

# Current interpretations and scientific rationale of the ozone usage in dentistry: A systematic review of literature

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## ABSTRACT

In the era of antibiotic resistance, a naturally occurring substance is needed to completely cure the infection without any toxic side-effects; a responsibility that “O<sub>3</sub> or Ozone” seems to implement sincerely. Ozone gas has a high-oxidation potential and has the capacity to stimulate blood circulation and the immune response. It is a great supplement to conventional therapeutic dental modalities. Treatment may be achieved by increasing the resistance of the tooth against the microbial activity and reducing the extent of microbial activity. In addition to the recent materials and techniques, the therapeutic actions of ozone may provide beneficial results by reducing the demineralization of the tooth. Its bactericide, virucide and fungicide effects are based on its strong oxidation effect with the formation of free radicals as well as its direct destruction of almost all microorganisms. This potentially beneficial agent has been used in dentistry also. Ozone has a wide application in dentistry which includes treatment of carious lesions, root canal disinfection, wound healing impairments after surgical interventions, plaque control, disinfection of dentures, etc., The purpose of this article is to summarize the mechanism of action and different modalities of ozone therapy in the practice of dentistry.

## Key words

Heal Ozone, oral microorganism, ozone

## INTRODUCTION

The word ozone was first introduced by Schonbein in 1840. He subjected oxygen to electrical discharges and noted “the odor of electrical matter.” Schonbein concluded that the odor was due to a gas which he named ozone, from the Greek Ozein. Ozone is a gas composed of three atoms of oxygen and presented naturally in the upper layer of the atmosphere in abundance. Ozone protects living organisms by surrounding the earth at altitudes of 50,000–100,000 feet.<sup>[1]</sup> It is a blue gas, with a strong odor and absorbs the harmful ultraviolet rays present in the light spectrum from the sun and protects the living creatures from the ultraviolet rays.<sup>[2]</sup> It has got a high-oxidation potential which is 1.5 times greater

than chloride when used as an anti-microbial agent. It also stimulates blood circulation, and the immune response.<sup>[3]</sup> Medical ozone is a mixture of the purest oxygen and purest ozone. According to its application, the ozone concentration may vary between 1 and 100 µg/ml (0.05-5%). The ozone therapist determines the complete dosage according to the medical/dental indication and the patient’s condition.<sup>[4]</sup> It has been used in the medical field since long due to its extremely strong oxidant property that oxidizes nearly all surfaces to the highest oxidation stage.<sup>[5]</sup> Ozone is a gas, so it penetrates very well even into such tissues and spaces that are not easily accessible. It is used as a circulatory enhancement and stimulation of oxygen metabolism, disruption of tumor metabolism and to kill pathogens.<sup>[3]</sup> Introduction of ozone therapy has true revolutionized dentistry.<sup>[6]</sup>

Three different systems of generating ozone gas<sup>[2,5,7]</sup>

- Ultraviolet system produces in low concentrations of ozone used in esthetics, saunas, air purification
- Cold plasma system used in air and water purification
- Corona discharge system produces a high concentration of ozone.

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The route of ozone administration is topical or 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. Commercially available ozone generator: CurOzone USA Inc. (Ontario, Canada) developed the HealOzone, which is now distributed by KaVo Dental (KaVo, Biberach, Germany), for use in dentistry.<sup>[8]</sup> Ozone is a powerful oxidant capable of interacting as metabolic and immune modulator, as well as anti-microbial agent. Multiple microbiological and the biochemical studies justified that there are no doubts about the effectiveness of ozone in bacterial reduction. Among other things, ozone is used to purify drinking water and water in dental equipment and for sterilizing instruments for medical use.<sup>[4]</sup>

## METHODS OF LITERATURE SEARCH

In this era of information and technology, a number of internet-based tools are available that can genuinely retrieve biomedical information. Some of the renowned internet-based popular search engines (Google, Yahoo), scholarly search bibliographic databases (PubMed, PubMed Central, Medline Plus, Cochrane, Medknow, Ebsco, Science Direct, Hinari, WebMD, IndMed, Embase), and textbooks were explored until Jan 2014 using MeSH (Medical Subject Headings; PubMed) keywords such as “Ozone,” “Oral microorganism,” “HealOzone,” “Dentistry.” The search was limited to reviews, systematic researches and meta-analyses in differently dental journals published over the past 40 years in English and Spanish. A total of 87 articles were identified, however, after examining the titles and abstracts, this number was finally condensed to 35 articles.

