Ozone applications in dentistry: an overview

Junaid Ahmed, Almas Binnal, Bijina Rajan, Ceena Denny, Nandita Shenoy
Department of Oral Medicine and Radiology, Manipal College of Dental Sciences, Mangalore, Karnataka, India

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Corresponding Author
Nandita Shenoy
Department of Oral Medicine and Radiology, Manipal College of Dental Sciences, Mangalore - 575 001, Karnataka, India. nandita.shenoy@gmail.com

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Abstract
Ozone therapy has been successfully used in the medical field for treatment of various diseases, for more than 100 years. Researches have shown the efficacy of both gaseous and dissolved ozone in eradicating a wide range of bacteria, bacterial spores and viruses. Ozone could also help in healing wounds, treatment of radiation-induced mucositis and osteoradionecrosis by increasing the blood supply and through modulation of inflammatory mediators. Despite of these advantages, therapeutic ozone’s application in dentistry is limited because of its possible side effects on upper respiratory system. Dental practitioners need to know the proper usage of modern pharmaceutical methods like ozone, that can provide better patient care and considerably cut down the time and cost of treatment.

INTRODUCTION
Ozone (O₃) is a naturally occurring gaseous molecule made up of three oxygen atoms [1]. The word ozone originates from the Greek word “ozein”, which means odor. At room temperature, ozone is a blue gas with a characteristic smell that could be noticed in air even at concentration of 2 ppm. It was first used by the German chemist, Christian Friedrich Schonbein (1799-1868), in 1840 [2]. Extensive research done in this field has resulted in a wide range of application, both in the industrial and clinical field. Use of ozone was initially limited for industrial purpose, mainly for the disinfection of water. The first reported medical application is the use of ozone for treating gaseous, post-traumatic gangrene in German soldiers during the 1st world war. Ozone has been successfully used in medicine for more than 100 years to now because of its microbiologic properties. It was first used in dentistry by the German dentist Edward A. Fisch, in Zurich, Switzerland for the treatment of infected wound cavities and chronic periodontal disease, in 1933 [3]. Following this, the use of ozone therapy has been advocated in dentistry for the past 6 decades. Studies have examined ozone’s effect on dental caries and primary root caries, periodontitis, disinfection of denture surfaces, wound healing and as an antimicrobial, antiviral, and antifungal agent in the oral cavity [4, 5].

Ozone generators
Medical grade ozone is a mixture of pure oxygen and pure ozone in the ratio of 0.05% to 5% of O₃ with 95% to 99.95% of O₂. Due to the instability of the O₃ molecule, medical grade ozone must be prepared immediately before use. Within less than an hour after preparation, only half of the mixture would remain as ozone while the other half would be transformed into oxygen. As a result, it is impossible to store ozone over long periods of time. O₃ can be associated with a vehicle with aqueous properties to promote the conversion more quickly, while to retard the conversion it can be associated with a vehicle with more viscous properties, thereby providing control [6].

In clinical settings, ozone generators are used to produce ozone from medical oxygen via an electrical field that simulates the natural production of ozone at
the time of lightening. This 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 [7].

Mechanism of action of ozone

Ozone is a thermodynamically highly unstable compound that decomposes to pure oxygen depending on system conditions like temperature and pressure [8]. Ozone is the third most potent oxidant after fluorine and per sulfate and has a half-life of 40 min at 20°C [9]. Potential applications of ozone in the clinical practice of dentistry and medicine is based on the actions such as antimicrobial (bactericidal, viricidal, and fungicidal), anti-inflammatory, immunomodulating, biosynthetic (activation of the metabolism of carbohydrates, proteins, lipids), bioenergetic, antihypoxic, analgesic and hemostatic effects. The main antiviral actions of ozone are the change of the capsid and the irreversible destruction of viral DNA [10]. However, ozone does not have the same strength of action on every germ. For example, enteroviruses [11], rotaviruses [12], hepatitis A [13] and human immunodeficiency viruses [14] are more ozone-sensitive than poliomyelitis and coxsackieviruses. The antibacterial effect of ozone is based on the inhibition of their metabolic activity and the lysis of bacterial cell wall [15, 16]. In bacterial cultures, Escherichia coli and Candida albicans are more ozone-sensitive than Staphylococci.

Research on the use of ozone in combatting bacteria typical for dental diseases has shown that the gas has an oxidizing effect on these bacteria and is bactericidal [17]. Whereas an in vitro study in which evaluation of antibacterial effect of ozone was done after 2 months of disinfection with ozone on Streptococcus mutans and Lactobacillus casei showed that ozone has a significant antibacterial effect against S. mutans but L. casei was found to be more resistant to ozone [18].

