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Antimicrobial Effects of Ozone in Dentistry: Mechanisms, Clinical Applications, and Safety Considerations: A Narrative Review

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Abstract

Background: The use of ozone (O3) as an additional antimicrobial substance in dentistry is widespread; however, just because something works in the lab doesn't mean that it works on people. **Objectives:** To evaluate the modes of action, administration, clinical application, and safety of ozone in dentistry, with a clear demarcation of laboratory vs. clinical evidence. **Results:** Ozone in medicine is generated from oxygen using corona discharge and delivered as a gas, ozonized water, oil, or gel. The antimicrobial activity depends on concentration, time of exposure, organic load, and biofilm presence. Laboratory studies have shown that there is more biofilm resistance and less effectiveness of root canal disinfection than with sodium hypochlorite. The clinical uses of medical ozone include caries, periodontitis, oral surgery, pediatric dentistry, and musculoskeletal pain therapy. Data on caries treatment are very insufficient. In a meta-analysis published in 2025 based on 13 randomized studies, there were moderate benefits in probing depth and the gingival index, but no effect on bleeding, plaque, or attachment level.

Conclusion: There is insufficient scientific data to substantiate the use of ozone as a stand-alone therapy or as an alternative to conventional treatment methods. Ozone can be used as an adjunct therapy in a controlled manner, preferably in a clinical study setting, along with conventional practices.

Keywords: ozone; dental caries; periodontitis; endodontics; biofilm; preventive dentistry.

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1. Introduction

Ozone is an allotrope of oxygen consisting of three oxygen atoms. Ozone absorbs a considerable share of solar ultraviolet light in the stratosphere; at the ground level, due to the high oxidizing activity of ozone, it has found application in water purification, food storage, disinfection, and in medicine as well [1,2]. In dentistry, ozone can be used as an antimicrobial, anti-inflammatory, and healing substance; however, the validity of this idea varies considerably depending on the type of ozone

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preparations and applications [2–4]. There are some clinical reviews dedicated to ozone [5,6].

The rationale for using ozone in dentistry is grounded on the following reasons: the microbic origin of conditions such as caries, periodontal and endodontic diseases; the need to develop better control of oral biofilms; the popularity of minimally invasive treatment strategies. As ozone has an oxidizing effect on numerous cellular targets at the same time, the resistance of microorganisms to ozone is unlikely to develop. Although this assumption is convincing, it has not been proven yet, and does not provide a clear answer to the question concerning the superiority of ozone to antimicrobials [3,7].

Preventive dentistry aims to inhibit the onset and development of oral diseases. Modalities include risk assessment, biofilm control, fluoride treatment, fissure sealant application, nutritional counseling, and professional preventive care, leaving operative procedures to be performed on disease-causing lesions. As caries and periodontal diseases are biofilm-induced, the non-surgical treatment of early lesions is an important goal [8]. Therefore, agents that can influence biofilm formation without the removal of hard tooth tissue are favorable [5,7]. However, the question is not whether ozone will kill the microbes in vitro. The issue is about the clinical benefits of ozone and its risks as part of preventive care.

Ozone research includes in vitro and animal experiments, clinical trials, and reviews. Laboratory studies can establish if ozone can influence microbes or cells in vitro. In addition, clinical trials alone can prove that ozone can be beneficial for patients [6]. Thus, any antimicrobial effects achieved in the laboratory cannot be considered proof of the efficacy of ozone treatment. Modern systematic reviews point out great variability in ozone concentration, administration, exposure time, controls, and endpoints [9–11].

The current literature review examines the physical and chemical properties of ozone along with the modes of antimicrobial action; discusses the application of ozone in dentistry, differentiating between laboratory and clinical research; highlights the differences between gaseous ozone, ozone dissolved in water, oil ozonation, and ozone gel; considers the possible utilization of ozone in preventive dentistry; and addresses safety concerns. This work is an interpretive synthesis as opposed to a systematic review and meta-analysis (see Section 9.3).

2. Historical Background

Ozone was first characterized by Christian Friedrich Schönbein in 1839; it got its name from the Greek ozein, “to smell” [3,12]. Later, it has been used for water purification and sanitization purposes as well as for disinfection of wounds contaminated with bacteria, in particular, during World War I [2,12]. Ozonized water has been utilized in dentistry in the first half of the twentieth century; special equipment to use it locally was invented much later [2]. Such a historical background explains the current interest in ozone, but it does not prove its efficiency.