## HISTORICAL BACKGROUND

Christian Friedrich Schönbein, a German Chemist, is regarded as the father of ozone therapy. When he passed an electrical discharge through water, a strange smell was produced, which he called ozone, derived from the Greek word “Ozein” which means odor. In 1857 Joachim Hansler, a German physicist and physician, along with German physician, Hans Wolff, developed the first-ozone generator for medical use. In 1860, Monaco first used it in water treatment plants. Dr. Lender in 1870 purified blood in test tubes by using O<sub>3</sub>. Later, O<sub>3</sub> application gained as a popularity as a therapeutic procedure throughout Europe and America. In 1881, it was used as a disinfectant in the treatment of diphtheria. Dr. Charles Kenworthy, a Florida physician, in 1885, published his experiences with ozone in the Florida Medical Association Journal In October 1893, Ousbaden, Holland became the first city to utilize a water treatment plant using ozone. In World War I and II it was used to treat wounded soldiers in the trenches. In early 20<sup>th</sup> century Food and Drug Act, revised its use and effect in the field of medicine. A German dentist,

Dr. E.A. Fisch, in 1950, used ozonated water for dental procedures and pioneered its use in medicine.<sup>[4]</sup>

## Mechanism of action of ozone

There are several actions of ozone such as anti-microbial, anti-inflammatory, analgesic, immune-stimulating, anti-hypoxic, detoxicating, bio-energetic, and biosynthetic (activation of the metabolism of carbohydrates, proteins and lipids) actions.<sup>[2]</sup> Anti-microbial action: The anti-microbial effect of ozone results from oxidation of microbial cellular components.<sup>[9]</sup> It does not damage healthy human body cells because they have free radical scavengers like superoxide dismutase, catalase, hydrolase and antioxidant nutrients like Vitamin C, E, beta-carotene, selenium, methionine, glutathione which inhibit the uncontrolled activity of free radicals, and thus all healthy cells are protected. Only unhealthy cells such as cancer cells which have lost this protective mechanism and organisms such as bacteria, viruses, fungi, parasites which are devoid of these antioxidants and scavengers are destroyed.<sup>[2]</sup> The ozone oxidant potential induces the destruction of cellular walls and cytoplasmic membranes of bacteria.<sup>[10,11]</sup>

Anti-inflammatory and analgesic action: Ozone helps in the synthesis of biologically active substances such as interleukins, leukotriene's and prostaglandins which is beneficial in reducing inflammation and pain. The infection or inflammation is positively charged (acidic) and ozone is negatively charged (basic) so the chemistry of infection and inflammation attracts ozone to the area.<sup>[12]</sup> Immune-stimulating action: The electromagnetic action of ozone stimulates and modulates immune system particularly lymphocytes producing interleukins. It also activates the function of macrophages and increases sensitivity of microorganisms to phagocytosis.<sup>[13]</sup>

Anti-hypoxic action: Ozone brings about the rise of PO<sub>2</sub> in tissues and improves transportation of oxygen in the blood, which results in a change of cellular metabolism activation of aerobic processes (Glycolysis, Krebs's cycle, B-oxidation of fatty acids) and use of energetic resources. Ozone acts as a super-oxygenator, bringing oxygen to tissues, assisting the body in its natural healing process. Bio-energetic and biosynthetic action: Ozone activates mechanisms of protein synthesis, increases amount of ribosomes and mitochondria in cells, elevating functional activity and regeneration potential of tissues and organs.<sup>[14]</sup> Ozone act by killing bacteria at the carious lesion and oxidizing organic material within the carious dentin. Ozone in the gaseous or aqueous phase has been shown to be a powerful and reliable anti-microbial agent against bacteria, fungi, protozoa and viruses. It is generally accepted that the oxidant potential of ozone induces the destruction of cell walls and cytoplasmic membranes of bacteria and fungi. During this process, ozone attacks the glycoproteins, glycolipids and other amino acids and inhibits and blocks the enzymatic

control system of the cell. This results in an increase in membrane permeability, the key element of cell viability, leading to immediate functional cessation. Then ozone molecules can readily enter the cell and destroy the microorganism.

