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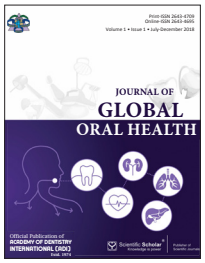

Review Article

Ozone: A paradigm shift in dental therapy

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Received : 16 July 19
Accepted : 27 July 19
Published : 25 September 19

DOI
10.25259/JGOH_56_2019

Quick Response Code:

ABSTRACT

Objectives: Ozone has been used in medicine for over a century, but its clinical applications in dentistry have just begun to be explored. The effects of ozone either as gas, water, or oil in the treatment of dental diseases such as caries, periodontitis, and hypersensitivity have been investigated and the results are promising. Thus, the objective of this review is to shed light on the recent clinical oral applications of ozone and summarize the various research findings regarding the use of ozone in dentistry. This review would enable researchers to know the background of ozone in dentistry and to help them formulate new and improved protocols to study the possible applications of ozone in clinical dentistry.

Data Sources: Pertinent literature on the application of ozone to treat various dental diseases was thoroughly searched using Medline, PubMed, Central, Cochrane, and Embase.

Conclusion: Clinical use of ozone is a minimally invasive approach toward the prevention and control of oral diseases. The present literature review observed encouraging results on the use of ozone in various modalities of dental treatments. However, the use of ozone in dentistry needs further investigation using controlled clinical trials, with sufficient, follow-up period and standardized measurements to establish ozone therapy as a standard treatment modality in dental practice.

Keywords: Caries, Endodontics, Antimicrobial, Ozone, Periodontal disease

INTRODUCTION

Ozone also called trioxygen is an allotropic form of oxygen and an unstable gas which occurs naturally by the action of ultraviolet rays on oxygen in the outer atmosphere. Ozone derives its name from the Greek word "ozein" which means "to smell," named after its characteristic odor usually detected by human nose at 0.02 or 0.05 ppm.

It is known to be a potent oxidizer and has the ability to oxidize any known biological entity.[1] The principal action of ozone is its antimicrobial effect on bacteria, virus, and fungi,[2] besides its immunomodulatory, anti-hypoxic, biosynthetic, and anti-inflammatory properties [Figure 1].[3-6]

Ozone has been used in the field of medicine for over a century as a disinfectant, to purify blood, and during the World War I it was used to treat gangrene, burn wounds, osteomyelitis, fistulas, and many other infections.[7] E. A. Fisch, a German dentist, was the first person to use ozone for disinfection and to aid healing in his own practice; following his footsteps, Dr. Payr started using ozone routinely during surgeries.[8] Thenceforth, ozone has been accepted as an alternative and complimentary therapy. Medical-grade ozone is essentially a composition of 0.1–5% ozone and

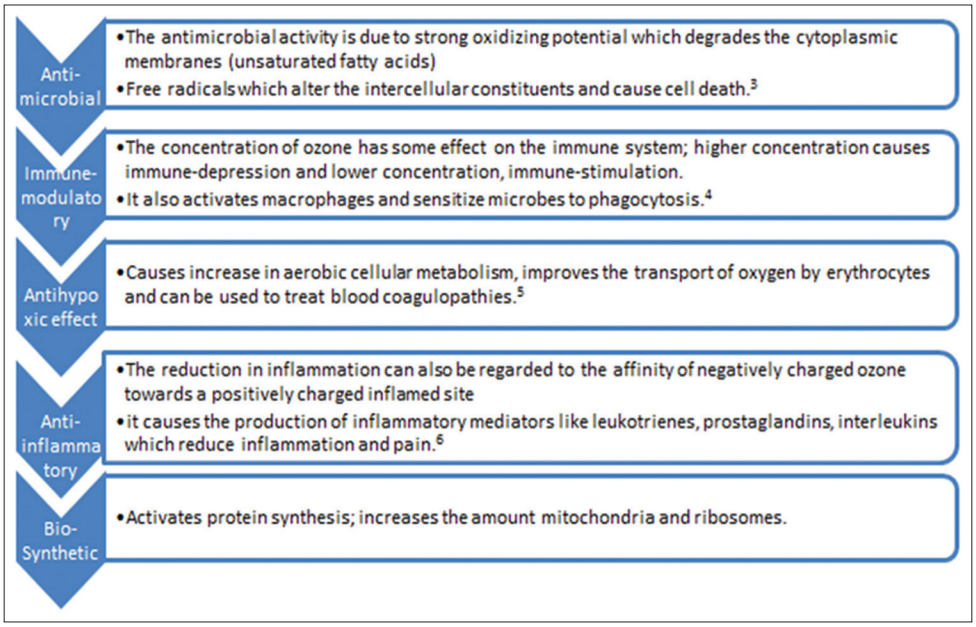

Figure 1: The various actions of ozone on biological tissues.

