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Ozone applications in dentistry: A review

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Abstract

Ozone (O_3) therapy has been applied in medicine and dentistry for many years and has become increasingly widespread. Ozone, composed of three oxygen atoms (O_3), is a strong antioxidant and a highly effective antimicrobial agent. Ozone gas has high oxidizing properties and exhibits a 1.5-fold higher antimicrobial effect than chloride. Its use has become popular in many fields of dentistry in recent years, owing to its various properties. It is categorized as one of the non-invasive, atraumatic, protective, and preventive treatment modalities that have been improved by modern dentistry, and its acceptability among patients has increased as a result. Ozone is an antimicrobial, analgesic, and biosynthetic agent that stimulates the immune system, enhances blood circulation capacity, and positively affects oxygen transport mechanisms. It influences both cellular and humoral immunity. All three forms of ozone (gaseous, oil, and solution) can be used in dentistry. It is indicated for the treatment of approximately 300 different pathological conditions. Ozone is used in endodontics (irrigation solution, intracanal medicament, abscess cases, disinfection), periodontology (gingivitis, periodontitis, periimplantitis, surgical injuries, prophylaxis), oral pathology (stomatitis, aphthous ulceration, candidiasis, herpes lesions), oral, dental, and jaw surgery (implantation, reimplantation, simple-to-complicated tooth extraction, homeostasis, wound healing, temporomandibular joint (TMJ) surgery, osteonecrosis cases), prosthetic dental treatment (disinfection of fixed and removable prostheses), restorative dental treatment (caries lesions, dentine hypersensitivity, cracked tooth, bleaching), orthodontics (remineralization and prophylaxis of white spot lesions), pedodontics (caries lesions, root canal treatment, positive psychological impact, short treatment duration), and sterilization of dental instruments and units. This review aimed to describe the usage fields and effects of ozone in dental applications, provide insights into clinical practices in other fields of dentistry, and introduce newly conducted in vitro and in vivo studies.

Keywords: Ozone, ozone therapy, dentistry, disinfection

1. Introduction

In 1785, Van Marum discovered an unusual odor when electric sparks were generated near a static electric machine and named it the “odor of electricity” (1). In 1840, the German chemist Christian Friedrich Schönbein discovered the presence of this odor and named it “ozein”, which means "to smell" in Greek (1). In 1857, the first ozone generator was developed by Werner von Siemens in Germany (2). The first medical application of ozone was performed by Dr. Lender in 1870 to clear the blood in test tubes. Thereafter, it became commonly used in America and Europe (3). It was used as a therapeutic agent for diphtheria in 1881. It was used in the treatment of gangrene and wounds of the soldiers in the I. and II. World Wars (4). In 1974, Wolff invented the mechanism by which blood directly contacts an oxygen-ozone gaseous mixture (ozonated autohemotherapy) (5). The use of ozone was legalized in the USA at the beginning of the 20th century (4). The dentist Dr. Fisch was the first physician who started to regularly use ozone in dental practice in 1930. In 2001, Dr. Sieg Fried wrote a book on the use of ozone in medicine (4). Ozone has been used in different fields of medicine and dentistry for almost a hundred years (6). Currently, it is administered in 16 countries as a treatment method with validated acceptability (7).

It is used in ophthalmology, viral diseases, bacterial and fungal infections, age-related degeneration, orthopedics, dermatology, hematology, and neurodegenerative diseases, and further studies on its use are ongoing (8).

2. Chemical properties

Ozone is a natural compound composed of three oxygen atoms (9). Its molecular weight is 47.98 g/mol. It is an unstable molecule because one oxygen atom continually detaches/attaches from/to two oxygen molecules (Fig. 1). Therefore, it should be used immediately because of this property.

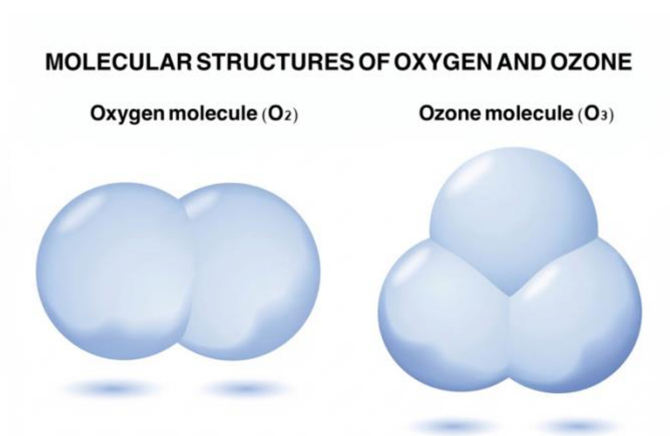

Figure 1. Representative drawings of oxygen and ozone molecules (10).

The half-life of ozone is 40 min at 20°C, whereas it is approximately 140 min at 0°C (2, 3). Ozone has a 1.6-fold higher density and a 10-fold higher water solubility than oxygen (49 mL in 100 mL water at 0°C (3).

Approximately 90% of atmospheric ozone gas is found in the stratosphere, located 20–50 km above the ground. The remaining amount is found in the troposphere, the part of the atmosphere closest to the ground (1). Ozone gas, which has a strong odor and blue color, absorbs harmful ultraviolet radiation in the light spectrum. Thus, it protects living organisms from UVA and UVB radiation (Fig. 2) (11).

Ozone tends to react with many organic and inorganic molecules, resulting in the formation of free oxygen radicals. Free oxygen radicals formed within physiological limits play a role in signal transduction pathways and immunity (12).

