Applications of Ozone in dentistry and Oral Health: A Systemic Review

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ABSTRACT

The concept of dental ozone therapy is significantly becoming a trend nowadays, O3 is pure ozone gas that has a soft sky-blue colour with a pungent smell extremely reactive, powerful oxidizing agent. It has many biomedical properties like antibacterial, immune-stimulating, synthesis of Igs, etc. There are various uses of ozone in the field of dentistry, and the objective of this review is to shed light on clinical dental applications of ozone and summarize the research findings regarding the use of ozone in dentistry.

Keywords: Ozone, Dentistry, Dental Diseases, Oral Health

INTRODUCTION

Ozone (O3) is an allotrope of Oxygen (O2) is a natural but unstable molecule. The concept of dental ozone therapy is significantly becoming a trend nowadays in some countries and is considered one of the most effective treatment methods in terms of disinfecting the harmful microorganisms in the oral cavity, and due to all of this, therapy is getting trendy these days. Before going into the detailed application of ozone in dentistry let us first describe the chemical and physical properties of ozone.

Physical & chemical properties of ozone

The pure ozone gas has a soft sky-blue colour with a pungent smell. The molecular weight of O3 is 48 in comparison to the oxygen diatomic molecule that is 32. It occurs naturally in small amounts in the Earth’s stratosphere, where it absorbs UV rays and thus protects the living beings on earth because UV radiation can cause severe damage to living organisms. Ozone is 1.5 times denser than diatomic oxygen and is much more reactive than the O2 gas and act as an extremely powerful oxidizing agent, thus can be used as a bleaching agent for organic compounds, used as a strong germicide to sterilize drinking water. In the large metropolis, ozone, mixed with other compounds like NO2, acidic compounds, CO, etc has become the main toxicant for the lungs, eyes, nose and, to a lesser extent, the skin.
Biomedical properties of ozone

Ozone leads to oxidative stress in cells because of its ability to produce free radicals deriving from the liperoxidation of cell membranes, protein oxidation, enzymatic inactivation, the destruction of DNA, and cell apoptosis. It and so its safety and toxicity depend upon its concentration level. Also, healthy cells have antioxidant enzymes in their cell membranes, such as superoxide dismutase, catalase, glutathione peroxidase, etc. There are also antioxidants such as vitamin C, vitamin E, etc. present in the extracellular matrix fluids, plasma and these antioxidants protect the healthy cells from being oxidized by ozone but on the other hand pathogens such as Bacteria, Viruses, Fungi, and Parasites have little or no antioxidant enzymes in their cell membranes. This makes them vulnerable to oxidants. An oxidant (ozone) will destroy the cell membrane of the pathogen resulting in a disinfecting or sterilizing effect. Ozone leaves no toxic byproducts like chlorine compounds in vivo or ex vivo. Ozone therapy has been widely used in everyday clinical practice over the last few years, clinical evidence has suggested that ozone therapy may play a major role in the treatment of other conditions such as vascular and immune diseases.

Ozone disrupts the integrity of the bacterial cell envelope through oxidation of the phospholipids and lipoproteins and in fungi it inhibits cell growth at certain stages and in the case of viruses, the O₃ damages the viral capsid and upsets the reproductive cycle by disrupting the virus-to-cell contact with peroxidation, thus it acts as an antimicrobial due to its oxidative properties. Also, the benefits of ozone on the body include strengthening the immune system, stimulating white blood cells, preventing infections and immune system deficiencies by destroying fungi, bacteria and viruses. It also helps to counteract cell mutations, thereby preventing some types of cancer. Oxygen/ O₃ mixture was also found to prolong the appearance of arrhythmia induced by potassium chloride, aconitine, etc., in laboratory animals like rats. Some of the most common applications include subcutaneous injections to treat pain and inflammation in localised areas such as joints and muscles. It can be used to treat skin disorders like eczema, acne and pimples where skin treatment with ozone is given using a localised blowing method with oxygen and ozone. Besides this there are many more uses of ozone therapy like in toxins elimination from the body, skin treatments, weight loss management, arthritis and inflammation, disinfecting wounds, activating the immune system, herniated discs management, treating cancer and now in dentistry also. Thus, potential effects of ozone are -

Antimicrobial activity, damage to the cytoplasmic membrane, oxidation of intracellular contents, specific to microbial cell, effective in antibiotic resistive strain, immuno-stimulating, activates the cellular and humoral immune system, synthesis of immunoglobulin’s, enhanced phagocytosis activity, activation of biological antioxidants, analgesic, anti-hypoxic and detoxicating, activation of the aerobic process (Krebs cycle, glycolysis, oxidation of fatty acids), synthesis of interleukins, leukotrienes and prostaglandins, synthesis of immunoglobulins.