The study conducted by Guinesi et al [19] evaluated the presence of ozone as well as by-products of ozonation such as formaldehyde in ozonated oils (sunflower oil, castor oil and almond oil) and propylene glycol. A complete absence of ozone and presence of formaldehyde was observed in all the samples tested suggesting that the healing and antibacterial effect of ozonated oil could be attributed to products formed by ozonation of mineral oils such as formaldehyde and not to the ozone itself.

USES OF OZONE IN DENTISTRY

Ozone has a wide range of application in dentistry. Ozone has been applied for treatment of early carious lesions, sterilization of cavities, desensitization of extremely sensitive teeth, root canals, periodontal pockets, enhancing epithelial wound healing such as ulcerations and herpetic lesions, bleaching of discolored root canal treated teeth, treatment of peri-implantitis, irrigation of extraction sockets and as a rinse for the avulsed teeth or as a denture cleaner and decontamination of used dental instruments.

Wound healing

Ozone promotes wound healing of both soft tissue and hard tissues [20]. Irrigation of extraction socket with ozonated water could considerably reduce the post-extraction healing time. Use of ozonated water as a cooling and rinsing medium during surgical removal of third molar can reduce the occurrence of infectious complications after the procedure [21]. It accelerates the wound healing in aphtous ulcers, herpes labialis, acute necrotizing ulcerative gingivitis and other gum infections. Ozone is found to be useful in the healing of infectious wound after radiotherapy.

Ozone therapy was found to be beneficial for the treatment of the refractory osteomyelitis in head and neck. It has been shown that ozone has antimicrobial effect against methicillin resistant Staphylococcus aureus, which is one of the main pathogenic microorganisms involved in osteomyelitis [22, 23]. Thus ozone can be used as an alternative to hyperbaric oxygen therapy after the removal of the bone sequestra. In alveolitis, there is accelerated healing by irrigation with ozonated water after removal of the necrotic pulp and debris under antibiotic coverage.

Ozone therapy has shown its efficacy in preventing the development of osteonecrosis in the jaws of patients of whom oral surgery during bisphosphonate treatment cannot be avoided. The combination of ozone therapy with antibiotics and surgery could be considered effective in the treatment of jaw osteonecrosis [24].

Aphtous ulcers

Recurrent aphtous ulceration is a common mucosal disorder that can be painful and debilitating for the patients. A case report by Logan [25] had demonstrated the beneficial use of topical application of ozone using the HealOzone appliance (Kavo Dental GmbH, Biberach/Riss, Germany) in a patient with long standing aphtous ulceration involving the lateral border of the tongue. The topical application of ozone provided an effective means of producing resolution of clinical symptoms related to aphtous ulceration for this patient. The use of topical ozone for the treatment of recurrent aphtous ulceration requires further investigation before it can be advocated as a valid treatment option for these lesions. In the meantime however, topical ozone application may be a further option for patients with aphtous stomatitis for whom other treatment options have been exhausted or for whom systemic treatment is contraindicated.
In another study with aqueous ozone, Cardoso et al. [26] found that in gastric ulcer models induced by stress, there was a significant reduction in the incidence of ulcers types I, II and III.

Mucositis

Mucositis is one of the most common adverse reactions of radiation therapy for head and neck cancers and chemotherapy. It is characterized by a painful inflammation and ulceration of the mucous membranes of mouth and lining of the digestive tract [27]. Chemotherapy and/or radiation therapy interfere with the normal turnover of epithelial cells, leading to mucosal injury; subsequently, mucositis can also occur from indirect invasion of gram-negative bacteria and fungal species because most of the cancer drugs cause changes in blood counts [28]. Since infection may have an important role in the pathophysiology of oral mucositis, several antimicrobial agents have been investigated for their efficacy in preventing and treating this condition. Currently, no single intervention completely prevents or treats oral mucositis. Treatment of established mucositis remains a challenge and focuses on a palliative management approach. Topical anesthetics, mixtures, and mucosal coating agents have been used, despite the lack of experimental evidence supporting their efficacy [29]. While the evidence base for ozone therapy for secondary effects of chemotherapy or radiotherapy is currently being investigated, studies that used gaseous and aqueous ozone application alone have not been adequately represented in the literature [30].