3. Physicochemical Properties and Generation of Ozone

3.1. Structure and properties

Ozone (O3) is an angular triatomic molecule with a molecular mass of 48 g/mol. Ozone occurs as a colorless gas having a characteristic smell and is a very good oxidizing agent. The thermodynamic instability of ozone leads to the conversion of ozone into diatomic oxygen depending on various parameters like temperature, humidity, air flow, concentration, and surroundings. In case of dissolution in water, parameters like pH, temperature, and the presence of dissolved organic/inorganic compounds affect the process of decomposition of ozone, and thus ozonized water needs to be prepared just before use. The half-life of ozone varies according to the conditions of

experiments and is applicable only to specific conditions [1,12].

3.2. Generation

The source of the feed gas for ozone generation in medicine and dentistry is pure oxygen. The corona discharge technique is the most common one owing to the availability of precise control of the concentrations of produced gas; there are also other types of ozone generators based on UV light and cold plasma technologies [3]. Pure oxygen ensures low gas mixture contamination and all gas stream components should be resistant to intense oxidation. The tissue dose depends on the generator concentration, flow, exposure time, and the quality of the seal at the interface of the delivery system.

4. Mechanisms of Antimicrobial Action

Ozone kills microorganisms by oxidation of their cells. It attacks the lipids of cell membranes, changes the permeability of cell membranes, and oxidizes proteins, enzymes, and other cellular targets, rendering them dysfunctional. The prevalence of such mechanisms depends on the type of microorganism, the type of ozone used, its concentration, and other factors.

Ozone is active in vitro against a range of bacteria and fungi [14-15], but biofilms are a different matter. Cells in an established biofilm are protected by the extracellular matrix and by organic material that consumes ozone before it reaches them. In one study, 5-ppm ozone water was strongly active against planktonic Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus mutans and Porphyromonas gingivalis, yet biofilms of the same species lost only a small fraction of their bacteria after repeated exposure; a significant reduction required continuous low-flow application [14]. In another, ozonized saline reduced multispecies peri-implant biofilms on titanium by about 1.7 $\log_{10}$, and only at the highest concentration tested [16]. Results obtained with suspensions therefore cannot be carried over to the clinic.

It has also been suggested that ozone oxidizes acids produced by cariogenic bacteria, such as pyruvic acid, and so buffers the local environment against demineralization [5]. This remains a hypothesis and does not show that ozone can reverse cavitated caries. Some skepticism should be cast on statements regarding the inability of microorganisms to acquire resistance to ozone, as its non-specificity might lower the risk, but this has never been investigated in an oral cavity setting.

The issue of relative sensitivity of microorganisms and host cells to ozone is still ambiguous. Host cells have their own antioxidant system that counteracts oxidative damage, which includes the activation of the Nrf2 signaling pathway; yet, this fact does not mean ozone is harmless to oral tissues. There were studies conducted in vitro which demonstrated that ozonated water of 2 and 4 mg/L was compatible with human dental pulp cells, while concentrations of 8 and 16 mg/L caused a significant decrease in viability after 48 hours [17]. It is evident that cell damage depends on ozone concentration.

It should be noted that most information presented in this paragraph is based on laboratory studies that cannot be applied to clinical practice.

5. Delivery Systems and Forms of Ozone

Ozone in dentistry is used in various forms such as gaseous ozone, ozone water, ozonated oil, and ozone gels, which have also been tested [18–20] (Table 1). A variety of gels are based on ozonated oils, causing some overlap in this case. What matters is the particular product and its composition, the amount of ozone contained, and how it is released. It cannot be taken for granted that results of one product are transferable to others. Mixtures of oxygen and ozone were investigated for pain relief and musculoskeletal disorders but are not approved dental treatments [6,21].

Table 1. Forms of ozone used or investigated in dentistry

Form	Investigated dental uses	Important considerations
Gaseous ozone	Localized application to carious lesions and root surfaces; selected periodontal sites [2,10].	Requires a sealed delivery interface and effective suction or containment; inhalation exposure must be prevented.
Ozonated water	Irrigation of periodontal pockets and root canals; disinfection of denture-base resin, peri-implant surfaces and dental unit waterlines [15,16,22–24].	Short-lived and generated immediately before use; activity depends on concentration and organic load.
Ozonated oil	Topical application to oral tissue, for example ozonated olive oil [18]; application to extraction sockets and other wound-related uses have been reported [2,25].	Composition and ozone content vary between products; clinical evidence is limited.
Ozonated gel	Investigated as an adjunct to periodontal therapy in two randomized trials [19,20].	May contain ozonated oil; composition and release vary between products; clinical evidence is limited.
Oxygen–ozone mixture	Investigated in masticatory muscle pain and temporomandibular conditions [21].	Evidence is preliminary; route, dose, and indication require careful scrutiny.