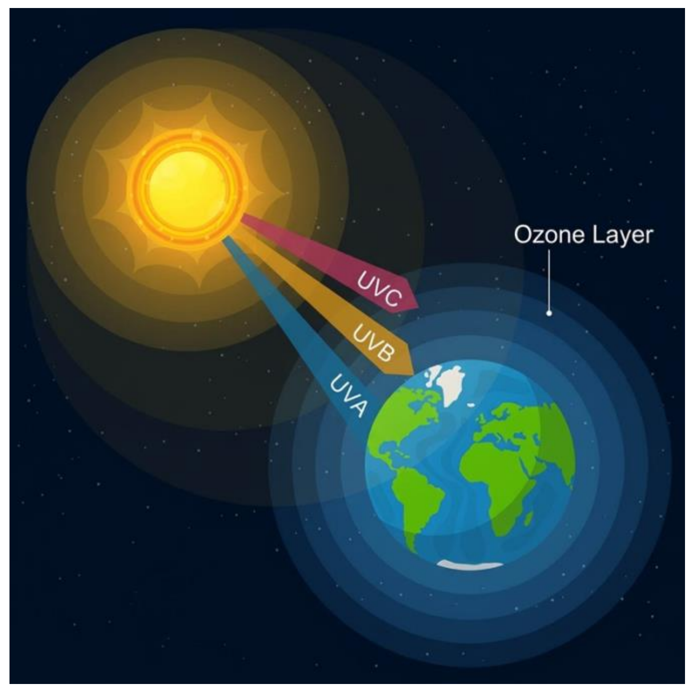

Figure 2. UVA radiation from the sun almost reaches the Earth’s surface. A major portion of UVB radiation is absorbed by the ozone layer. UVC radiation does not reach the Earth (10).

3. Biological properties and antimicrobial effects

Ozone has antimicrobial, immunostimulatory, blood-circulation-enhancing, biosynthetic, analgesic, detoxification, and bioenergetic effects on the human body (8). Ozone is an effective and reliable antimicrobial agent against bacteria, fungi, protozoa, and viruses (9). Ozone exerts its effects against microorganisms via neutralization, destruction of the cell wall, or inhibition of reproduction (Fig. 3) (9, 13).

Figure 3. Benefits and effects of ozone therapy.

Consequently, ozone penetrates cells because of its increased membrane permeability, impairs enzyme activity, and leads to cellular dysfunction. This causes microbial death (13, 14). Ozone has been reported to be effective in bacterial inactivation even at a concentration of 0.1 ppm. It particularly affects fungi during the budding stage, inhibiting their growth. It affects viruses by damaging the viral capsid (15).

Another effect of ozone occurs on the oxygen metabolism. It elevates red blood cell count by stimulating the production of 2,3-diphosphoglycerate. Consequently, it increases glycolysis. Ozone increases the oxidative carboxylation of pyruvate in the Krebs cycle and aids in the oxidation of NADH and cytochrome C (16). It also stimulates the production of free radical scavengers (glutathione peroxidase, catalase, and superoxide dismutase) (17). Ozone enhances cellular and humoral immunity by promoting macrophage activation and cytokine release (18). In leukocytes, it induces the production of interferons (IFN-α, IFN-ß, IFN-γ), interleukins (IL-1ß, IL-2, IL-6, IL-8), Tumor Necrosis Factor (TNF-α), and growth factors (such as Platelet-Derived Growth Factor [PDGF] and Transforming Growth Factor Beta 1 [TGF-ß1]) (19, 20).

4. Toxicity

Inhalation of ozone gas may exert toxic effects on the human body, particularly on the organs of the respiratory system. Several complications may occur, such as euphoria, upper respiratory tract irritation, nausea, vomiting, shortness of breath, circulatory disorders, and cardiac problems (21, 22). Ozone may be administered in the oral cavity at a maximum concentration of 0.01 ppm. The patient should be transferred to a lying position if intoxication develops during vitamin E and N-acetylcysteine therapy, and treatment of vitamin E and N-acetylcysteine should be administered (23). Ozone is contraindicated in pregnant patients and those with hyperthyroidism, advanced degree anemia, severe myasthenia, glucose-6-phosphate dehydrogenase deficiency, acute alcohol intoxication, myocardial infarction, and ozone allergy. Ozone gas has strong oxidizing properties; therefore, all materials in contact with it should be ozone-resistant, such as glass, silicone, and Teflon (21).

5. Ozone production

Ozone is produced naturally in two ways. The first method of ozone production occurs via electric sparks following weather events. An oxygen molecule is converted into two oxygen atoms via electrical discharge. Each oxygen atom combines with a natural oxygen molecule to form ozone (Fig. 4) (23).

Second, ultraviolet (UV) rays emitted by the sun interact with oxygen in the stratosphere due to electrical sparks. Therefore, the stratosphere contains the greatest amount of absorbed UV radiation and the greatest amount of ozone (23).

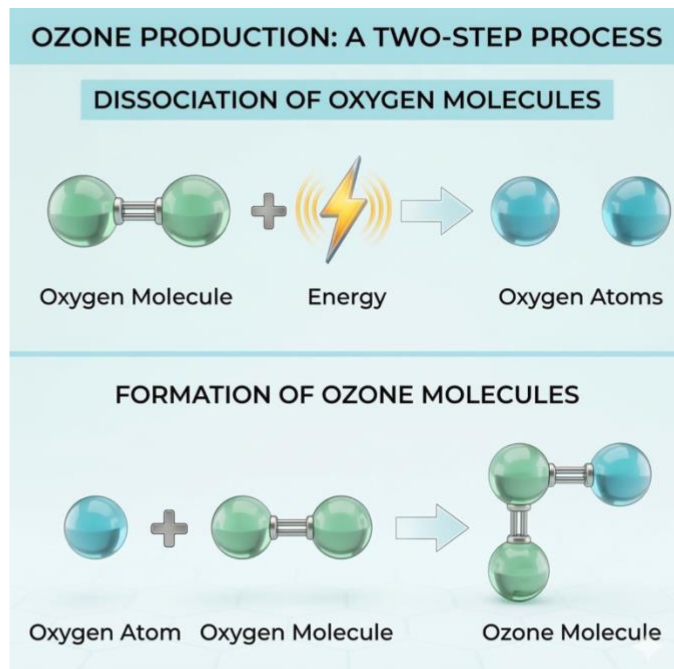

Figure 4. Ozone (O_3) is formed by the combination of an oxygen atom and an oxygen molecule.