A case report by Shenberg and Blum [31] demonstrated gaseous and aqueous ozone therapy for treatment of mucositis secondary to chemotherapy/radiotherapy. The treat-ment protocol involved application of ozone in both aqueous and gaseous forms. Ozone in a gaseous form was provided at 40 to 60 seconds per lesion. The gaseous ozone concentration was 2100 ppm, with a flow rate of ozone/air mix at 5 meter/second. The aqueous solution of ozone bubbles and water is 2 to 4 ppm. The patient gargled with the aqueous solution for 1 to 2 min. Patient responded positively, enabling her to eat normally, eliminating pain medication, and improved the quality of life. It is difficult to extrapolate for large patient cohorts from a single case study, so further research into the therapeutic use of gaseous and aqueous ozone is indicated.

Temporomandibular joint disorders

Intra-articular administration of ozonated water has been found to be a successful alternative therapy for the management of different joint diseases. In this method, ozone gas is bubbled through water and the mixture is injected directly between the joints. It is used primarily by physicians in Germany, Russia and Cuba to treat arthritis, rheumatism and other joint diseases [32]. This treatment modality has been used by some of the practitioners for the management of temporomandibular joint (TMJ) disorders. A number of TMJ disorders occur due to inflammation secondary to bacteria, viral or fungal infections. Ozone gas not only kills the organisms, but reduces the inflammation and stimulates new cartilage growth.

A randomized control study was conducted by Daif [33], involving 60 individuals with bilateral internal derangement of the TMJ and disc displacement with reduction. The patients were divided randomly into two groups. First group was treated with direct injection of ozone into the superior joint space. Each joint received 2 ml of ozone oxygen mixture. The ozone gas concentration was 10 μg/mL. The second group received non-steroidal anti-inflammatory drugs and muscle relaxants. Injection was given 2 times per week for 3 weeks. 87% of the patients who received ozone gas injection into the joint space either completely recovered or improved. However, further clinical and experimental studies are required to provide direct evidence for its mechanism of action and to substantiate the results.

Osseointegration and periimplantitis

Dental implant therapy has become the ultimate standard for replacement of missing teeth. An adequate and steady plaque control regimen must be ensured for the prevention of periimplantitis. Ozone kills the microorganisms causing periimplantitis and shows a positive wound healing effect due to the increase of tissue circulation. Gaseous ozone or ozonized water shows an increased healing compared to wound healing without ozone therapy.

An in vivo study conducted by El Hadary et al. [34] has evaluated that short-term administration of cyclosporine A, when administered with topical ozonated oil, may influence bone density and the quality of dental implant osseointegration. Therefore, topically applied ozonated oil may influence bone density and the quality of osseointegration around dental implants.

Ozone in prosthodontics

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. Gaseous ozone is used to disintegrate smear layer and to disinfect the prepared tooth. Denture stomatitis can be controlled by topical application of ozonated oil over tissue surface and over denture surface [35].

A study conducted by Arita et al. [36] showed that application of ozonated water may be useful in reducing the number of Candida albicans on denture
plates. The heat-cured acrylic resins were cultured with *C. albicans*. After treatment of flowing ozonated water, the number of attached *C. albicans* was counted. In some experiments, the test samples were treated with ozonated water in combination with ultrasonication. After exposure to flowing ozonated water (2 or 4 mg/l) for 1 min, viable *C. albicans* cells were nearly nonexistent. The combination of ozonated water and ultrasonication had a strong effect on the viability of *C. albicans* adhering to the acrylic resin plates.

**Effect of ozone on periodontium**
Ozone has antimicrobial activity against periodontal pathogens. Bezrukova *et al* [37] reported that ozone reduced the growth of Actinobacillus actinomycetemcomitans, Bacteroides forsythia, Treponema denticola, Porphyromonas gingivalis, and Prevotella intermedia; however, no information was provided about application time or dose. Brauner [38] investigated the therapeutic effects of ozonated water by irrigating the periodontal pockets of 40 patients with 10 ml of ozonated bi-distilled water, daily, for 4 weeks, resulting in an enhancement of the sulcus bleeding index, plaque index, and sulcus fluid rate, without any observed adverse effects; the exact concentration of ozone in the water and the contact time were not reported. In a clinical and microbiological study of 16 patients over an 18-day time-period, Kshitish and Laxman [39] found a higher percentage reduction of several clinical indices (plaque, gingival, and bleeding indices) upon irrigation of periodontal pockets with ozonated water, when compared with 0.2% chlorhexidine (CHX). The antimicrobial results, however, were conflicting. Antimicrobial effects of ozonated water, but not of CHX, were observed against *A. actinomycetemcomitans* and *C. albicans*, but no effect on *Porphyromonas gingivalis* or *Tannerella forsythensis* was seen for either agent. Another randomized controlled trial conducted in twenty-two subjects with periodontitis using ozone nano-bubble water irrigation as an adjunct to mechanical subgingival debridement revealed that this type of treatment may be a valuable adjunct to periodontal treatment [40].