5.1. Comparative appraisal of the principal forms

The four main forms are not interchangeable, and none of the sources reviewed compares them head-to-head in patients, so they cannot be ranked by clinical effectiveness. The comparison below therefore deals with the type and strength of the evidence, practical aspects of delivery and safety (Table 2).

Gaseous ozone has been studied most in caries. Laboratory work has exposed cariogenic bacteria and enamel to the gas [26,27], and all seven clinical studies in a recent systematic review on primary teeth used gaseous ozone [10]. The delivered dose depends on generator output, flow rate, exposure time, and the seal of the delivery cup (Section 3.2). Its limitations include the lower susceptibility of biofilm organisms [14], poorer performance than sodium hypochlorite in a recent endodontic comparison [23], dose-dependent cytotoxicity of ozone preparations in vitro [17], and an inhalation hazard that calls for dedicated devices with effective suction [2,5].

Ozonated water. Most studies have used it as an irrigant, rinse, or disinfectant. It is active against planktonic oral pathogens in vitro [14], and ozone ultrafine bubble water inhibited early Candida albicans biofilms on denture-base resin [15]. The same type of preparation killed Porphyromonas gingivalis and inactivated its virulence factors with little toxicity to human gingival cells [13]. Clinically, subgingival irrigation with ozonized water has been compared with saline as an adjunct

to mechanical debridement in chronic periodontitis [22]. Its main drawback is instability, since activity depends on concentration, organic load, and the aqueous vehicle [1,12]. In a recent in vitro comparison of endodontic disinfectants, ozonated water did not significantly reduce Enterococcus faecalis or Streptococcus mutans [23].

Ozonated oils and gels are best considered together because many gels are oil-based. Ozonated olive oil is used as a topical preparation [18]. In periodontal patients, ozonated gels have been compared with chlorhexidine gel after mechanical therapy in two split-mouth randomized trials. Both treatments improved clinical parameters; chlorhexidine did better for attachment level and gingival index at 3 months in the smaller trial, whereas the larger trial found no differences between groups [19,20]. Ozonated oil placed in extraction sockets has also been compared with dexamethasone [25]. Because composition and release differ from product to product, results for one formulation should not be extrapolated to another.

The choice of form should therefore follow the indication, the evidence available for that indication and the safety profile of the form, not an assumption that one form is better in general. Comparative trials are needed to settle questions of effectiveness.

6. Dental Applications and Evidence

For each application, laboratory and animal findings are reported separately from clinical evidence; the former show biological plausibility, not benefit to patients.

6.1. Dental caries and restorative dentistry

Caries is the most widely studied dental use of ozone and the one most relevant to prevention.

Laboratory evidence. In an in vitro study, 80 s of gaseous ozone (40 μg/mL) or ozonated water (60 μg/mL) reduced Streptococcus mutans, Streptococcus sobrinus, Lactobacillus casei and Actinomyces naeslundii from about 10^6 to 10^1 CFU/mL, although results varied considerably between replicates; 2% chlorhexidine eliminated all four organisms [26]. Low-concentration ozonated water showed antibiofilm activity against S. mutans, alone and combined with photodynamic therapy [31], yet in a separate model S. mutans biofilms were much less susceptible than planktonic cells [14]. Gaseous ozone also reduced S. mutans significantly in another study, but less than sodium hypochlorite did [23].