Ozone can be applied in gaseous, aqueous, or oil forms.

Ozone gas: It can be produced using either an open- or closed-suction system. The closed suction system is most commonly used because toxication may develop during the operation of an open system (24). Oxygen is converted to ozone in this system. Ozone is delivered to a hand instrument, including a silicone cup. Ozone cannot escape from the instrument because of its fit to the tooth. Ozone is collected back into the instrument after application and converted to oxygen (4, 25). Ozone in gaseous form can be generated using various devices. These devices can operate using four different mechanisms (23, 26).

I. **Ultraviolet system:** This system produces ozone at low concentrations via the emission of UV light at 185 nm (23). It is used for aesthetic purposes, saunas, and air purification (11, 27, 28).

II. **Corona Discharge System:** It provides ozone production at high concentrations. Oxygen passing through a corona discharge system via electrical rays is converted into ozone (26). It is easy to use. Ozone production can be controlled. It is the most commonly used system in medicine and dentistry (23).

III. **Cold plasma system:** It is used for the purification of air and water. It is composed of a unit containing a halogenated glass cathode tube that provides high electricity by inducing an ionic current. There is a second unit around this tube that is not directly exposed to the current. Ozone is produced in the plasma placed within the tube (23, 26).

IV. **Electromagnetic system:** It comprises a glass tube in which an oxygen current passes through and a system that includes metal cables passing through and around it. An electromagnetic field is generated by a high-voltage source (26).

6. Dental ozone generators

HealOzone: It has been developed by CurOzone USA Inc. (CurOzone USA Inc., Ontario, Canada; distributed by KaVo, Biberach, Germany). It is used in dental practices. It contains a closed-circuit system (Fig. 5).

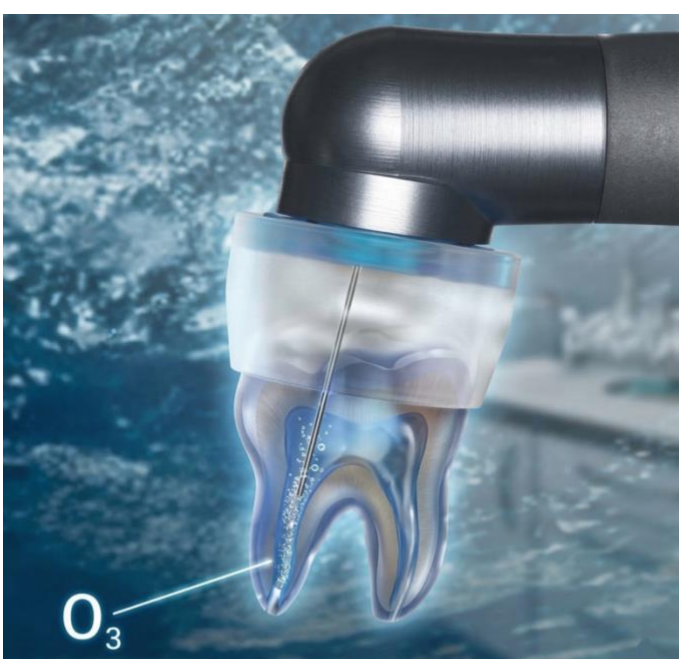

Figure 5. Use of HealOzone for disinfection in the root canals (29).

The effect of excess gas is reduced by ions when subjected to an emulsion (30). The device contains an air filter, a vacuum pump, an ozone generator, a leakage-proof silicone cup, and a hand instrument covered with a hose (31). Five different sizes of silicone cups are provided to fit teeth with different shapes and sizes (Fig. 6).

A minimum application time of 20 seconds is recommended. However, the company recommends a 60-second application for each canal in the standard treatment.

Figure 6. Ozone can be easily administered to many patients (32).

After ozone application, remineralizing agents (fluoride, calcium, zinc, phosphate, and xylitol) should be applied to the tooth surface (31). The company recommends an application time of 3 min and a resting time of 7 min. The main components of ozone devices are the oxygen supply, air supply, air dryer, differential pressure sensor, ozone generator, handpiece, tube, moisture trap, ozone neutralizer, and vacuum pump.

Prozone: This is preferred in endodontics and periodontology because of its tissue-compatible dosing features. It is easy to use (33). Successful results have been obtained, particularly in the treatment of peri-implantitis cases and endodontic infections. Prozone (W&H Dentalwerk, Bürmoos, Austria) provides a hygienic environment in applying ozone by directing it to the pockets owing to replaceable plastic attachments (Perio tips or Endo tips) (Fig. 7) (34).

Figure 7. Prozone device (35).