During orthodontic treatment, gingival inflammation occurs along with an increased production of Lactate dehydrogenase (LDH) enzyme in the gingival crevicular fluid. A single sub gingival irrigation of ozonated water can effectively reduce gingival inflammation in orthodontic patients. Ozone irrigation had also found to reduce the load of LDH enzyme in GCF suggesting that it can be used for plaque control in orthodontic patients [41].

**Ozone for treatment of dental caries**
Ozone in gaseous and aqueous phase has a disruptive effect on cariogenic bacteria like *Streptococcus mutans* and *Streptococcus sobrinus*. Ozone can convert pyruvic acid produced by cariogenic bacteria, to acetic acid which can buffer the cariogenic acid and cause demineralization of the carious lesion [42]. Effect of ozone is more in reverting non-cavitated lesions when compared to the cavitated ones [43]. Ozone treatment alone or combined with a remineralizing solution was found to be effective for remineralization of pit and fissure caries [44]. Ozone can be used for the disinfection of the prepared cavity. Assessment of influence of ozone gas and ozonated water application on resin-dentin bonds had shown that it can be used before bonding procedure with no deleterious effect on bond strength [45]. Kivanc *et al* [46] conducted a study to evaluate the effects of application of ozone and Nd:YAG laser on glass-fiber post bond strength and found that it has no adverse effect on the bond strength. Few studies have also shown the complete reversal of leathery root caries after the application of ozone [47]. While few laboratory and short duration clinical studies have suggested that ozone may be effective for the treatment of root caries or killing of oral micro-organisms, the clinical evidence of ozone in the treatment of dental caries is not compelling [48]. It is more important in pediatric dentistry where it could help in patient anxiety and better patient compliance. Ozone can be used as a viable adjunct to fluoride containing desensitizers for the desensitization of hypersensitive dentin [49].

**Bleaching**
Ozone can be successfully used for the bleaching of root canal treated tooth. Conventional ‘walking bleaching’ requires much more time and results are not often satisfactory. Moreover, whitening more severe stains, such as those caused by systemic ingestion of tetracycline, constitutes a challenge. Ozone can be successfully used for lightening the yellowish tinge of tetracycline-stained rat incisors. An experimental study conducted by Tessier *et al* [50] used application of ozone for 3 to 5 min to rat lower incisors and found good results.

**OZONE TOXICITY**
Ozone inhalation can be toxic to the pulmonary system and other organs. There are a number of good experimental studies showing that exposure by inhalation to prolonged tropospheric ozone damages the respiratory system and extrapulmonary organs. The skin, if extensively exposed, may also contribute to the damage. Known side-effects are epiphora, upper respiratory irritation, rhinitis, cough, headache, occasional nausea, vomiting, shortness of breath, blood vessel swelling, poor circulation, heart problems and at a time stroke [51]. Because of ozone's high oxidative power, all materials
that come in contact with the gas must be ozone resistant, such as glass, silicon, and Teflon. If ozone intoxication occurs the patient must be placed in the supine position, and treated with vitamin E and n-acetylcysteine [52].

Contraindications

The different contraindications of ozone include pregnancy, glucose-6-phosphate dehydrogenase deficiency (favism), hyperthyroidism, severe anemia, severe myasthenia, active hemorrhage, acute alcohol intoxication, recent myocardial infarction and ozone allergy. Prolonged inhalation of ozone can be deleterious to the lungs and other organs but well tolerated in some conditions. A review. Quintessence Int 2011; 18:15-18.

CONCLUSIONS

Different studies conducted in the field of dentistry in the past decade have shown the beneficial role of ozone in treating different oral and dental conditions. But its use is still considered limited to date. It could be mainly due to the described possible side effects of ozone gas on upper respiratory system during intra-oral application and due to the lack of long-term studies. Ozone can be considered as a therapeutic option only if it can be applied by preventing it from entering the respiratory tract and avoiding unnecessary contact with the tissues, achieving a perfect seal is sometimes challenging. This has to be achieved by using silicon cups of appropriate size in every cases being treated. In addition barriers must be improvised by the dentist to achieve a seal if the silicone cup alone is inadequate. If a seal cannot be achieved traditional dentistry must be used instead. Moreover, information regarding the therapeutic dosage and duration of application of ozone is still controversial. Additional clinical trials are required to standardize the dosages and application time of dosage in every aspect of dentistry.

REFERENCES


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