Clinical evidence. In a randomized trial of 92 young adults with 546 initial approximal lesions, in-office ozone, home-use nano-hydroxyapatite gel and the two combined were compared. The combination produced the highest radiographic remineralization rate at 1 year (69.3% versus 36.5% with nano-hydroxyapatite alone), but demineralization was evident again at 2 years [29]. In orthodontic patients, adding ozone and/or octenidine to professional cleaning and fluoride varnish was associated with the lowest proportion of patients with white spot lesions in the combined-treatment group; lesions still developed in every group, and ozone was never tested without fluoride varnish [30]. A systematic review and meta-analysis of 12 randomized trials (695 patients; 1,227 cavities) rated the certainty of evidence as very low and concluded that ozone could not be recommended for caries treatment. Ozone reduced bacteria less than chlorhexidine in children and about as much in adults; it reduced bacteria more than fissure sealants, but the difference had disappeared by final excavation [11]. A systematic review limited to primary teeth found seven clinical studies, all using gaseous ozone: four were at high risk of bias, two at low risk, and one raised some concerns, and heterogeneity ruled out meta-analysis. Ozone was determined to be comparable to other treatments, with no reported negative side effects, but further studies were suggested [10]. In an analysis in 2025, this was also confirmed [6].

Table 2. Comparative appraisal of gaseous ozone, ozonated water, ozonated oils, and ozonated gels in dentistry

Aspect	Gaseous ozone	Ozonated water	Ozonated oil	Ozonated gel
Main uses investigated	Carious lesions and root surfaces; selected periodontal sites [2,10].	Irrigation of periodontal pockets and root canals; disinfection of denture-base resin, peri-implant surfaces and waterlines [15,16,22,24].	Topical application, e.g., ozonated olive oil [18]; application to extraction sockets reported [25].	Adjunct to periodontal therapy [19,20].
Evidence cited here	Laboratory: cariogenic bacteria, enamel, and endodontic models [23,26–28]. Clinical: caries trials [29,30] and systematic reviews [10,11].	Laboratory: planktonic and biofilm oral bacteria, denture-base resin, peri-implant biofilm, waterlines [13–16,24]. Clinical: a periodontitis study comparing ozonized water with saline irrigation [22].	Limited; not clearly separable from gels in the sources cited.	Two split-mouth randomized trials versus chlorhexidine gel in periodontal disease [19,20].
Main practical limitation	Dose depends on device settings and sealing of the interface; reduced effect in biofilms [14].	Unstable; generated immediately before use; activity depends on concentration and organic load.	Composition and ozone content vary between products.	Composition and release characteristics vary between products.
Safety considerations	Respiratory irritation on inhalation [2,5]; dose-dependent cytotoxicity in vitro [17].	Not risk-free; depends on concentration, contact time, route, and tissue condition [17].	Safety data are limited; depend on formulation, method of use, and exposure.	Safety data are limited; depend on formulation, method of use, and exposure.
Main evidence gaps	Standardized dose and exposure; patient-relevant outcomes; adverse-event monitoring.	Standardized concentration and contact time; clinical comparators.	Product characterization; clinical studies of oils specifically.	Product characterization; adequately powered trials.

Enamel, dentine, and adhesion. Application of gaseous ozone for 40-50 seconds is known to increase the hardness of the enamel in vitro [27]. On the other hand, evidence concerning the effects of ozone on adhesion seems to be less promising. An 80-second exposure resulted in reduced bond strength between four restorative materials and enamel/dentin compared to the 20-second exposure, which had no impact on the bond strength [32]. A 10-second ozone exposure significantly decreased microtensile bond strength to dentin [26]. These results are the outcome of in vitro research, but nevertheless point to an incompatibility of ozone therapy and adhesion procedures.

Interpretation. A fall in viable bacteria in infected dentin is a surrogate endpoint; it does not mean that the lesion has healed or arrested. The contribution of ozone when it is combined with remineralizing agents remains unclear [29]. Ozone should not replace fluoride, sealants, selective caries removal or restoration.

6.2. Periodontology and peri-implant diseases

In periodontology, ozone has been tested as an adjunct to non-surgical therapy, delivered as ozonated water irrigation, as a gas, or as a gel.

Laboratory evidence. In vitro, ozone preparations are active against oral and periodontal pathogens [13,14]. For peri-implant disease, ozonized saline was tested on single- and multispecies biofilms grown on titanium. Only the highest concentration (80 µg/NmL) was effective, reducing counts by about 2.8 $\log_{10}$ in single-species and 1.7 $\log_{10}$ in multispecies biofilms, compared with 1.4 and 1.2 $\log_{10}$ for 0.12% chlorhexidine [16].

