

The European Cooperation of Medical Ozone Societies warns from direct intravenous injections of ozone/oxygen gas that should not be practiced due to the possible risk of air embolism.^[9]

OZONE GAS APPLICATION

Ozone generating equipment converts oxygen to ozone. The ozone is thereafter led to a hand piece

fitted with a silicone cup. Differently shaped silicone cups are available that correspond to the form of various teeth and their surfaces. This ensures close contact between the silicone cup and the carious area of the tooth so that the ozone does not escape. The ozone is led through the silicone cup over the tooth for a minimum of 10 secs. The ozone in the silicone cup is collected again and reconverted to oxygen by the apparatus.^[10]

OZONE AQUEOUS SOLUTION

The following properties of ozone are used in this case:^[10]

- Disinfectant and sterilizing effect;
- Hemostatic effect, especially in cases of hemorrhages;
 - Accelerated wound healing, improved oxygen supply and support of metabolic



Fig. 2: Ozone treatment in Periodontitis

OZONE OIL

Ozonated oils are pure plant extracts, through which pure oxygen and ozone are passed. The plant extracts undergo a chemical reaction to form a thick, viscous oil, or in some cases, a petroleum jelly-like product. The final product contains ozonides. This method of external application is harmless.^[10]



Fig. 2: Ozone treatment in Peri-implantitis

MECHANISMS OF ACTION

There are several potential actions of Ozone, which are applied in the clinical practice of dentistry and medicine, such as antimicrobial (bactericidal, viricidal and fungicidal), anti-inflammatory, immunostimulating, antihypoxic and detoxicating,

biosynthetic, (activation of the metabolism of carbohydrates, proteins, lipids) bio energetics, hemostatic etc.^[11]

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.^[12,13] Ozone seems to render the spores defective in germination, perhaps because of damage to the spore's inner membrane.^[14]

Virus

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

Fungal and Protozoa

Ozone inhibits cell growth at certain stages.^[17]

Effect on Blood Cells

Ozone reduces or eliminates clumping of red blood cells and its flexibility is restored, along with oxygen carrying ability. There is a stimulation of the production of glutathione peroxidase, catalase, and superoxide dismutase which act as free radical scavengers.^[18,19]

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. Ozone reacts with the unsaturated fatty acids of the lipid layer in cellular membranes, forming hydrogen peroxides (H₂O₂), one of the most significant cytokine inducers.^[20,21]

Platelets

H₂O₂ generated by blood ozonation activate phospholipase C, phospholipase A₂, cyclo oxygenases and lipooxygenases, and thromboxane synthetase, allowing a step increase of intracellular Ca²⁺, release of prostaglandin E₂, prostaglandin F_{2a}, and thromboxane A₂ with irreversible platelet aggregation.^[22,23]

ADVANTAGES OF TOPICAL OZONE THERAPY

There is always a chance of development of resistance against antibiotic. Pathogens on the other hand, cannot overcome oxidative challenges of ozone. In addition, there is evidence that ozone directly inactivates bacterial toxins, while

antibiotics do not. Indeed, toxins are major contributors to bacterial tissue destruction.^[10]

BIOCOMPATIBILITY OF OZONE

A study investigated cytotoxic effects of gaseous ozone and aqueous ozone on human oral epithelial (BHY) cells and gingival fibroblast (HGF-1) cells compared with established antiseptics chlorhexidine digluconate (CHX) 0.2%; sodium hypochlorite (NaOCl) 5.25%, 2.25%; hydrogen peroxide H₂O₂ 3%. Aqueous ozone revealed the highest level of biocompatibility of the tested antiseptics.^[24] The metabolic activity of L-929 mouse fibroblasts was high when the cells were treated with ozonated water, whereas that of significantly decreased when the cells were treated with 2.5% NaOCl.^[25] Irrigation of the root surface of avulsed teeth did not reveal a negative effect on periodontal ligament cell proliferation. Another study demonstrated that odontoblastic cells exhibited inflammatory responses against bacterial lipopolysaccharides (LPS). Ozonated water improved LPS-induced inflammatory responses.^[26]

CLINICAL APPLICATIONS OF OZONE IN DENTISTRY

With all the evidence of different actions and lack of toxicity Ozone is developed into a new non-invasive tool for the treatment of diseases in medicine and dentistry.