Ozone can attack many biomolecules, such as the cysteine, methionine and histidine residues of proteins. By oxidizing the biomolecules featured in the dental tissues, ozone has severely disruptive effect on cariogenic bacteria, resulting in the elimination of acidogenic bacteria. The strongest naturally occurring acid produced by acidogenic bacteria during cariogenesis is pyruvic acid. Ozone can decarboxylate this acid to acetic acid. It has been shown that remineralization of incipient carious lesions can be encouraged when the production of acetic acid or other high-pKa acids found in resting plaque, buffers plaque fluid.<sup>[14]</sup> Ozone therapy appears to be a safe, economical, effective treatment for patients with cardiovascular disorders based on biological responses that improve blood circulation and oxygen delivery to ischemic tissue owing to the concerted effect of NO and CO and an increase of intraerythrocytic 2,3-diphosphoglycerate level. By improving oxygen delivery, it enhances the general metabolism. It up-regulates the cellular antioxidant enzymes and induces HO-1 and HSP-70 and induces a mild activation of the immune system and enhances the release of growth factors from platelets. It also procures a surprising wellness in most of the patients, probably by stimulating the neuro-endocrine system.<sup>[15]</sup>

### Indications

- Arterial circulatory disorders
- Immunodeficiency and Immune dysbalance - Additive therapy in carcinoma patients diseases caused by viruses (e.g.,: Hepatitis)
- Inflammatory conditions
- Rheumatic diseases
- External ulcers and skin lesion
- External ulcers and skin lesions
- Dentistry.

Ozone is also used in the pharmaceutical industry, food processing industry, fabrics and cosmetics.<sup>[16]</sup>

### Clinical applications of ozone in dentistry

With all the evidence of different actions and lack of toxicity ozone is developed into a new noninvasive tool for the treatment of diseases in medicine and dentistry.<sup>[17]</sup>

## TREATMENT OF 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. Pyruvic acid, that is produced by bacteria and implicated in the progression of caries, is oxidized by ozone to acetate and carbon-di-oxide. This treatment is an alternative therapy to conventional drilling and filling for noncavitated deciduous carious lesion. The infusion of ozone into noncarious dentin prevented biofilm formation *in vitro* from *Streptococcus mutans* and *Lactobacillus acidophilus* over a 4 weekS period. 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*, *Lactobacillus casei* and *Actinomyces naeslundii*. Ozone is also found to be effective against the microflora associated with primary root caries lesions. Application of ozone during 40 s, and the use of remineralizing products can arrests the progression of noncavitory root caries.<sup>[16]</sup> It also oxides volatile sulphur compounds precursor methionine to its corresponding sulphoxide and thus prevents malodor associated with root caries. The use of ozone is as simple and effective to treat root caries in medically compromised patients and elderly people.<sup>[18]</sup>

### Role in endodontic

The aim of conventional root canal therapy is to provide a clean, prepared root canal that facilitates the placement of an adequate root filling. There may be multiple canals, frequently linked by a “web” of accessory canals. There is the so-called “apical delta” and the common lateral canals. Until recently, the dental profession relied on irrigants reaching these areas to disinfect and dissolve organic debris where it is impossible to instrument mechanically. In endodontic treatment instead of using irrigation chemicals (NaOCl), ozonated water can be used for irrigation.<sup>[19]</sup> Ozone was found to be effective against endodontic pathogenic microorganisms like *Enterococcus faecalis*, *Candida albicans*, *Peptostreptococcus micros* and *Pseudomonas aeruginosa* disinfecting of root canals and dentinal tubules.<sup>[20]</sup> Ozone also eliminates the distinctive anaerobic odor associated with some chronically infected teeth. Before the final fill of the canals, the files are coated with ozonated olive oil for lubrication and disinfection and the canals are prepared and then irrigated with ozonated water and dried. Before filling, a slow insufflations (45–60 s) into each canal with moderate/high concentration of ozone gas. Insufflation of ozone electrochemically travel into the lateral canals and dentinal tubules killing the microbes. Nagayoshi, Kitamura *et al.* examined the effect of ozonated water against *E. faecalis* and *S. mutans* infections and found a significant reduction in the viability of these organisms invading dentinal tubules. Ozone will also penetrate through the apical foramen