Ozonytron-X, -XL, -XO, -XP/OZ, and -XPO: The plasma therapy devices of the Ozonytron product line are designed for dentistry practice (Figs. 8, 9, 10, 11, and 12). They contribute to long-term healing. Specifically, plasma treatment is performed with plasma electrodes, plasma tips, and/or plasma tooth pieces. For instance, the essential device, Ozonytron-X, allows treatment only with plasma electrodes, whereas the All-in-One Ozonytron-XPO device and the Ozonytron-XP/OZ device support the use of all applicators. It can be used in the treatment of periodontal pockets, endodontic therapies, and bleaching.

Figure 8. Ozonytron-X device (36).

The Ozonytron-XL (two-in-one ozone therapy system) provides a second internal ozone gas generator in addition to plasma probes. It has a continuous insufflation pistol that can produce ozone at concentrations up to 66,000 ppm for root canal and sulcus operations (Fig. 9).

Figure 9. Ozonytron-XL device (36).

Figure 10. Ozonytron-XO device (36).

The Ozonytron-XP (multifunctional programmable digital therapy system) includes updatable ready-to-use software for dermatology, wound care, gynecology, and dentistry. It can be used without a power supply. Full-jaw bite plates are available for dental applications. The Ozonytron-OZ (vacuum ozone insufflation unit) provides a full-jaw bite plate system specific for dentistry. Bleaching can be performed in 15 min.

The efficacy of Prozone, Ozonytron-XP, and Ozonytron-OZ against *S. mutans* and *L. acidophilus* was compared in a study. Prozone demonstrated the lowest efficacy, whereas Ozonytron-XP and Ozonytron-OZ were found to be more successful. Ozonytron-OZ exhibited a treatment success rate of 99% for both species when applied for 180 seconds. Whereas Ozonytron-XP exhibited a treatment success rate over 95% for both species in a shorter time (30 seconds) (37).

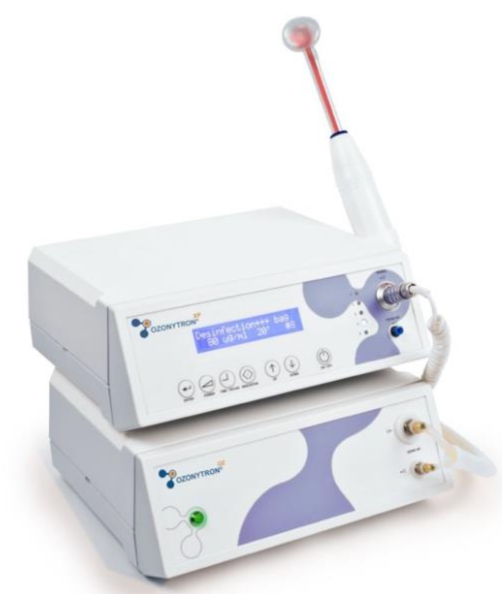

Figure 11. Ozonytron-XP/OZ Device (36).

Figure 12. Ozonytron-XPO device and mouthpiece (36).

Ozonated water: It is known to be effective against Gram-positive, Gram-negative, and plaque bacteria (38). Although its efficacy is lower than that of gaseous ozone, it is recommended as a safe treatment under conditions where gaseous ozone is inappropriate (13, 24). It can also be used as a mouthwash for halitosis and periodontal diseases (25). Additionally, it is preferred for its hemostatic effect, wound-healing properties, and cost-effectiveness (24, 38, 39).

Ozonated oil: It is obtained from herbal essences containing pure oxygen and ozone. A chemical reaction forms ozonides as the final product (25). It is used externally (4). Its use is recommended for bacterial and fungal infections owing to its antibacterial and antifungal efficacy. It is commercially available under the names Oleozone and Bioperoxoil in the market (Fig. 13) (30).

Figure 13. Ozonated oil (40).

7. Use of ozone in dental applications

7.1. Use in endodontics

The importance of irrigation agents and antimicrobials in endodontics cannot be debated. Ozone is recommended as an alternative irrigant owing to its cytotoxicity, unpleasant taste and odor, allergenic potential, and leading to unexpected consequences, such as the corrosive effect of sodium hypochlorite (NaOCl), although it is an excellent irrigant agent (41). Another commonly used irrigant is chlorhexidine. Chlorhexidine does not have a tissue-dissolving property. It cannot remove the smear layer. In addition, it may cause desquamation and coloration of the oral mucosa (42, 43). Therefore, the use of ozone in endodontics as an antimicrobial agent has been investigated. Ozone affects and removes the smear layer and widens dentin tubule diameters by opening them (4). Ozone is used as a disinfection agent, irrigation solution, and intracanal medicament in endodontics. It should also be noted that ozone has a postoperative pain-reducing effect (44). All three forms of ozone (gaseous, oil, and aqueous) can be used in dentistry (45, 46). Its gaseous form shows antimicrobial effects.

A significant reduction in the population of pathogenic microorganisms was observed when gaseous circulation was applied for 2–3 min at a flow rate of 0.5-1 L/min and a volume of 5 g/mL (47). The aqueous form of ozone provides tissue regeneration and bone healing when used as an irrigation agent (4). Nagayoshi et al. used ozonated water and 2.5% sodium hypochlorite against *E. faecalis* and *S. mutans* in a study conducted on extracted bovine teeth. They found that antimicrobial efficacy was similar; however, ozonated water was less cytotoxic (38). Studies have demonstrated that ozone is effective against many genera, such as *Mycobacterium, Staphylococcus, Pseudomonas, Enterococcus, Escherichia coli, Peptostreptococcus, and Candida* (48). Its oil form can be used as an intracanal medicament in infected nephrotic ducts (4).