USES IN ORAL MEDICINE

Soft tissue lesions like Herpes, Aphthae, Removable denture ulcers, Cuts, Cheilitis, Candidiasis, Cysts and Traumatic wounds can be treated with either Ozonated water or oils. The disinfectant and healing properties help in the healing of these lesions.^[6] Ozonated oil applied on herpes labialis and mandibular osteomyelitis demonstrated faster healing times than conventional protocols.^[27] Ozone, in these cases, neutralizes herpes virions by direct action, thus inhibiting bactericidal suprainfections, and stimulating the healing of tissues through circulatory prompting. Ozone has been proven to be one of the most powerful oxidants we can use in dentistry.^[10]

USES IN ORAL SURGERY

Ozone was found to accelerate the healing of the wounds.^[28] After a tooth is extracted or any surgical procedure the area is irrigated and insufflated which promotes faster healing without complications. Ozone therapy is found to be beneficial for the treatment of the refractory osteomyelitis in the head and neck in addition to treatment with antibiotic, surgery and hyperbaric oxygen. It also increases the

benefits of surgical and pharmacological treatments causing complete healing of the lesions. A noninvasive surgery with pre and postsurgical cycles of Ozone therapy consisting of eight sessions lasting 3 minutes each besides antibiotics and antifungal therapies has been applied for the treatment of bisphosphonate induced osteonecrosis of jaw.^[29]

USES IN PERIODONTIA

The effect of Ozone water on oral microorganisms and dental plaque were studied. Dental plaque samples are treated with 4 ml of Ozone water for 10 sec and was observed that gram +ve and gram -ve oral microorganisms and *Candida albicans* in pure culture as well as bacteria in plaque biofilm are killed, hence it was used to control oral microorganisms in dental plaque.^[30] 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. 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. And also there is reduction in the plaque index, gingival index and bleeding index by using ozone irrigation when compared to chlorhexidine.^[32] Periodontal disease is a multifactorial disease. The sulci and pockets are irrigated with ozonated water to reduce the initial microbial load and insufflated with Ozone gas. The patients are also given ozonated oil to apply topically to the soft tissue. Silicon tray isolation technique can also be used where Ozone is introduced into the tray which fits the arch through the port of the tray. Excess gas is evacuated by a small evacuator which is attached to the outlet valve.^[6]

USES IN PROSTHODONTICS

Disinfection of dentures is necessary to prevent denture stomatitis. The exposure of dentures to Ozonated water and ultrasonication had antimicrobial activity against *C. albicans*,^[32,33] there was no significant difference in antimicrobial activity against *C. albicans* by using both ozonated water with ultrasonication and commercially available denture cleaners. Gaseous O₃ was proved to be clinically useful for disinfection of dentures.^[32] Reflectance, surface roughness and weight were measured after O₃ exposure of 20 mg/h caused a slight change in the Au-Cu-Ag-Pd alloy in

terms of measured reflectance, but the changes were significantly less than those caused by acid-electrolyzed water & one of the commercial denture cleaners. Methicillin-resistant *Staphylococcus aureus* (MRSA) and *E coli* T1 phage virus bacteria was $3.1 \times 10(3)$ CFU/mL at the beginning of the experiment, fell to $1.0 \times 10(0)$ CFU/mL 10 min later.^[34]

USES IN ENDODONTICS

In endodontic treatment instead of using irrigation chemicals (Naocl), Ozonated water can be used for irrigation. A Japanese study published in 2004 demonstrated the antimicrobial activity of Ozone in root canal treatment without any tissue toxicity. The study also shown that there was high metabolic activity of the associated fibroblasts indicated an increase in the healing process.^{35, 36} Procedure includes, the canals are prepared with files lubricated with ozonated oils and irrigated with ozonated water and dried. Before filling, a slow insufflation 45-60 sec into each canal should be done with concentration of Ozone using about 30 ml.^[6] In a study the aqueous form of Ozone was found to be less cytotoxic than gaseous Ozone.^[6] Ozonated oils like Ozonated sunflower oil, olive oil and ground nut oil was efficient in canal sterilization than the conventional irrigation by the Sodium hypochlorite and Sodium peroxide combination. In a study on permeability of oral microorganisms and dental plaque, both gram +ve and gram -ve bacteria were killed by Ozonated water (0.5-4 mg/l). Gram -ve bacteria such as *Porphyromonas endodontalis* and *Porphyromonas gingivalis* were more sensitive to Ozonated water than gram +ve oral Streptococci and *Candida albicans* in pure culture and Ozonated water was proved to have bactericidal activity against bacteria in plaque biofilm. But it was found that even after 20 minute of contact time of Ozonated water, gaseous Ozone and antiseptic agents did not have antibacterial effect on *Enterococcus Faecalis*.^[35] Single visit treatment of infected root canals with and without ozonotherapy has resulted in complete remission of periapical lesions.^[36]