and enter into the surrounding and supportive bone tissue, encouraging healing and regeneration of bone. In root canal treated teeth, crown discoloration is a major esthetic problem, especially in anterior teeth. Teeth whitening can be done using ozone gas due to its strong oxidizing properties. After removing the root canal filler material from the pulp chamber, the canal is sealed tight at the level of cemento-enamel junction. Now a bleaching paste or a cotton pellet moistened in the bleaching solution is packed in the chamber and sealed with glass ionomer cement. Then the crown is irradiated with ozone for minimum of 3-4 min. For bleaching of the entire dentition, tray technique can be used. This ozone treatment bleaches the teeth within minutes. Noncarious hypersensitivity is due to many contributing factors among which attrition, erosion, abfraction, bite pressure, gum recession are common. Smear layer present over the tooth surface prevents the penetration of ionic calcium and fluoride deep into the dentinal tubules. Ozone removes the smear layer, opens up the dentinal tubules, broadens their diameter and allows calcium and fluoride ions flow into tubules easily, deeply and effectively to plug dentinal tubules, preventing the fluid exchange through these tubules. Quick relief from root sensitivity has been documented after ozone spray for 60 s followed by mineral wash on to the exposed dentine in a repetitive manner.<sup>[21]</sup> In a study on permeability of oral microorganisms and dental plaque, both Gram-positive and Gram-negative bacteria killed by ozonated water (0.5–4 mg/L). Ozonated water also have bactericidal activity against bacteria in plaque biofilm.

### Periodontics

Ozonated water (4 mg/L) was found effective for killing Gram-positive and Gram-negative oral microorganisms and oral *C. albicans* in pure culture as well as bacteria in plaque biofilm and useful to control oral infectious microorganisms in dental plaque.<sup>[15,22]</sup> Ozonated water can be used in the ultrasonic water reservoir, also as a pretreatment rinse before scaling and root planning and pockets are irrigated using syringe and canula in nonsurgical curettage. This process will reduce the initial pathogenic load on the patient locally and systemically. After treatment, each pocket and sulcus is insufflated with ozone gas which directly goes into tissues, sterilizing the area.<sup>[2,23]</sup> 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. Ozone can inactivate microorganisms causing periodontitis and also has an antifungal effect when compared to chlorhexidine, but did not show any antiviral effect. A study of the effect of ozonated water on proliferation of cells in the periodontal ligament has resulted in the decontamination of root surface, without negative effect on the remaining periodontal cells on the root surface. And also there

is a reduction in the plaque index, gingival index and bleeding index by using ozone irrigation when compared to chlorhexidine.<sup>[24]</sup> Healing and bactericidal properties makes it useful as a subgingival irrigant. For the prevention of peri-implantitis, an adequate and steady plaque control regimen must be ensured. Ozone also 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.<sup>[25]</sup> Ozonated oil is used as a safe therapeutic alternative in patients with acute necrotizing ulcerative gingivitis. Healing and bactericidal properties makes it useful as a subgingival irrigant.<sup>[16]</sup> The use of ozone around implants not only effectively sterilizes the surface of both implants and bone, but also initiates the reparative mechanisms allowing tissue regeneration around implant surface.<sup>[26,27]</sup>

### Prosthetic dentistry

A common occurrence found in full denture wearers is denture stomatitis, mainly due to *C. albicans*. This can be controlled by topical application of ozonated oil over the tissue surface and over denture surface. The disinfecting action of ozone is also used to clean denture. Advice patients to soak dentures in ozonated water for at least 10 min after removal and rinse them before inserting into mouth.<sup>[28]</sup> Reflectance, surface roughness and weight, were measured after O<sub>3</sub> 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 and one of the commercial denture cleaners. Methicillin-resistant *Staphylococcus aureus* and *Escherichia coli* T1 phage virus bacteria was 3.1 × 10<sup>3</sup> (3) CFU/mL at the beginning of the experiment, fell to 1.0 × 10<sup>0</sup> (0) CFU/mL 10 min later.<sup>[7]</sup> 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. There is also some evidence on the effectiveness of aqueous ozone application in adjunct to aminoalcohol for decontamination of the implant surfaces.<sup>[29]</sup> Ozone therapy in implantology helps in bone regeneration. The socket is prepared conventionally, and ozone is bubbled into the socket for about 40 s, followed by placement of the implant into the socket. This prevents infection and enhances bone regeneration.<sup>[6]</sup>

### Oral surgery

Ozone was found to accelerate the healing of the wounds. After a tooth is extracted or any surgical procedure, the area is irrigated and insufflated with ozone 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.<sup>[7,30]</sup> Ozone has a positive influence on bone metabolism and reparative process of the bone.



Ozone therapy in the management of bone necrosis or in extraction sites during and after surgery in patients treated with bisphosphonates may stimulate cell proliferation and soft tissue healing.<sup>[31]</sup> In alveolitis, there is accelerated healing by irrigation with ozonated water after removal of the necrotic plug and debris under antibiotic coverage. The use of ozone also eliminates dry alveoli and postextractional pain.