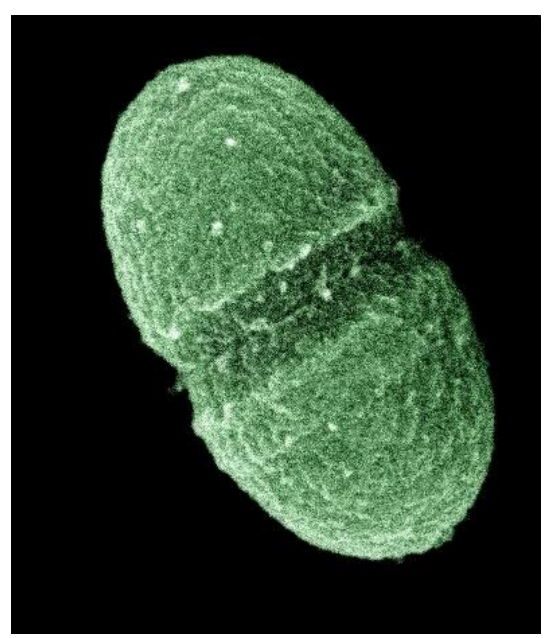

Figure 14. Microscopic image of *E. faecalis* (49).

Hems et al. evaluated the efficacy of ozone against *E. faecalis* and used both gaseous and aqueous ozone. As a consequence, aqueous ozone began to show an antibacterial effect against planktonic *E. faecalis* after 240 seconds. However, it has been reported that the efficacy of aqueous ozone against *E. faecalis* in the biofilm was low (50).

Silveira et al. conducted an animal study on extracted infected canine teeth and found that ozonated oil was successful at a rate of 77% when used as an intracanal medicament. The treatment success rate was 74% in the specimens treated with $Ca(OH)_2$ in the other study group (48).

In accordance with results from other studies, the antibacterial efficacy of ozone gas was higher than that of KTP and Er: YAG lasers but lower than that of NaOCl. Ozone is considered more effective. Ozone is considered a more efficient irrigation agent for canal disinfection when applied in combination with other irrigation agents during root canal treatment than when applied alone (51-53). It has also been reported that ozone gas can be safely administered under conditions where NaOCl is not indicated (53). Because ozone provides the most effective results in the presence of a low amount of organic debris, its use is recommended prior to the final stage at the end of irrigation and preparation procedures (54).

Estrela et al. compared the antimicrobial efficacy of ozonated water, ozonated gas, 2.5% NaOCl, and 2% chlorhexidine in human root canals in their study. Consequently, none of the agents was effective against *E. faecalis* after 20 min of contact (55).

Kaptan et al. found no significant difference between the teeth treated concomitantly with 2% NaOCl and ozone gas and the teeth treated with 5.25% NaOCl and $Ca(OH)_2$ without ozone gas. In addition, the *E. faecalis* biofilm was eradicated in the group treated with a combination of 2% NaOCl, $Ca(OH)_2$, and ozone gas.

Another conclusion of this study was that treatment can be achieved with a lower cytotoxic effect owing to repeated ozone gas application, allowing the use of low doses of NaOCl (56).

Rossi-Fedele et al. have examined the pulp tissue dissolution in NaOCl and ozone gas. The results revealed that the pulp tissue dissolved only in the groups applied with NaOCl. In addition, a 2-fold faster dissolution rate was reported with the combined application of NaOCl and ozone gas compared with NaOCl alone (57).

In a study by Reddy et al., ozonated sesame oil was more effective against C. albicans than $Ca(OH)_2$ when used as an intracanal medicament. The combined use of both irrigants revealed the lowest effect (58).

Another contribution of ozone to endodontic treatments is its novel finding that it increases the shear bond strength of root canal filling materials. A previous study reported that ozone increased adhesion to dentin and had a positive effect on the bonding of both AH Plus and EZ-Fill, while increasing the bonding of AH Plus to a greater extent (59).

Ozonated oil is recommended as an alternative to direct pulp capping agents. Ozone causes less irritation (60). Postoperative pain may result from tissue irritation that can develop at any time during root canal therapy. The subject of decreasing postoperative pain by reducing the mediators causing pain in the tissue and increasing local blood circulation was also evaluated using ozone treatment (61).

7.2. Use in restorative dentistry

Owing to its atraumatic and non-invasive nature for dental applications, ozone has gained popularity in restorative dentistry (23). Ozone can be used in the following fields of restorative dentistry (8):

- The prophylaxis of caries and treatment of the caries at baseline
- The cases of hypersensitive dentin
- Cracked tooth syndrome
- Bleaching treatment

It has been reported that, as a result of in vitro studies involving ozone treatment, the microbial count significantly decreased in the lesions of cases with pit-fissure and root caries at baseline (39, 62-64). Ozone showed the highest effect on the smallest and non-cavitated caries, whereas it exhibited a lower effect on caries near the gingival level compared with other regions (62). Ozone also contributes to caries remineralization (65). It achieves this by changing the acidic flora formed due to bacterial activity to a normal pH level. Ozone oxidizes pyruvic acid to acetate and carbon dioxide. It removes proteins from the caries lesion and facilitates the diffusion of calcium, fluoride, and phosphate ions into the lesion (66, 67).

Holmes examined the biomolecular structure of caries lesions before and after ozone treatment and reported that acids produced by bacteria shifted to a more alkaline state as a result of oxidation with ozone, thereby forming a suitable environment for remineralization, and he has evaluated the effect of ozone on root surface caries in a randomized clinical trial and observed that caries surfaces were hardened in 100% of the patients by testing the surface hardness in the cases at the end of the 12th month (68).