95–99.6% pure oxygen,[7] and in dentistry it has been used either as a gas, water, or oil to treat a plethora of conditions.

The objective of this article was to update the recent clinical oral applications and summarize the various research findings regarding the use of ozone in dentistry. This review would enable researchers to know the background of ozone use and to help formulate new protocols to study the possible applications of ozone in clinical dentistry.

Use of ozone in dental therapeutics is truly a paradigm shift in the management of oral and dental infections. Its various applications pertaining to dental diseases are summarized below.

Ozone in caries management

Dental caries is the most common chronic disease known to affect humans, which is multifactorial in origin. Conventionally, caries has been treated using a surgical approach based on blacks philosophy of "extension for prevention." It was followed until the latter part of the 20th century which could be attributed to the lack of understanding of the caries process and in particular the ability of dental tissues to remineralize. By the end of the 20th century, a new concept of minimal intervention in caries management emerged which emphasized the concept of remineralization of demineralized enamel and dentin.[9] With the introduction of minimal intervention in caries management, came the idea of the use of ozone to aid in biofilm control and remineralization of early-stage caries as described below.

Effect of ozone on biofilms

The use of ozone to treat dental caries was introduced in early 2000; since then several *in vitro* and *in vivo* studies have established its effectiveness in treating primary root caries, occlusal pit and fissures caries as well as initial enamel caries. Ozone, in a gaseous or aqueous form, has been found to be effective in removing biofilm and its associated bacteria.[10] Cariogenic microflora, such as *Streptococcus mutans*, *Lactobacillus casei*, and *Actinomyces naeslundii*, have been inactivated within the 60s of exposure to ozone gas,[11] and ozonated water at a concentration of 0.1 ppm was found effective in reducing plaque microbial load.[12] In an *in vitro* study, ozone exhibited bactericidal activity with 10s exposure either as gas or water on root caries and as gas on *S. mutans* and *Streptococcus sobrinus*.[13,14] When used at a concentration of 0.5–4 mg/l, it effectively prevented plaque formation by both Gram-positive and Gram-negative bacteria as well as *Candida albicans*.[15] While 80s exposure to ozone on deep cavities reduces the residual microbial load significantly, 40s exposure significantly reduced *S. mutans* counts.[16] In a case of oral candidiasis, ozonated water (5–10 ml; 25 μg/ml) used as 1 min oral rinse showed superior effectiveness over clotrimazole in reducing candidial counts and establishing a carrier state.[17]

Remineralization of caries lesions with ozone

The remineralizing effect of ozone on cavitated caries lesion is well established. Baysan *et al.* 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 follow-up, ozone-treated lesion significantly rehardened compared to controls,[18] and at 12 months follow-up 47% of ozone-treated lesions rehardened whereas none of the lesions in the control group had reversed.[19] Similar result was observed when 178 non-leathery primary root caries lesions were treated with ozone gas (2100 ppm for 10s) or air along with daily use of the remineralizing patent kit and evaluated at 3, 6, 12, and 18 months. After 18 months, all the ozone-treated lesions had reversed while in the control group, only one had reversed, and 37% had worsened clinically.[20] Open single surface lesions treated with ozone in anxious children exhibited increased tactile hardness values at 4, 6, and 8 months compared to baseline, whereas no change in the hardness value was observed in the control group.[21]