### Oral medicine

Soft tissue lesions such as 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.<sup>[7]</sup>

## DENTAL OZONE GENERATORS; HEAL OZONE<sup>[19]</sup>

The ozone unit for dental use was initially developed by CurOzone Inc. (Canada) and subsequently manufactured under license and distributed by KaVo Dental GmbH and Co. (Germany) under the name "HealOzone." Its use has been pioneered by Professor Lynch *et al.* at Queen's University in Belfast, Northern Ireland, and Barts and the London Queen Mary's School of Medicine and Dentistry in London, UK. It converts oxygen to ozone.<sup>[15]</sup>

## HEALOZONE PROCEDURE

The HealOzone procedure consists of a package which includes: The application of ozone gas, the use of remineralizing agents, a patient kit and information on oral hygiene. The HealOzone device comprises an air filter, vacuum pump, an ozone generator, a handpiece fitted with a sealing silicone cup and a flexible hose. The procedure usually takes between 20 and 120 s per tooth. Immediately after ozone application the tooth surface is treated with a remineralizing solution (reductant) containing fluoride, calcium, zinc, phosphate and xylitol dispensed from a 2-ml ampule.<sup>[32]</sup> Patients are also supplied with a patient kit, which consists of toothpaste, oral rinse and oral spray, all containing fluoride, calcium, zinc, phosphate and xylitol, and aims to enhance the remineralization process. HealOzone application for the treatment of noncavitated lesions is usually repeated at 3 and 6 months.<sup>[33]</sup>

### The OzoTop

The OzoTop is a free-flow ozone delivery system using a corona discharge. It is a compact, easy to use tabletop unit. Due to the delivery system of the OzoTop, root canals and periodontal pockets can be penetrated easily. The system may be used in all cases where point of placement disinfection is needed, including periodontology, endodontology, restorative, implantology, aphthous ulcers/herpes, gerodontology (dentures) and

impression materials. The system utilizes ambient air, which is filtered and dried before passing over a ceramic plate where a high voltage is applied, and ozone is produced. Ozone is applied at 6, 12, 18, 24 s, depending on which treatment is required. High-volume suction is required as this is an open system.<sup>[17,34]</sup>

### Ozone toxicity

Ozone inhalation can be toxic to the pulmonary system and other organs. Complications caused by ozone therapy are infrequent at 0.0007 per application. Known side-effects are upper respiratory irritation, rhinitis, cough, headache, occasional nausea, vomiting, shortness of breath, blood vessel swelling, poor circulation, heart problems and epiphora.<sup>[4]</sup> Prolonged inhalation of ozone can be deleterious to the lungs and other organs but well calibrated doses can be therapeutically used in various conditions without any toxicity or side-effects.<sup>[8]</sup> European cooperation of medical ozone societies prohibited the intravenous injections of ozone gas due to risk of air embolism.<sup>[7,18]</sup>

### Cure for ozone intoxication

The patient must be placed in the supine position. The patient should inhale the humid oxygen and treated with Vitamin E, ascorbic acid and n-acetylcysteines.

### Contradictions<sup>[4]</sup>

1. Pregnancy
2. Glucose-6-phosphate-dehydrogenase deficiency (favism)
3. Hyperthyroidism
4. Severe anemia
5. Severe myasthenia
6. Acute alcohol intoxication
7. Recent myocardial infarction
8. Hemorrhage from any organ
9. Ozone allergy.

## CONCLUSION

Ozone therapy allows a new vision, which complies with needs and demands of the public for noninvasive, effective dental care and it is truly a paradigm shift in dental practice. Ozone therapy has opened new vistas in treatment modalities for dental patients of all ages and applicable to a wide range of conditions of intra oral hard and soft tissues. It is especially suitable to the younger patients who are often scared of "drilling" and find conventional treatment unacceptable. The ozone therapy has been more beneficial than present conventional therapeutic modalities that follow a minimally invasive and conservative application to dental treatment. The elucidation of molecular mechanisms of ozone further benefits practical application in dentistry. It is applicable to a wide range of conditions of the intra-oral hard and soft tissues. The treatment of carious lesions is effective and made much more acceptable for the patient. 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 effect. Scientific support demonstrated by various studies shows ozone therapy as a potential therapy in the field of medicine and dentistry. According to Cochrane database, there is a lack of consistency between different outcome measures and the absence of reliable evidence that the application of ozone gas reverses the decay. Nevertheless *in vivo* randomized and well controlled clinical trials are the requirement of the day to establish it as a standard therapy.

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## Announcement

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