OZONE THERAPY AND DENTAL CARIES

The application of Ozone therapy in the treatment of dental caries is extensively studied and many studies have proved its effectiveness in the treatment of pit and fissure caries, root caries and interproximal caries. Ozone is delivered through a hand piece, which is equipped with a silicon cup. The cup is applied directly to the tooth so that it

forms a tight seal at the application site. The mechanism of action is due to its microbiological properties and its ability to oxidize the bacterial cell wall.^[11,37] Pyruvic acid, that is produced by bacteria and implicated in the progression of caries, is oxidized by Ozone to acetate and carbon dioxide. This treatment is an alternative therapy to conventional drilling and filling for non cavitated deciduous carious lesion. The infusion of Ozone into non-carious dentin prevented biofilm formation in vitro from *S. mutans* and *Lactobacillus acidophilus* over a 4 week period.^[38] Some studies have demonstrated that 40 s application of Ozone is sufficient to kill different concentrations of *S. mutans* and application of 60 s has almost completely eliminated *S. mutans*, *L. casei* and *A. naeslundii*.^[39] Ozone is also found to be effective against the microflora associated with primary root caries lesions. In a study the aqueous form of Ozone was found to be less cytotoxic than gaseous Ozone.^[40] But it is reported to have a minimal effect on the viability of different bacterial species organized in a cariogenic biofilm. According to some studies the application of Ozone gas to non-cavitated carious lesions does not significantly reduce the number of viable bacteria in the underlying infected dentin. But it provided strong evidence that the mechanism by which Ozone application might be effective is not mediated by direct killing of bacteria in infected dentin.^[41] Ozone treatment either alone or combined with a remineralizing solution was found to be effective for remineralization of initial fissure caries lesions.^[42,43] But randomized double blind standardized clinical studies are still required to establish Ozone therapy in the treatment of dental caries. But it can be used in conjunction to the conventional treatment modalities.

OZONE AND DENTAL UNIT WATER LINES

Dental unit water line (DUWL) contamination has become a concern.^[44,45] Water becomes stagnant when the units are not in use. Detachment of microorganisms, splatter, and aerosols from dental procedures may possibly infect health care personnel.^[45] Szymanska identified moulds, bacteria, and yeasts in biofilms which are hazardous to the health care worker and other patients during treatment.^[46] Opportunistic pathogens were cultured from the mains water. Another study suggested that DUWL biocides may adversely affect adhesion of resin to enamel.^[47] Ozone has been used for purification of water due to its efficiency and lack

of side effects. Kohno *et al.*, published their results that indicated acidic electrolyzed water could be applied as an appropriate measure against bacterial contamination of the DUWL.^[48] In model dental unit water lines, ozone achieved a 57% reduction in biofilm and a 65% reduction in viable bacteria in spite of being used in a very low dose and with a short time of application.^[49]

USES IN IMPLANTOLOGY

The use of ozone in implantology helps in bone regeneration. The socket is prepared conventionally and the ozone is bubbled into the prepared socket for about 40 sec. This is followed by placement of implant into the socket. This prevents infection and enhances bone regeneration. Also in cases of peri-implantitis the studies have shown promising reports of regeneration and eliminate infection around the implant.^[50]

CONTRAINDICATIONS FOR OZONE THERAPY

Ozone therapy is still being ignored by most of medical establishment because of facts that gaseous ozone is quite toxic and has strong oxidative properties. Along with the specified uses of ozone there are certain conditions where ozone therapy is contraindicated namely.^[51]

- Pregnancy
- Glucose 6 phosphate dehydrogenase deficiency
- Hyperthyroidism
- Severe anemia
- Severe myasthenia
- Ozone allergy
- Recent myocardial infarction
- Hemorrhage from any organ
- Acute alcohol intoxication.

OZONE TOXICITY

Overwhelming evidence shows that the bronchial-pulmonary system is very sensitive to ozone and this gas should never be inhaled. 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 O₂/O₃, an application prohibited by the European Society of Ozone therapy since 1983. Known side effects are epiphora and upper respiratory irritation, rhinitis, cough, headache, occasional nausea, and vomiting.^[10]

CONCLUSION

The use of ozone has opened new vistas in treatment modalities. Now, one can focus on the site

of infection rather than the whole body. Also most people suffer anxieties about being treated for tooth decay or more precisely; they fear the injections and drills. But, now, with ozone treatment this is all the thing of past. Studies have shown that 99 percent of all the bacteria causing tooth decay have been eliminated after 10 secs of ozone exposure and even 99.9 percent bacteria after 20 secs exposure. Thus, treating patients with ozone cuts off the treatment time with a great deal of difference, eliminates the bacterial count more precisely, and moreover, it is completely painless, so increasing the patients' acceptability and compliance. Ozone, definitely, seems to be a promising treatment modality for various dental problems in future. On the other hand we have to keep in mind that presently ozone is an adjunct to other conventional treatment modalities and should be used in combination until more research shows its benefits in independent usage.

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