Ozone has been used to remineralize non-cavitated pit and fissure caries. In a clinical trial, sealant placed following ozone treatment exhibited highest remineralization effect when compared to all other untreated groups.[22] Similar trend was observed in a split-mouth study in which 258 pit and fissure caries lesions in primary teeth received ozone gas (2100 ppm) treatment for 10s followed by application of xylitol and fluoride. When the lesions were monitored using electrical caries monitor (ECM), at 12 months, the ozone-treated group exhibited significant improvement in lesion reversal indicated as improvement in the ECM scores compared to controls.[23] In a clinical study, Huth *et al*.[24] carried out a spilt-mouth randomized clinical trial to evaluate the effectiveness of 40s ozone exposure to reverse non-cavitated pit and fissure caries. Fifty-seven pairs of lesions on contralateral molars were included in the study and randomly divided into ozone (ozone gas for 40s) and control (no treatment) groups and followed up for 3 months. Caries reversal in ozone-treated lesions was significantly higher than the control in high caries risk individuals; however, the difference was not statistically significant when the whole population was included.[24] Samuel *et al*. found ozone to have significantly improved the remineralizing potential of nanohydroxyapatite in remineralizing initial enamel caries in *in vitro* and *in situ* study.[25,26] Contrary to previous reports, Nie *et al*. reported inability of ozone to remineralize enamel lesions in an *in vitro* study.[27] Similar observation was reported by Duggal *et al*. when ozone in combination to a reductant kit failed to inhibit the demineralization of enamel and dentin subjected to cariogenic challenge *in situ* compared to the kit containing high fluoride.[28]

Mechanisms of action of ozone

The principal action of ozone is believed to be antimicrobial; although, ozone gas had failed to reduce the number of bacteria in the dentin of non-cavitated lesions.[29] Hence, an alternate mechanism for the effect of ozone on non-cavitated lesions was postulated. The surface enamel is more resistant to demineralization due to post-eruptive maturation, but the demineralization process causes increased porosity on the surface making the subsurface enamel more susceptible to mineral loss and lesion formation. Enamel is composed of 1% (w/v) organic content that covers the minerals acting as a barrier to diffusion.[30] Thus, it can be postulated that a potent oxidizer and proteolytic agent like ozone can disrupt the organic content in demineralized enamel and enhance the diffusion of remineralizing agents. Moreover, ozone disrupts the cariogenic bacteria in biofilm and alters the ecological niche, making it difficult for the cariogenic organism to recolonize against the normal commensals.[31] The caries process is essentially a disruption in the harmonious balance between demineralization and remineralization. Pyruvic acid is one of the principal contributors to decreasing pH toward caries activity,[32] but ozone oxidizes pyruvic acid to acetate and carbon dioxide thereby promoting remineralization because acetate has higher pKa and favor pH buffering in resting plaque.[33]

The physical properties of enamel are not affected by ozone at a concentration of 90 and 120 μg;[34] but exposure to ozone gas for 40s dehydrated sound enamel and enhanced its microhardness.[35] However, the effect of ozone on demineralized enamel is still unclear and needs to be explored. The conclusion from each study toward the use of ozone in caries management is summarized in Table 1.

Ozone in periodontology

Periodontal disease is one affecting the supporting structures of teeth. It usually begins as gingivitis and in a small proportion of cases progresses to periodontitis. However, it is ultimately the host response and bacterial, genetic variance which decides the transition and severity of the disease.

In a clinical study, 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 planing (SRP). The following therapy; pocket depth, plaque, gingival indices, and bacterial count were reduced significantly in the quadrant treated.[36] In a similar study, SRP alone or in combination with ozone therapy on salivary matrix metalloproteinase and clinical parameters was assessed in chronic and aggressive periodontitis, but no significant difference was reported between the interventions.[37] A clinical trial involving 41 patients with chronic periodontitis, investigated the effect of SRP followed by irrigation with either ozonated water or distilled water on the plaque, gingival index, bleeding on probing, probing pocket depth, gingival recession, clinical attachment loss, and C-reactive protein expression in serum at baseline and 3 months post-therapy. Except for gingival index, other parameters expressed significant improvement in both the

Table 1: Summary of the studies on the effect of ozone in cariology.