Ozone applications in dentistry

Dentists can apply ozone in the form of gas, water or oil. It has proven useful in treating several different dental problems:

According to Krammer, a German dentist, aqueous ozone can be used:
1. As a powerful disinfectant
2. To control bleeding
3. To cleanse wounds in bones and soft tissues
4. To improve healing by increasing the local supply of oxygen to the wound area
5. To increase the metabolic processes related to wound healing as ozonated water can increase the temperature in the wound area.

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Due to these activities ozonated water can be used in candidiasis, gingivitis and as a disinfectant to rinse the oral cavity. The use of ozone in dentistry is described briefly below-

Wound healing - University of Basel, Switzerland conducted a study of immune-histochemical, and micromorphological examinations of the wounds of the oral mucosa in which it was found that the patients who applied ozonized water on their wounds showed an acceleration of wound healing and earlier wound closing than patients who applied regular water and did not receive treatment.7

Dental caries management - Colonization by Streptococcus mutans can cause dental decay if they grow within deep fissures of the tooth, while Streptococcus sobrinus play a primary role in smooth-surface decay but when these bacteria were subject to ozone from an ozone-generating device, there was a significant reduction in ozone-treated samples.8

So, ozone’s antibacterial properties may help prevent small cavities from growing larger in the pits and fissures on the biting surfaces of the back teeth. Additionally, ozone may be helpful in disinfecting areas of decay underneath tooth restorations. Study trials have shown that non-cavity root caries can be reversed and arrested of progression which eliminates the need for removal and it just requires the routine application of ozone for 40 seconds, following by the use of remineralizing products.9 The remineralizing effect of ozone on cavitated caries lesion is well established. The research conducted a clinical trial evaluating the clinical reversal of root caries with 10s exposure to ozone gas at 2100 ppm, followed by 5s application of xylitol and fluoride. After 6 months of follow-up, ozone-treated lesion significantly rehardened compared to controls.10

Oral lichen planus - Lichen planus is an inflammatory condition that affects the oral mucous membranes with clinical features of white, lacy patches or red swollen lesions and open sores in the gum. The application of gaseous ozone has been proven to be effective in increasing wound healing after high-dose radiotherapy and this therapy has shown very good results in the resolution of symptoms at the end of the treatment and thus shows its potential to replace steroid treatment.11

Herpetic Infections – As we all know that HSV-1 is mostly responsible for causing oral-facial herpes, the combination of the orthodox antiviral agents with ozone therapy plus minor autohemothepathy and topical application of ozonated oil is useful in the management.12

Ozone in prosthodontics - One of the most common problems associated with denture use is stomatitis that is mainly caused by C. albicans. A denture cleanser releasing ozone bubbles with a concentration of 10 ppm has been developed and is effective in reducing the number of C. albicans following a 30–60 min exposure.13

Periodontal problems – Gingivitis and periodontitis are the common problems in the periodontics and are the major cause of loss of tooth among the population and also leads to other discomforts to patients like swelling or tenderness, loose teeth, bleeding, pus, sensitivity, halitosis, malocclusion, etc. Ramzy et al found that irrigation with ozonated water in patients with aggressive periodontitis with scaling & root planning was effective in improving the clinical parameters; periodontal pockets in patients with aggressive periodontitis were irrigated once a week for 4 weeks with 150 ml of ozonated water for 5–10 min post scaling and root planning and following this therapy; pocket depth, plaque, gingival indices, and bacterial count were reduced significantly in the treated quadrant. Also, Karapetian et al (in vitro study) conducted a study for effect of ozone on peri-implantitis and found that there was a maximum reduction in bacterial counts (Table 2).14
Halitosis – halitosis is also known as bad breath and one of the causes of halitosis is bacteria present in the oral cavity that forms volatile sulfur compounds such as H2S that causes the oral malodor and some of these bacteria are the main culprit in perio diseases and caries. And since, ozone is antimicrobial in nature also and acts as a disinfectant, it can be useful in minimizing the foul smell from the mouth by killing the microbes.15

Dentin hypersensitivity - Dentin hypersensitivity causes sharp, short pains that are caused by exposed dentin when it is in contact with thermal, tactile, chemical, or osmotic stimuli. There may be a lingering aching discomfort after the stimuli are removed. The hydrodynamic theory states that dentin is permeable throughout the tubules and when the dentinal fluid movement increases, sensitivity occurs. A supporting study proved that there was an average of 55% decrease in pain level after ozone treatment.16

Temporomandibular joint disorders - The temporomandibular joint is a hinge that connects your jaw to the temporal bone on the skull. As we have already studied that ozone therapy is useful in the management of inflammatory