Baysan et al. applied an ozonated solution for 10 and 20 seconds in their in vitro study and examined the populations of *S. mutans* and *S. sobrinus*. The results revealed that the bacterial count dropped below 1% after 10 sec, whereas bacteria were removed at a rate of 99% after the 20-second treatment. This condition is defined as the conversion of ozone's disinfecting property into a sterilizing property (69). The application of ozone for 40 sec and the use of agents that support additional remineralization could stop the progression of root surface caries without the formation of cavitation and substantially remove S. mutans (67). It has been reported that a 60-second application completely removed L. casei and *A. naeslundi* in addition to *S. mutans* (70). Another study reported that the most successful antibacterial efficacy of ozone could be achieved with an 80-second application (64).

However, Zaura et al. reported in their in vitro study that ozone could not induce remineralization in demineralized dentin (71).

Another innovative approach in restorative dentistry is the combined use of ART and ozone. The advantages of the combined use of these two techniques can be summarized as follows (72):

- Chair time is shorter compared with the conventional caries removal technique.
- Pulp perforation risk is lower than that of the conventional caries removal technique.
- Post-treatment period is asymptomatic and aesthetically more acceptable.
- This is more psychologically acceptable.

Another advantage of ozone is that it can help overcome anxiety and fear, particularly in patients and children with anxiety, because it is an atraumatic and relatively easily acceptable treatment method (8, 73, 74).

It should be applied in combination with restorative dental treatment for localized caries lesions with cavitation formation. In addition, patients should be instructed to focus on their diet to support oral hygiene and reduce carcinogenicity (4).

Another impact of ozone is the oxidation of sulfur compounds into sulfides, which affects root-surface caries and suppresses oral malodor.

Ozone is recommended as a simple and effective treatment method for patients at risk of medical complications and for the elderly (75, 76).

Ozone can be administered based on lesion severity and used in conjunction with Diagnodent to assess caries risk in the early stages.

Table 1. The example of the case-treatment procedure in the study (77).

Caries Severity Index	Diagnodent reading	Clinical diagnosis	Radiographic interpretation	Treatment plan
1	<10	May be a sound tooth	Normal	10 sec O_3/Seal fissures if indicated with GIC or flowable composite
2	10-16	White spot lesions	Normal (lesion not seen on x-rays)	40 sec O_3 and remineralization therapy. Air abrasion and/or seal fissures
3	20-24	Carious lesion at EDJ	May not be visible on x-rays	Air abrasion/etch/40 sec O_3 therapy and restoration with GIC/composite
4	25-29	Caries involving 1-2mm of dentin	May/may not be visible on x-rays	Remove infected dentin, leave affected dentin. Etching—60 sec O_3 therapy and restore with GIC/composite/light cure GIC
5	>30	Caries involving >2 mm of dentin	Mostly visible on x-rays	Remove infected dentin to leave affected dentin, ozone exposure for 60 sec. depending on remaining dentin thickness, liner/base, and restoration.
6	>99	Deep carious lesion, may/may not involve pulp.	Visible on x-rays and assessing pulp vitality	If vital, indirect pulp capping is advised. Expose O_3 for 120 sec and seal with GIC. After 1 month, reassess, and if remineralization is evident, it can be restored with a permanent restoration.
Recommended ozone concentration: 3.5-5 g/mL and flow rate: 0.5-1 L/min.				

After the application of ozone has become widespread in the field of restorative dentistry, its effects on restorative materials have attracted attention. Studies on this topic have shown that ozone has no negative effect on the bonding of restorative materials (78, 79). The physical and mechanical properties of dentin and enamel are not affected by 60-second and 40-second ozone treatments, respectively (76, 80). However, a 2-min ozone application causes roughness on the enamel (81). Studies have demonstrated that the use of ozone as a cavity disinfectant has no disadvantages.

Çehreli et al. reported that the ozone group had lower microleakage and that sealants penetrated better, as observed in the SEM images (82). To date, no definitive conclusion has been drawn regarding the effect of ozone on microleakage. Some studies have shown that ozone has no negative effect on the penetration and microleakage of fissure sealants (80, 81, 83) and that ozone increases enamel microhardness.

Ozone can also be used in bleaching treatments because it is an oxidizing agent. It is safe for use because it is fast, effective, easy to use, and harmless (84-86).

In addition, Tessier suggested that ozone can also be used for internal colorations as a result of his study (87). In the bleaching technique using ozone gas for external colorations, all jaw arches can be processed with lingual surfaces. This is achieved using a spoon-shaped end applicator (Fig. 15) (88).

Figure 15. Ozonytron device and spoon applicator (88).

Ozone can be used in cases with hypersensitive dentin. Its action mechanism on a hypersensitive tooth occurs by penetration through open tubules of the hypersensitive and allowing the minerals that will come through saliva and remineralizing agents to enter the tooth (8). According to the results of a study, pain decreased at a rate of 55% after ozone treatment in cases of hypersensitive dentin (89).

Cracked tooth syndrome is characterized by cracks extending into the dentin layer of a vital posterior tooth, potentially reaching the pulp. Ozone exhibits its effect by the same action mechanism encountered in the cases with hypersensitive dentin (Fig. 16) (26, 90). It reduces the symptoms of cracked tooth syndrome and yields better treatment outcomes when used in combination with fluoride (91).