Clinical studies. Several trials have combined ozone with scaling and root planing and reported improvements in some parameters [19,20,22]. A meta-analysis of 13 randomized controlled trials (n = 655) showed the following pooled benefits of ozone therapy: reduced probing depth (weighted mean difference: -0.26 mm; 95% CI: -0.48 to -0.05; I^2 = 78%) and gingival index (-0.15; 95% CI: -0.24 to -0.07). Bleeding on probing, plaque index, and clinical attachment level showed no benefits. The authors emphasized that the findings should be interpreted cautiously considering the low number and small sample sizes of the studies and possible risks of bias and heterogeneity [9]. Few data have been gathered regarding peri-implant diseases: a systematic review of 17 studies published in 2023 had just two on implants. In one of those studies, the success rate of ozone treatment was not significantly different from controls (50% vs. 36.6%, respectively) [33].

Interpretation. The findings are mixed and should not be read as proof of efficacy. Differences of a fraction of a millimeter, pooled from heterogeneous trials, do not by themselves establish clinical benefit. Mechanical biofilm disruption, scaling and root planing, and good home plaque control remain the basis of periodontal treatment; ozone is at most an adjunct.

6.3. Endodontics

Because of its oxidative antibacterial action, ozone has been proposed as an adjunctive irrigant or gaseous disinfectant in endodontics [28].

Laboratory and ex vivo evidence. Most studies have tested ozone against endodontic organisms such as Enterococcus faecalis in extracted teeth or in vitro. A systematic review of eight studies (seven ex vivo and one randomized clinical trial) found that ozone reduced the microbial load significantly less than sodium hypochlorite, and that adding it to chemomechanical preparation did not improve on sodium hypochlorite alone [28]. A 2026 in vitro study gave similar results: sodium hypochlorite, alone or in combination, eliminated E. faecalis and S. mutans; gaseous ozone produced a smaller but significant reduction; ozonated water had no significant effect; and combining gaseous ozone with sodium hypochlorite added nothing [23]. Ozone is therefore not superior to sodium hypochlorite.

Clinical evidence. Clinical data are scarce. The systematic review cited above identified a single randomized trial and concluded that ozone should neither replace nor supplement sodium hypochlorite for reducing the microbial load [28]. Changes in patient symptoms are not a measure of canal disinfection and should not be used as evidence of antimicrobial effect.

Interpretation. The studies comparing ozone with sodium hypochlorite [23,28] show no advantage for ozone and do not support its use in place of standard endodontic disinfection.

6.4. Oral surgery

In oral surgery, ozone has been proposed for irrigation, wound care and the control of postoperative pain and inflammation [2]. A meta-analysis of four randomized trials (133 patients) of adjuvant ozone after removal of impacted mandibular third molars found lower pain scores at 24 hours and 7 days and lower analgesic intake, but no significant effect on facial swelling or trismus; the authors rated the evidence as low quality [34]. In a randomized study of 60 patients undergoing mandibular transalveolar molar extraction, ozonated oil placed in the socket gave pain and swelling scores similar to dexamethasone on days 1 and 7, with greater pain relief on day 3 and better wound healing [25]. A 2025 systematic review of clinical trials across dentistry also examined the effect of ozone on healing and pain [35].

Interpretation. These are small studies with different methods and outcome measures. A benefit on one outcome (pain) without an effect on others (swelling and trismus) is not enough to claim effectiveness. Ozone should be regarded as investigational or adjunctive, not as a substitute for standard surgical asepsis and care.

6.5. Prosthodontics and denture hygiene

Laboratory evidence. Denture biofilms containing Candida albicans may lead to denture stomatitis. It was found from in vitro investigations that the use of ozone ultrafine bubbles water (9-11ppm) decreased the viability of C. albicans in 24-hour biofilms on PMMA denture base material while inhibiting the formation of biofilms without changing the surface properties of the material [15].

Clinical evidence. In this study, no research regarding the efficacy of ozone usage in denture cleanliness was found.

Interpretation. Ozonated water should be considered for clinical trials as part of denture care protocol, even if experimental results cannot prove clinical efficiency.

6.6. Pediatric dentistry

The use of ozone has been recommended in pediatric dentistry because it allows for rapid application of the therapy locally, without drilling or anesthesia [2,10]. Even though this feature can be advantageous for anxious and difficult-to-manage children, convenience alone is not sufficient evidence of effectiveness.