### Table 2: Studies on the use of ozone in periodontics

<table>
<thead>
<tr>
<th>Form of ozone</th>
<th>Authors</th>
<th>Findings</th>
<th>Experimental design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ozone water</td>
<td>Ebersberger et al., 2002 1,2</td>
<td>2 min irrigation with ozonated water (4 mg/ml) leads to mechanical cleansing, decontaminates the root surface, no negative effect on periodontal cells remaining on the tooth surface</td>
<td>23 freshly extracted completely erupted third molars randomly treated by irrigation with ozonated water for 2 min or irrigation with a sterile isotonic saline (control group). The periodontal cells of these teeth studied immunohistochemically to mark PCNA.</td>
</tr>
<tr>
<td>Ozone water</td>
<td>Nagayoshi et al., 2004 3,4</td>
<td>Ozonated water is effective for killing Gram-positive and negative oral microorganisms and oral Candida albicans in pure culture as well as bacteria in plaque biofilm</td>
<td>Dental plaque samples were treated with 5 mL of ozonated water for 30 s.</td>
</tr>
<tr>
<td>Ozone water</td>
<td>Ramzy et al., 2005 5,6</td>
<td>High significant improvement regarding pocket depth, PI, GI, and reduction in bacterial content reported in sites treated with ozonized water</td>
<td>Periodontal pockets in 22 patients suffering from aggressive periodontitis (age range from 13 to 25 years) were irrigated with 250 mL of ozonized water over 1-3 min once weekly using a blunt tipped sterile plastic syringe.</td>
</tr>
<tr>
<td>Ozone water</td>
<td>Huth et al., 2006 7,8</td>
<td>Aqueous ozone is less cytotoxic than gaseous ozone or established antimicrobials</td>
<td>Aqueous form of ozone, as a potential gaseous or established antimicrobials (CHX 2%, 0.2% NaOCl 3-25%, 2.25% H2O2 3% were compared.</td>
</tr>
<tr>
<td>Gaseous ozone</td>
<td>Müller et al., 2007 9,10</td>
<td>Only 5% hypochlorite solution was able to eliminate all bacteria effectively. Usage of gasform ozone or PDT was not able to reduce significantly or completely eliminate bacteria in the biofilm</td>
<td>Mature 6 species oral biofilms treated with gasform vacuum ozone or vacuum alone, PDT and antimicrobial solution immersions of biofilms for 60 s in 0.2% and 2% chlorhexidine or 0.5% and 3% hypochlorite solution.</td>
</tr>
<tr>
<td>Ozone water</td>
<td>Kshithish and Laxman 2006 11,12</td>
<td>A higher percentage of reduction in PI (90%), GI (29%) and bleeding index (29%) using ozone irrigation as compared to chlorhexidine</td>
<td>A randomized, double-blind, crossover split-mouth study on 16 patients suffering from generalized chronic periodontitis. Subgingival Irrigation of each half of the mouth with either ozone or chlorhexidine was done at different time intervals.</td>
</tr>
<tr>
<td>Ozone water</td>
<td>Doodad et al., 2011 13</td>
<td>Ozone application serve as potent atraumatic, antimicrobial agent to treat periodontal disease nonsurgically both for home care and professional practice</td>
<td>Oral irrigation with ozonated water, 0.2% chlorhexidine and 2% peroxide solution done in patients with chronic periodontitis.</td>
</tr>
<tr>
<td>Gaseous ozone</td>
<td>Hauser-Gerspach et al., 2012 14</td>
<td>Gaseous ozone showed selective efficacy to reduce adherent bacteria on titanium and zirconia without affecting adhesion and proliferation of osteoblastic cells</td>
<td>The antimicrobial efficacy of gaseous ozone on bacteria adhered to saliva-coated titanium and zirconia disks served as substrates for the adherence of Streptococcus sanguinis and Porphyromonas gingivalis was evaluated. The test specimens were treated with gaseous ozone [(490 ppm, 33 mL/l) for 6 and 24 s.</td>
</tr>
<tr>
<td>Ozone NBW3</td>
<td>Hayakorn et al., 2013 15</td>
<td>Subgingival Irrigation with NBW3 is valuable adjunct to periodontal treatment</td>
<td>Clinical and microbiological effects of NBW3 irrigation as an adjunct to subgingival debridement for periodontal treatment.</td>
</tr>
<tr>
<td>Ozone olive oil</td>
<td>Shoukaheb and Ali 2014 16,17</td>
<td>The results showed improvement in all clinical parameters in (Group II). Whereas SRP alone resulted in a significant improvement only up to 1 month for BOP, PPID and CAL parameters and up to 3 months for the PI and GI scores as compared to baseline values</td>
<td>Thirty patients were randomly selected and equally divided into: Group I received SRP only, Group II received SRP and ozonated olive oil gel (Ozoxal). Subgingival application of olive gel was performed following initial SRP and at 1, 3, 14, and 21 days. Clinical measurements and plaque samples for PCR were recorded at baseline, 1, 3 and 6 months after treatment.</td>
</tr>
<tr>
<td>Ozone water</td>
<td>Cane et al., 2015 18</td>
<td>Statistically significant reduction in 6 microbial species and for CBT in sites treated with ozone therapy in comparison with SRP alone. Results were obtained with a single local application of ozone therapy just after SRP and with a molecular contrast 3rd day after treatment</td>
<td>The efficacy of supportive periodontal therapy alone versus Aquacut® ozone therapy used in association with SRP in the treatment of chronic periodontitis in 20 adult patients were compared; a split mouth design.</td>
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</table>