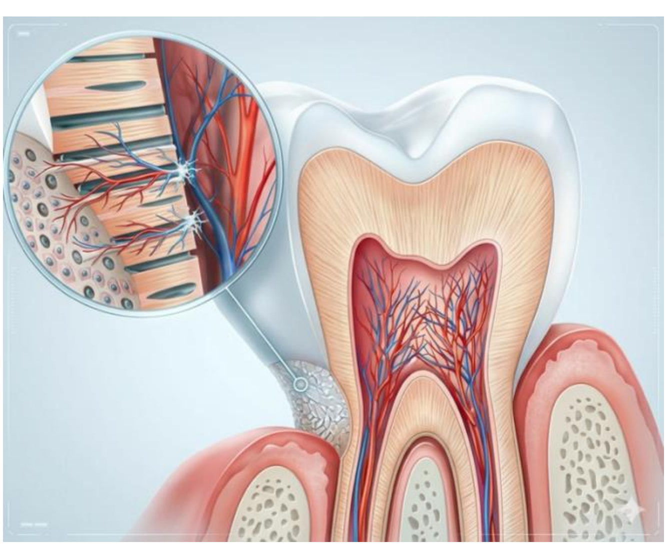

Figure 16. The effect of ozone on penetrating the open tubules in hypersensitive teeth (90).

7.3. Use in pediatric dentistry

The application of ozone in pedodontics is not different from the prescription indications of the other branches of dentistry. It suggests advantages, such as ease of use, tolerability, rapid action mechanism, and a promising, successful treatment process. It is a facilitating alternative for both physicians and patients (15). Dahnhardt et al. reported in their study on pediatric anxiety patients that anxiety and fears of children decreased at a rate of 93% after caries treatment with ozone was introduced to practice (74).

Meanwhile, the use of ozonated water is indicated during replantation in frequently traumatized cases, particularly in avulsed teeth in children. It has high biocompatibility with periodontal, epithelial, and gingival fibroblast cells and causes no harm to these cells (92, 93).

7.4. Use in prosthetic dentistry

Ozone is commonly used as a disinfecting agent in prosthetic tooth treatment. Prosthetic stomatitis, which is often observed in patients who use prostheses, is a condition caused by C. albicans localized in the microbial dental plaque. Ozonated oil, ozonated water, or ozone gas can be used to control plaque accumulation (94, 95). Ozonated oil can be applied directly to the tissue or topically to the prosthesis (67).

Some studies have shown that ozonated gas is more effective than ozonated water for disinfecting prostheses (67). Arita et al. reported that ultrasonically activated ozonated water decreases the count of C. albicans and can be used to clean prostheses (96). Although ozone gas is preferred for disinfection of prostheses in clinical environments, ozonated water can be recommended as a home-type disinfectant. For this purpose, it is recommended that patients remove their prostheses and soak them in water for 10 minutes.

Patients should be warned to rinse the prostheses before reuse (97, 98). Ozonated water is recommended as a surface disinfectant in implantology, in addition to amino alcohols (23). In addition to its decontamination effect, it also contributes to bone regeneration, prevents infection, and facilitates recovery of the implant socket (99). Ozone, used in cases with hypersensitive dentin, is recommended for the same purpose to reduce hypersensitivity prior to cementation in prepared teeth (89).

7.5. Use in oral, dental, and jaw surgery

Ozone can be used in many surgical conditions. There is a broad range of applications, from simple tooth extractions to serious jaw infections. It positively affects wound healing (100). It is recommended for disinfecting the socket after tooth extraction (65). It can be used for disinfection of the related area and tooth root during replantation, and for treatment of soft tissue lesions (herpes simplex, aphthous ulceration) (34, 101). Patients with herpes labialis at the baseline stage underwent ozone therapy for 40–60 seconds and were followed up. It was observed that pain significantly decreased and the lesion healed in 3 days in the patients (5). Additionally, it decreased the incidence of dry socket and postoperative pain (67). Ozonated oil has been used to treat the related area in cases of alveolitis (102). The efficacy of ozonated oil and antibiotics was compared in a study conducted on patients with alveolitis. It was observed that the patients treated with ozonated oil recovered more quickly (23).

Ozone application provides regeneration in the soft and hard tissues of patients after implant surgery, patients with chronic osteomyelitis, and those who have used bisphosphonates. It decreases the incidence of complications, such as osteonecrosis (4, 103, 104). Oxygenation decreases due to radiotherapy in the maxilla and mandible, and the recovery of the related region may be delayed after extraction due to inadequate vascular support. Ozone can be used to support recovery in such cases (1).

Full and partial recovery were observed in eight and four of the 12 multiple myeloma patients with jaw osteonecrosis who were administered ozone for 15 days in addition to antibiotic treatment, respectively (105).

Agrillo et al. reported that tooth extraction with ozone application is a safe treatment option for patients who developed osteonecrosis following bisphosphonate use (106). Kazancıoğlu et al. evaluated the effects of ozone application on pain, swelling, and trismus following third molar surgery. They concluded that postoperative pain decreased, whereas swelling and trismus were unaffected (107). In another study, no significant difference was detected between topical chlorhexidine and ozone application in terms of wound infection and alveolitis during third molar surgery (108). Ozone may be an alternative to hyperbaric oxygen therapy owing to its strong oxidizing properties. Bacteria in contact with ozone can be recognized by granulocytes and the complement system, and the phagocytic ability of polymorphonuclear cells increases (109).

Another field of use for ozone in surgery is in TMJ arthrocentesis cases (Fig. 17). Hammuda et al. reported that ozone is a successful conservative approach as a biostimulatory and anti-inflammatory therapeutic agent for healing TMJ internal irregularities (110).

Daif has reported that the application of ozone gas neutralizes free radicals that accumulate in the TMJ and elevates cellular physiological performance by increasing ATP production, thereby providing control over disease progression and enabling repair of damaged tissues (111).

Although ozone is an effective treatment method that has achieved recovery in many patients, it can cause serious complications in certain disease processes. It is particularly applied in herniated and disc disorders, and complications such as vision loss, vertebrobasilar insufficiency, and gas embolism (112-114).