Author, Year	Objective	Type of study	Conclusion supporting the use of ozone	
			Positive	Negative
Open carious lesions				
Baysan *et al.*, 2004[13]	Effect of ozone on bacteria and clinical severity of PRCL	*In vitro*	10 or 20s exposure significantly reduces the microbial count and reverses the lesion	Nil
Baysan *et al.*, 2000[14]	Assess the antimicrobial efficacy of ozone gas on PRCL	*In vitro*	10 or 20 s exposure to ozone gas is significantly effective on PRCL compared to controls	Nil
Baysan *et al.*, 2007[18]	Efficacy of ozone application with or without root sealant in healing leathery root caries evaluated at 1, 3, and 6 months.	*In vitro*	After 6 months, lesions hardened only in ozone group. At all follow-ups, the ECM and DIAGNOdent exhibited improvement only in the ozone group.	Nil
Baysan *et al.*, 2002[19]	Evaluate the clinical reversal of root caries after application of ozone gas for 10s at 2100 ppm, following which xylitol and fluoride were applied for 5s at 1, 3, and 6 months.	*In vitro*	At 12 month follow-up, 47% of lesions in ozone group hardened compared to none in the control group.	Nil
Holmes 2003[20]	Effect of ozone with daily use of remineralizing agents on the clinical severity of PRCL	*In vitro*	PRCL can be treated noninvasively using ozone and remineralizing agents.	Nil
Dähnhardt *et al.*, 2006[21]	Ability of ozone to reverse caries lesion in open single surface lesions among children (mean age 5.96 years)	*In vitro*	The tactile hardness value in ozone treated group improved, whereas in control group no change was reported.	Nil
Non cavitated carious lesions				
Unal and Oztas, 2015[22]	Remineralization effectiveness of three sealants on initial fissure caries with or without ozone use	*In vitro*	Greatest remineralization was shown by Ozone+Aegis sealant.	Nil
Abu Naba 2003[23]	Evaluate the effect of ozone or no ozone to improve the clinical severity and ECM scores on the initial pit and fissure caries.	*In vitro*	Ozone treated samples showed significant improvement	Nil
Huth *et al.*, 2005[24]	Effect of ozone on the initial pit and fissure caries compared to untreated control teeth.	*In vitro*	At 3 months ozone-treated groups revealed significant lesion reversal than controls only in the high-risk group.	The difference in caries lesion reversal was not significant when compared for the whole population.
Nie *et al.*, 2007[27]	The ability of ozone to remineralize demineralized bovine enamel.	*In vitro*	Nil	Ozone has no effect in remineralization of enamel.
Duggal *et al.*, 2012[28]	Effect of remineralizing agent with and without ozone to inhibit demineralization of human enamel and dentin in a cariogenic challenge.	*In situ*	Nil	Ozone has no additional effect in inhibiting the demineralization of enamel and dentine when compared to a remineralizing treatment.
Samuel *et al.*, 2014[25]	Ability of ozone to enhance the remineralization of n-HAP on artificial enamel caries	*In vitro*	Ozone significantly improved the remineralizing potential of n-HAP	Nil
Samuel *et al.*, 2016[26]	Ability of ozone to heal initial enamel caries	*In vitro*	Ozone significantly improved the remineralizing potential of n-HAP	Nil

(Contd...)

Table 1: *(Continued)*

Non cavitated carious lesions				
Author, Year	**Objective**	**Type of study**	**Conclusion supporting the use of ozone**	
			Positive	**Negative**
Anti-microbial action				
Baysan *et al.*, 2000[14]	Effect of ozone on *S. mutans* and *Streptococcus sobrinus*	*In vitro*	10s exposure reduced *S. mutans* and *Streptococcus sobrinus* on saliva-coated glass beads.	Nil
Polydorou *et al.*, 2006[16]	Antibacterial effect of ozone gas on *S. mutans*	*In vitro*	Ozone showed significant antimicrobial activity against *S. mutans*	40 s ozone was less effective compared to 80s exposure in reducing *S. mutans* counts.
Baysan *et al.*, 2007[29]	The ability of ozone to eliminate bacteria in non cavitated dentine lesions	*In vitro*	Nil	Ozone was not effective in reducing the bacterial count in non cavitated dentinal lesions.
Nagayoshi *et al.*, 2004[15]	Bactericidal activity of ozone against oral microorganisms in suspension and dental plaque	*In vitro*	Ozonated water instantaneously destroyed *S. mutans* and it also prevented the accumulation of plaque	Nil

ECM: Electrical caries monitor, n-HAP: Nanohydroxyapatite, PRCL: Primary root caries lesions, *S. mutans: Streptococcus mutans*

groups and no additional benefit of ozone water irrigation following SRP was reported in the treatment of chronic periodontitis.[38]