Clinical evidence. Results are contradictory in the pediatric literature. In 2024, a systematic review was performed that revealed seven clinical trials using gaseous ozone in primary teeth; four were found to be at high risk of bias [10]. In the caries meta-analysis, the efficacy of ozone in reducing bacteria was inferior to that of chlorhexidine in children [11].

Interpretation. Ozone therapy cannot replace fluoride treatment, dietary recommendations, plaque removal, fissure sealing, and restoration therapy. The lack of inhalation hazard is especially crucial in pediatric patients.

6.7. Tooth bleaching

Laboratory evidence. Among human molar enamel-dentine discs, treatment with either ozone or violet light caused the smallest color shift, while a combination of ozone and 35% hydrogen peroxide resulted in the maximum color shift; enamel roughness was similar in all cases [36].

Interpretation. One lone laboratory study alone cannot conclude whether or not ozone is effective and safe for whitening of teeth. In the absence of clinical evidence, ozone-mediated whitening should be considered experimental.

6.8. Temporomandibular disorders and masticatory muscle pain

Clinical evidence. In a double-blind randomized trial, 40 women with myofascial masticatory muscle pain received either high-frequency bio-oxidative ozone therapy or a sham treatment. Pain intensity and pressure pain thresholds improved in both groups at 1 and 3 months, more so with ozone (VAS improvement of 67.7% versus 48.4%). The marked improvement with sham treatment, however, weakens the comparison [21].

Interpretation. One small trial is not enough to make ozone a routine treatment for temporomandibular disorders. Larger, well-designed trials are needed.

6.9. Dental unit waterlines

Laboratory evidence. Dental unit waterlines are readily colonized by biofilm, and water at the start of the clinical day can carry 10^4–10^7 CFU/mL. In a laboratory study, low-concentration ozonized water (up to 0.4 mg/L, falling to tap-water levels within about 5 h) halved ATP levels in planktonic Candida albicans and deformed waterline bacteria, but its effect on waterline biofilms was not statistically significant and was smaller than that of 0.1% cetylpyridinium chloride. Six months of exposure caused no visible damage to brass, stainless steel, rubber, or tubing materials [24]. Ozonated water has also been discussed for waterline disinfection in broader reviews [2].

Interpretation. Ozone may have a role in waterline maintenance, but the data come from static laboratory conditions. Studies under clinical conditions and over longer periods are needed before it can be recommended.

6.10. Summary of the evidence

Table 3 summarizes the laboratory and clinical evidence for each application.

7. Ozone in the Context of Preventive Dentistry

7.1. Ozone in relation to well-established preventive and therapeutic interventions

The interventions that have been described above are well-established ones, and the present data do not show any justification for replacing them with anything else. In every single case, ozone was tested either as an adjuvant or experimental intervention. With regard to dental caries, there was only one study comparing the preventive intervention with ozone against a well-established intervention, using bacterial count as an endpoint and in relation to fissure sealants; however, the potential benefit of ozone was lost at the moment of final excavation [11]. There was no study on ozone in combination with fluoride varnish that tested ozone alone, thus raising the question as to whether ozone provides any benefits over fluoride- and sealant-based therapies in terms of arrest or development of lesions [30]. Table 4 provides the list of standard interventions and the status of ozone evidence in relation to every condition.

Table 3. Ozone use in dentistry: summary of lab and clinical studies

Application	Laboratory evidence	Clinical evidence	Overall interpretation
Dental caries (non-cavitated, fissure, and root caries)	Reduction of planktonic cariogenic bacteria with high variability; chlorhexidine more effective [26]; antibiofilm activity of ozonated water against S. mutans [31]; biofilms less susceptible than planktonic cells [14].	Randomized trials in approximal initial caries and in orthodontic patients, with ozone combined with other agents [29,30]; meta-analysis of 12 randomized trials: very low certainty, not enough to recommend ozone [11]; seven studies in primary teeth, four at high risk of bias [10].	Insufficient to support use as a stand-alone treatment; not a replacement for established caries management.
Enamel, dentine, and bonding	Increased enamel microhardness reported [27]; reduced bond strength with longer exposure [26,32].	No clinical evidence cited.	Laboratory evidence only; no general statement of compatibility is justified.
Periodontitis	Activity against selected oral microorganisms in vitro [13,14].	Adjunctive trials with scaling and root planing [19,20,22]; meta-analysis of 13 randomized trials: small gains in probing depth and gingival index, none in bleeding on probing, plaque index or attachment level [9].	Possible adjunct to mechanical therapy; certainty and clinical importance limited.
Peri-implant diseases	In-vitro study of ozonized saline on titanium biofilms [16].	Two implant-related trials within a systematic review; no firm conclusion [33].	Mainly laboratory evidence; clinical data very limited.
Root-canal disinfection	Systematic review: less microbial reduction than NaOCl and no added benefit as an adjunct [28]; in vitro: NaOCl eliminated E. faecalis and S. mutans, gaseous ozone was less effective and ozonated water ineffective [23].	One randomized clinical trial within a systematic review of eight studies [28].	Superiority over conventional irrigants not demonstrated; not a substitute for standard protocols.