Figure 17. The use of ozone gas as a stimulant in TMJ arthrocentesis.

7.6. Use in periodontology

Microbial dental plaque and specific bacteria (such as *A. actinomycetemcomitans*, *P. gingivalis*, and *T. Forsythia*) are major factors in the development of periodontal diseases (14). The use of ozone in periodontology is predominantly based on its antimicrobial and antiseptic properties. It eradicates the microorganisms that cause gingivitis, periodontitis, and peri-implantitis and accelerates tissue healing by increasing regional blood circulation (115, 116).

Studies have evaluated the effects of ozonated water on individuals with periodontal diseases. Brauner et al. have washed the periodontal pockets daily as part of routine care and followed up with the patients. Consequently, improvements were observed in the indices of hemorrhage, plaque, and pocket liquid (117).

Figure 18. Ozone improves periodontal indices positively.

Another study was conducted on patients who received orthodontic treatment. It was observed that gingival inflammation significantly decreased in patients who applied ozonated water to the subgingival region (118). In another study, ozonated water was applied to dental plaque, and a decrease in the S. mutans count was noted (119). Ozonated water was effective in controlling both gram-positive and gram-negative bacteria, as well as the population of *Candida albicans* (14, 120). Nagayoshi et al. examined the effects of ozonated water with three different concentrations (0.5, 2, and 4 mg/mL in distilled water) on cariogenic, periodontopathogenic, and endodontopathogenic microorganisms (*S. mutans, P. gingivalis, P. endodontalis, Aggregatibacter actinomycetemcomitans*, and *C. albicans*) in both biofilms and cultures. They reported that ozonated water was highly effective against gram-positive and gram-negative bacteria. Another outcome was that gram-negative bacteria were more sensitive to ozone (38).

Ozone demonstrates an antifungal effect compared to chlorhexidine; however, it has no antiviral effect. In addition, ozone has been shown to be more effective than chlorhexidine at reducing hemorrhage, dental plaque, and gingival indices (76). Ozonated water and ozonated gas were less effective than 2% chlorhexidine and more effective than 0.2% chlorhexidine in terms of antibacterial effects. Both antibacterial agents had no effect against A. *actinomycetemcomitans* (121). In a study conducted on patients with chronic periodontitis, ozonated and distilled water were used as irrigation solutions following phase 1 periodontal treatment. The patients were invited to compare the results three months later. Significant improvements were observed in all indices in both groups, except for the gingival index. No significant difference was found between irrigation with ozonated and distilled water (122).

Ozonated water can be used as an irrigation agent to prevent infection during the extraction of infected teeth. For the same purpose, ozonated oil can be used around the sutures at the wound site (123). Ozone, which has vasodilatory properties, acts as a positive wound-healing agent in the postoperative period and reduces pain by increasing blood flow to the tissue when applied in addition to conventional therapy in grafting surgeries (124). The use of ozonated oil has been shown to improve gingival health in patients with acute necrotizing ulcerative gingivitis (15).

Finally, studies have suggested that the use of ozonated water yields the greatest reduction in bacterial count compared with conventional or surgical treatments in patients with peri-implantitis (101, 125).

7.8. Use in orthodontics

White spot lesions may form because of the bonding agent applied before orthodontic treatment or within the first 4-week period after bracket placement (Fig. 19) (126). Therefore, ozone can be used in orthodontics for the prophylaxis of enamel (15). Ghobashy et al. have conducted a study to evaluate the effect of ozonated olive oil on the external surface around the orthodontic bracket. It was found that lower decalcification of the enamel occurred with the use of ozonated olive oil (127).

Figure 19. White spot lesions that formed around the bracket.

In contrast, some studies have suggested that ozone, which has a strong oxidizing property, may have a negative impact on the polymerization of resin-based adhesives. However, Çehreli et al. showed in a study on orthodontic patients that no reduction occurred in the shear bond strength of tooth surfaces treated with ozone (128).

Other usage fields: Ozone can be used as a reliable, effective, and non-toxic method for disinfecting dental units and waterways, which pose a major risk of contamination and infection (129). Ozone decreases the live bacterial count by 65% and the unexpected biofilm layer by 57% (25, 130). The presence of fungi and bacteria in the biofilm culture, and of these microorganisms, which may be infectious, poses a risk to healthcare staff (131).

Usage of ozone gas in medicine: Ozone gas used for medical purposes is a mixture of 95% oxygen and 5% ozone gas (12). Ozone gas is used for medical purposes as follows:

- Disinfection of the wound site and infections
- Inflammatory bowel diseases
- Pulmonary diseases
- Cardiovascular diseases
- Vision diseases
- Parkinson's and Alzheimer's diseases
- Chronic osteomyelitis
- Dermatological diseases
- Sleep problems
- Tinnitus
- Migraine and dizziness attacks
- Support for cancer treatments
- Stroke treatment

Contraindications: The use of ozone is inconvenient and contraindicated in pregnancy, glucose-6-phosphate dehydrogenase (favism) deficiency, hyperthyroidism, severe anemia, severe myasthenia, acute alcohol intoxication, myocardial infarction, hemorrhage in any organ, and ozone allergy (22, 27).

8. Conclusion

Contemporary dentistry is improving daily with the introduction of novel approaches. Ozone has benefits across many fields of dentistry and medicine based on its atraumatic nature. It has well-known antimicrobial, analgesic, immunostimulatory, and biosynthetic properties. It is indicated in many fields, such as the treatment of carious lesions, root canal irrigation, post-treatment wound healing, and disinfection. In particular, its acceptability by pediatric patients increases treatment compliance.

Further randomized controlled clinical and experimental studies are required to validate its reliability and definite indications.

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