The effect of 1 min exposure of ozone either as gas or water chlorhexidine (CHX) or saline on periodontal pathogens exhibited greater antimicrobial effect against *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Parvimonas micra* in planktonic compared to biofilm cultures. The antibactericidal activity of aqueous ozone (20 μg/ml) and ozone gas (≥4 mg [−3]) against periodontal-pathogens was significantly less compared to 2% CHX but were much effective than 0.2% CHX. However, none of the agents could significantly reduce the *Aggregatibacter actinomycetemcomitans* in biofilm cultures.[39] The influence of ozone with photodynamic therapy and antiseptic agents such as 2% CHX, 0.5%, and 5% hypochlorite on various organisms in a biofilm model was studied *in vitro*. About 5% hypochlorite was the only agent to exhibit significant bactericidal activity against organisms protected in the biofilm matrix.[40] Peri-implantitis is a unique situation and its management is complicated because of the complexity involved in decontaminating the implant surface, peri-implant tissue, and prevention of recolonization. Conventional, surgical or ozone therapy toward peri-implantitis was attempted and ozone-treated group caused a maximum reduction in the bacterial counts.[41]

Dental plaque is the primary causal factor for gingivitis, and if not removed on a daily basis can lead to gingivitis and later may progress into periodontal disease.[42] Professional cleaning followed by daily rinse of ozonated water was effective in reducing the severity of gingivitis and periodontitis. However, the use of ozone rinse alone was not sufficient to achieve adequate plaque control.[43]

Ozone possesses biosynthetic effect. This ability of ozone to proliferate periodontal cells was studied using immunochemistry following ozone exposure for 2 min after extraction. The expression of proliferation cell nuclear antigen and labeling index was comparatively high in the ozone group, but not statistically significant, but had no negative effect on periodontal cells.[44] Ozone causes vasodilatation and increases perfusion in tissues. Ozone therapy on de-epithelialized gingival graft improved the perfusion in graft site during the 1st week when evaluated using laser Doppler flowmetry. Furthermore, ozone-treated group reported less pain and better quality of life compared to graft alone, post-surgery.[45] The conclusion from each study toward the use of ozone in periodontology is summarized in Table 2.

Ozone in endodontics

The reliability of the use of ozone in endodontics is dependent primarily on its antimicrobial action. A randomized trial investigated the effectiveness of ozone gas and sodium hypochlorite/CHX in treating apical periodontitis and found no significant difference among the groups with regard to success rate, bactericidal action, periapical lesion size, and periapical index score at 6–12 months. Thus, ozone was considered an effective root canal disinfecting agent in treating apical periodontitis.[46] Similarly, the effect of ozone gas (1 g/m^{-3}) or water (5 μg/l), sodium hypochlorite, hydrogen peroxide, and CHX on enteropathogens in

Table 2: Summary of the studies on the effect of ozone in periodontology.

Periodontal disease				
Author, Year	**Objective**	**Type of study**	**Conclusion supporting the use of ozone**	
			Positive	**Negative**
Ramzy *et al.*, 2005[36]	Effect of ozonated water irrigation in patients with aggressive periodontitis	*In vitro*	Ozone treatment along with SRP was effective in improving the clinical parameters	Nil
Skurska *et al.*, 2010[37]	SRP alone or in combination with ozonated water irrigation on clinical parameters and MMP levels in subjects with chronic and aggressive periodontitis	*In vitro*	Nil	SRP with ozone water irrigation has no additional effect in improving the periodontal conditions of patients with CP and AP.
Al Habashneh *et al.*, 2015[38]	SRP alone or in combination with ozonated water on periodontal disease indicators	*In vitro*	Nil	SRP+ozonated water irrigation has no significant effect as compared to SRP+distilled water irrigation.
Huth *et al.*, 2011[39]	Antimicrobial action of ozone compared with regular antiseptics on periopathogens in planktonic/biofilm model.	*In vitro*	Aqueous ozone (20 μg/ml) or gas (≥4 g^3) was as effective an antimicrobial agent as 2% CHX	Ozone was ineffective in reducing the number of *Aggregatibacter actinomycetemcomitans*.
Muller *et al.*, 2007[40]	Antimicrobial activity of ozone and PDT	*In vitro*	Nil	Ozone and PDT had very poor cidal effects on the organisms in organized dental biofilm.
Karapetian *et al.*, [41]	Effect of ozone on peri-implantitis	*In vitro*	Ozone exhibited the maximum reduction in bacterial counts	Nil
Brauner A. 1991[43]	Effectiveness of daily ozone rinse following professional cleaning on gingivitis and periodontitis	*In vitro*	Ozone daily rinse following professional cleaning was found to be effective	Ozone rinse alone not sufficient to achieve plaque control
Biosynthentic effect				
Ebensberger *et al.*, 2002[44]	Ability of ozone to increase the proliferation of periodontal cells	*In vitro*	Ozone showed marginally greater proliferating index compared to saline	Results not statistically significant
Tasdemir *et al.*, 2016[45]	Effect of ozone on the first week healing period of de-epithelialized gingival graft	*In vitro*	Ozone therapy significantly improved the blood circulation, less post-operative pain and improved quality of life	Nil