Application	Laboratory evidence	Clinical evidence	Overall interpretation
Oral surgery	—	Meta-analysis of four randomized trials after third-molar surgery: less pain and analgesic intake, no effect on swelling or trismus, low-quality evidence [34]; trial of ozonated oil versus dexamethasone [25]; systematic review of clinical trials on healing and pain [35].	Inconclusive; investigational or adjunctive.
Denture hygiene	Reduced viable *C. albicans* in early biofilms on PMMA denture-base resin (ozone ultrafine bubble water) [15].	No clinical studies cited.	Laboratory evidence only.
Tooth bleaching	In human enamel–dentin blocks, ozone alone produced little color change but enhanced 35% hydrogen peroxide [36].	No human clinical evidence cited.	Experimental.
Temporomandibular / masticatory muscle pain	—	One randomized trial (n = 40) versus sham; sham group also improved [21].	Preliminary; not established routine care.
Dental unit waterlines	Reduced planktonic organisms; non-significant effect on waterline biofilm; no material damage over 6 months [24].	No clinical studies cited.	Laboratory evidence only.

Table 4. Proven methods of prevention and treatment that are not supplanted by ozone, and the investigated function of ozone.

Condition	Established measures to be retained	Investigated role of ozone and evidence status
Dental caries, including non-cavitated lesions and primary dentition	Fluoride, fissure sealants, dietary counseling, plaque control, selective caries removal, and restorative treatment where indicated.	Adjunct for non-cavitated lesions and disinfection; clinical evidence of very low certainty, with risk-of-bias concerns [10,11].
Periodontal disease	Mechanical biofilm disruption, scaling and root planing, and patient plaque control.	Adjunctive irrigation, gas or gel; outcomes mixed across parameters [9,19,20,22].
Peri-implant diseases	Established peri-implant therapy and plaque control.	Laboratory evidence and very limited clinical data [16,33].
Endodontic infection	Accepted endodontic irrigants and protocols.	Disinfection evidence is mainly laboratory-based, with one randomized trial; ozone is less effective than sodium hypochlorite [23,28].
Oral surgery	Standard surgical asepsis and postoperative care.	Investigational or adjunctive; inconclusive [34,35].
Denture stomatitis	Established denture-hygiene measures.	In-vitro evidence only [15].
Restorative procedures	Conventional operative care for cavitated lesions and standard adhesive protocols.	Laboratory studies on enamel and bonding; no clinical evidence cited [27,32].
Dental unit waterlines	Established waterline disinfection, flushing and monitoring protocols.	Laboratory evidence only [24].

7.2. Conditions for considering ozone within preventive care

The evidence supports only a cautious position. If ozone is used in preventive care at all, the authors suggest the following:

- Use ozone only as an addition to the measures in Table 4, never instead of them.
- Do not use it routinely. Given limited and heterogeneous evidence, restrict it to indications and protocols that have been tested clinically, or to well-designed research.
- Use validated dental devices with effective containment, especially for gaseous ozone and for children.

- Tell patients, and parents or caregivers, that ozone is an adjunctive treatment whose effectiveness has not been established.
- Do not use ozone to postpone operative, periodontal, or endodontic treatment that is indicated, because delay can allow disease to progress.

8. Safety, Toxicity, and Contraindications

Inhaled ozone irritates the respiratory tract. With gaseous dental applications, upper-airway irritation is mainly a risk for operators [5]. Reported effects of inhalation include cough, airway irritation, and headache, and inhalation should be avoided altogether because of the toxicity of ozone to the bronchi and lungs [2,5]. Gaseous ozone should therefore be delivered only with devices designed for dental use, through a well-sealed interface and with suction or capture of residual gas.