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arthritic pain conditions and also in case of TMJ dysfunction, studies showed that intra-articular ozone gas injection can treat internal derangement of the temporomandibular joint and the ozone gas was injected into the superior joint space.17

Intra-articular administration of ozonated water has been a successful alternative therapy for the treatment of different temporomandibular joint (TMJ) diseases. A randomized controlled study was conducted by Baysan A & Lynch E16 involving 60 individuals with bilateral internal disarray of the TMJ and disc displacement with reduction, 87% of the patients who received O3 gas injection in the joint space, recovered completely or presented improvements in the symptoms. However, further clinical and experimental studies are needed to provide direct evidence for its mechanism of action and to sustain the promising results obtained.17

The pain felt in the maxilla in the region of the apices of the posterior teeth can originate from infections and inflammations of the maxillary sinus, directly above the dental roots. In these cases, OZT can be applied through ear inflation, as well as by injections of low-concentration ozone gas into loose areolar tissues on buccal surfaces along the wall of the maxillary sinus. 25% of infections of the maxillary sinuses are of fungal origin. O3 having a high disinfection power, able to overcome the use of drugs.17

Teeth whitening – as we know that O3 is highly oxidative and also used to bleach various chemicals, the same property of O3 applies to teeth whitening. Also, one study conducted by Al-Omri et.al shows that the teeth bleached with O3 were much whiter than 38% of H2O2. 16

The efficacy of tooth whitening is a major concern in dental practice, since its cosmetic result is immediately noticeable, though it may not be the only aspect involved in a good facial appearance. However, whitening more severe stains, such as those caused by systemic ingestion of tetracycline, constitutes a challenge. Several tooth whitening agents and methods have been described in the literature for the treatment of tetracycline-stained teeth. Different bleaching agents have been utilized, e.g. carbamide peroxide or hydrogen peroxide plus carbamide peroxide. There are also variations in the way these agents are applied, such as exposure time, e.g., months of carbamide peroxide treatment; or concentration, e.g. 10%, 15% or 20% carbamide peroxide6. Additionally, the mode of activation or methods of application of the whitening compound may differ.18,19

In dentistry, ozone has proved to be successful in the treatment of root caries, non-cavitated fissure carious lesions, early carious lesions in teeth, dental surgery or following tooth extraction processes and reduction of pathogenic micro-organisms of carious dentine. Ozone has also been used to whiten teeth in individuals with dental sensitivity and mucosal ulcerations; in those who consume tobacco, coffee or chocolate; and in those who have extrinsically stained teeth due to brown-coloured melanoids or chlorhexidine use. A simple, safe and non-invasive ozone treatment would provide an alternative therapeutic agent to current methods; however, further morphological assessments will be required for its use in the dental clinic.20

Dry Socket - Ozone therapy following extraction significantly reduces the incidence of the dry socket because of its healing and disinfectant properties. Other uses of ozone in dentistry include Biofilm purging i.e elimination of bacterial pathogens, periodontal pocket disinfection and osseous disinfection, endodontic treatment as ozone was considered an effective root canal disinfecting agent in treating apical periodontitis, tooth extraction, gum recession (exposed root surfaces), pain control, infection control, tissue regeneration, etc.21

Routes of administration can be gaseous form, ozonated water i.e aqueous form or ozonized oil.

Contraindications of ozone therapy
All cases with Blood Coagulation Failure
Bleeding Organs
Thrombocytopenia
Uncontrolled hyperthyroidism
Acute alcohol intoxication
Pregnancy
Ozone Sensitivity / Allergy (very rare)
Hemorrhagic or Apoplectic Stroke
G6PD (extremely rare)
Side-effects of O3 therapy are18 Allergic skin reactions (very uncommon) weakness, slight dizziness (shortly during and after the administration of ozone therapy)

CONCLUSION
Dentistry is varying with the induction of modern science to practice dentistry. The ozone therapy has been more beneficial than present conventional therapeutics due to its multiple properties and uses in the field of dentistry either it is disinfection or the management of TMJ dysfunction. Also, it can be concluded that this therapy has very few contraindications and side effects so it would be well tolerated in most of the patients. However, further research is still needed to justify the routine uses of ozone in dentistry.

Conflicts of Interest:
All contributing authors declare no conflicts of interest.
REFERENCES