PDT: Photodynamic therapy, CHX: Chlorhexidine

suspension and root canal biofilm model was evaluated. Ozone gas and water, hypochlorite, and CHX were effective in completely eliminating suspended organisms, but lower concentration of ozonated water and peroxide was least effective. Total elimination of organisms in the biofilm was achieved after exposing them to higher concentration of ozone gas or hypochlorite for a minute or using a lower concentration ($4g/m^{-3}$) of ozone gas for at least 2.5 min, but aqueous ozone (20 μg/l) and 2% CHX almost eliminated the organisms in the biofilm. Thus, ozone efficacy was considered to be dependent on time, strain, and concentration for it to be effective against the organisms in suspension and biofilm.[47] The effect of ozone has been synergistic when used in combination with other agents to disinfect root canals. Sodium hypochlorite, 2% CHX and ozone gas individually had no efficacy against *Enterococcus faecalis* and *C. albicans* in infected canals; but a combination of 2% CHX irrigation followed by a 24s exposure to ozone gas completely eliminated them and this synergistic combination can be used in the treatment of infected root canals.[48]

However, few *in vitro* studies on the efficacy of ozone as root canal disinfectant are inconsistent. An *in vitro* study assessed the effect of ozonated water, gaseous ozone and 2.5% hypochlorite in inactivating *E. faecalis*, but none was

effective after a 20 min contact period;[49] Hems *et al*. found hypochlorite to possess superior cidal activity compared to ozonated water against *E. faecalis* in broth and culture.[50] Ozonated water when combined with sonication exhibited similar antimicrobial activity as that of 2.5% sodium hypochlorite irrigant and also found to be less cytotoxic against cultured fibroblast cells.[51] In a recent study, gaseous ozone was found to be less effective in reducing *E. faecalis* as compared to hypochlorite in an organized biofilm and was recommended to be used as an adjuvant in canal irrigation when hypochlorite is contraindicated.[52] The conclusion from each study toward the use of ozone in endodontics is summarized in Table 3.

Ozone on dentin hypersensitivity

Dentin hypersensitivity post-surgery was treated with ozonized oil or in combination with a calcium sodium phosphosilicate mineral wash. Following therapy, ozone alone was not effective, but in combination with mineral wash was effective in reducing dentinal hypersensitivity.[53] Ozone is also used in combination with other remineralizing agents (fluoride, CPP-ACP, and CPP-ACP+ Fluoride) to treat hypersensitivity in molar incisor hypomineralization (MIH). CPP-ACP is proven to be effective in the treatment of MIH, and ozone prolonged the action of CPP-ACP.[54] Ozone, in combination with a fluoride dentifrice, enhances tubular occlusion of dentin compared to a combination with oxalates and can be considered an effective adjunct in reducing hypersensitivity.[55] However, an evidence report following critical evaluation of a placebo-controlled triple-blind trial stated ozone has no effect on tooth hypersensitivity.[56]

Ozone in oral surgery

The use of ozone to prevent dry socket was investigated among 30 patients requiring bilateral surgical extraction of impacted lower third molars. Subjects were exposed to either intra-alveolar ozone for 12s or saline irrigation and evaluated at 48 h post-extraction and after 1 week. Ozone therapy following extraction significantly reduced the incidence (3.3%) of dry socket compared to controls (16.7%). Hence, ozone can reduce the incidence of dry socket and improve healing following surgical removal of third molars.[57] Application of ozone in combination with antibiotic therapy over a 15 day period was used to treat osteoradionecrosis of jaw following bisphosphonate treatment for multiple myeloma. Out of the twelve treated, eight had complete resolution and four had partial resolution,[58] ozone is also effective than low lever laser therapy in the treatment of oral lichen planus.[59]

Table 3: Summary of the studies on the effect of ozone in endodontics.