Non-gaseous preparations carry different risks, but they are not risk-free. Safety depends on concentration, contact time, formulation, method of application, and the condition of the exposed tissue. In vitro, the viability of dental pulp cells fell at higher concentrations of ozonated water [17]. The absence of reported adverse events in clinical trials is only weakly reassuring. The caries meta-analysis and the pediatric systematic review found no adverse events in the included trials, but these trials were small, short, and mostly at risk of bias, and none was designed to detect adverse effects [10,11].

Contraindications listed in the wider oxygen–ozone literature include pregnancy, glucose-6-phosphate dehydrogenase deficiency, uncontrolled hyperthyroidism, severe anemia, thrombocytopenia and bleeding disorders, and recent myocardial infarction [1,2]. These apply mainly to systemic administration and are not automatic contraindications to every local dental use. Risk should be judged according to the preparation, route, expected dose, the patient's medical history, the manufacturer's instructions and professional guidance. Some of these warnings rest on expert opinion rather than on high-quality dental trials.

9. Critical Appraisal, Limitations, and Future Directions

9.1. Critical appraisal of the evidence

The main limitations of the current literature are as follows:

- Most antimicrobial data come from in vitro tests using planktonic cells or simple biofilm models that do not reproduce the oral environment [14,26].
- For denture hygiene, waterline disinfection, enamel and bonding, and whitening, the evidence is laboratory-based; for peri-implant disease and root-canal disinfection, it is largely so. Such evidence cannot demonstrate clinical efficacy.
- Clinical trials differ widely in ozone concentration, exposure time, device, technique, co-interventions, controls and outcomes [6,11].
- Many trials are small, have short follow-up, or are at high risk of bias [10,11]; for caries, the most studied indication, the certainty of evidence is very low [11].
- In comparative studies where ozone was tested against conventional agents, ozone failed to show its superiority, as it exhibited a lower antibacterial effect compared to chlorhexidine in children [11], and proved to be inferior to sodium hypochlorite in the context of root-canal disinfection [23,28].
- In some of the studies, ozone was used along with other agents [29,30], while in other researches, the placebo group exhibited considerable improvement as well [21].
- Findings for one delivery form cannot be extrapolated to another, and no head-to-head trials compare gaseous ozone, ozonated water, oils, and gels.

- Long-term safety, cost-effectiveness, effects on the oral microbiome and the clinical relevance of laboratory antimicrobial activity are still unknown.

9.2. Future research

Future trials need to be appropriately powered and randomized, while also reporting the concentration, dosage, and duration of exposure to ozone in a uniform way, along with the results related to patients. Future trials ought to compare the treatment with the standard care available to see if there is any added benefit worth the expense and complications involved in such a treatment modality. In terms of preventive dentistry, the critical issue is whether the ozone provides any additional benefit apart from the existing fluoride and sealant methods in terms of lesion progression and prevention [6,9–11].

9.3. Limitations of this review

Narrative Review Study, This is a narrative review study. The sources used were not selected using a systematic approach, and therefore the sources used may be based on the opinions of the author(s). There might also have been other relevant studies that might have been ignored. Conclusions are interpretive. Most of the clinical evidence comes from systematic reviews and overviews, and the statements on risk of bias and certainty of evidence agree with those of the sources cited.

10. Conclusion

Ozone is a strong oxidant with clear antimicrobial activity in the laboratory, but its effect is limited in biofilm and root-canal models, and it has not produced conclusive clinical benefit. Clinical studies exist for caries, periodontitis, oral surgery, pediatric dentistry and masticatory muscle pain; for denture hygiene, waterline disinfection and whitening, the evidence is still confined to the laboratory, and for peri-implant disease and endodontic disinfection it is largely so. Across fields, the evidence is inconsistent and often at risk of bias, and for caries, the application most relevant to prevention, its certainty is very low. Gaseous ozone, ozonated water, ozonated oils and ozonated gels differ in their evidence base, handling and safety, and should not be treated as interchangeable. Currently, ozone is best regarded, at most, as a carefully controlled adjunct in selected settings or research protocols, not as a replacement for fluoride, fissure sealants, plaque control, restorative and endodontic care or periodontal therapy. Its inhalation hazard and potential cytotoxicity call for strict control of delivery and exposure. Adequately powered, standardized trials with long-term, patient-relevant outcomes are needed before broader recommendations can be made.

Declarations

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