Author, Year	Objective	Type of study	Conclusion supporting the use of ozone	
			Positive	Negative
Kist *et al.*, 2016[46]	Ability of ozone and sodium hypochlorite/CHX irrigation to treat apical periodontitis	*In vivo*	Ozone gas was as effective as hypochlorite/CHX in reducing the bacterial levels in the canal	Nil
Huth *et al.*, 2009[47]	Effect of ozone gas/water on enteropathogens in a biofilm	*In vitro*	High concentration of ozone gas and water were effective against the tested endo pathogens in suspension as well as biofilm.	Nil
Noites *et al.*, 2014[48]	Irrigation with hypochlorite, CHX or ozone alone or in combination against *E. faecalis* and *Candida albicans*	*In vitro*	2% CHX rinse followed by 24s exposure to ozone gas completely eliminated these organisms.	Ozone therapy alone was not effective against these organisms.
Estrela *et al.*, 2007[49]	Ant- microbial efficacy of ozone gas, water, CHX, and hypochlorite in root canals.	*In vitro*	Nil	Even application of ozone gas for 20 min was not effective against *E. faecalis*
Hems *et al.*, 2005[50]	Efficacy of ozone to kill *E. faecalis* in broth and biofilm	*In vitro*	Effective against *E. faecalis* in planktonic/suspension	Antibacterial not as that of hypochlorite against *E. faecalis*
Nagayoshi *et al.*, 2004[51]	Antimicrobial activity of ozone against *Streptococcus mutans* and *E. faecalis*	*In vitro*	Ozonated water under sonication was as effective as 2.5% hypochlorite.	Nil
Boch *et al.*, 2015[52]	Antimicrobial activity of gaseous ozone on *E. faecalis* in a biofilm	*In vitro*	Ozone effective against *E. faecalis* even in a biofilm.	Antimicrobial activity is less as compared to hypochlorite; hence, it can be used as an adjunct in endodontic treatment.

E. faecalis: Enterococcus faecalis, CHX: Chlorhexidine

Ozone in prosthodontics

One of the most common problems associated with denture use is stomatitis caused by *C. albicans*. Three studies were identified which evaluated the efficacy of ozone either in gaseous or aqueous form against *C. albicans* in denture. Ozone gas was found to be much effective than aqueous form to disinfect dentures,[60] but ozonated water immersion is also considered effective to reduce *C. albicans* in denture plates.[61] 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.[62]

Ozone toxicity

Ozone is a strong oxidizing agent and when inhaled is extremely toxic to the bronchio-pulmonary system. It can cause sore throat, dryness of mouth, coughing, potentiate asthma, and lung damage when inhaled.[63] It can also prove fatal when exposed to a concentration of 0.3 ppm for 15 min or 0.06 ppm, 8 h a day for 5 days.[64] Hence, ozone has no safety threshold as it is a toxic gas and can affect the respiratory system even at 120 ppb. Ozi-cure™ ozone delivery system is considered unsafe for dental use since the concentration of ozone surrounding the exposure was above the recommended levels; however, Healozone™ ozone delivery system was found to be safe.[65] Considering the risk involved, ozone water is less cytotoxic compared to gaseous ozone and other antimicrobials toward oral epithelial cells and gingival fibroblasts.[66]

CONCLUSION

The use of ozone to treat oral and dental diseases, indeed, is a paradigm shift in clinical practice. However, the effective use of ozone in routine dental practice is not yet universally accepted due to lack of adequate knowledge, training, and the conflicting evidence in literature. Although the result of the present literature review confirmed the absence of high-quality evidence to support the reported use of ozone in various specialties of dentistry, the results of existing studies are very encouraging and are putting ozone in the map of all-in-one and must have tools in dentistry. The previous reports were based on *in vitro* studies and few clinical trials with methodological flaws, smaller duration of follow-up and fewer subjects. Analyses in the majority of the involved studies were performed at the lesion level, which lacks sufficient validity. Thus, well-controlled double/triple-blind randomized trials, on larger sample, with sufficient follow-up period, standardized measurements and well-established analysis, are needed to establish ozone therapy as a standard treatment modality in dental practice.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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How to cite this article: Srinivasan SR, Amaechi BT. Ozone: A paradigm shift in dental therapy. J Global Oral Health 2019;2(1):68-77.