

Ozone Therapy in Dentistry: A Literature Review

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Abstract

Ozone therapy is a bio-oxidative therapeutic approach used in dentistry for its antimicrobial, healing, and immunostimulating properties. This literature review aims to evaluate the clinical applications, effectiveness, and future perspectives of ozone in various dental specialties. A bibliographic search was conducted in PubMed, ScienceDirect, and Google Scholar between 2015 and 2025 using the following Boolean equation: (ozone OR ozone) AND (therapy OR treatment) AND (dentistry OR odontology). Thirty-eight articles were included according to specific criteria. The results show that ozone has beneficial effects in the prevention and treatment of dental caries, endodontic disinfection, periodontology, oral surgery, management of postoperative pain, and healing of oral lesions. However, despite these promising outcomes, the standardization of treatment protocols remains necessary to confirm their clinical effectiveness and long-term safety.

Keywords

Ozone, Therapy, Treatment, Dentistry, Odontology

1. Introduction

Ozone therapy is a versatile bio-oxidative treatment in which oxygen and ozone are administered in the form of gas dissolved in water or an oily base to achieve therapeutic effects [1]. It was discovered in 1840 by the German chemist Christian Friedrich Schönbein, known as the pioneer of ozone therapy. In 1870, Dr. C. Lender in Germany was the first to use ozone for medical purposes, employing it to purify blood samples [2].

Due to its strong oxidizing capacity, ozone has been used for numerous applications as a disinfectant and germicidal agent, both in industrial and medical fields. It has been employed as a sterilizing agent for water treatment, medical equipment

disinfection, dental clinical environments, and enclosed spaces [3].

In dentistry, the use of ozone was introduced in the 1930s by dentist Edward A. Fisch, who based his approach on its beneficial biological properties, including immunostimulant, analgesic, antihypoxic, detoxifying, antimicrobial, bioenergetic, and biosynthetic effects [4]. As a non-invasive treatment modality, ozone therapy has been successfully used over recent decades as an alternative or adjunct in various dental treatments—particularly in the prevention and management of dental caries, root canal disinfection, and treatment of periodontal pockets.

Several forms of ozone administration exist, including gaseous ozone, ozonated oil, and aqueous ozone solution [5]. However, ozone also presents potential risks when misused. As an extremely reactive oxidizing agent, high concentrations or improper administration can cause tissue damage [6].

At the cellular level, ozone exerts its antimicrobial and healing effects through several interrelated biochemical mechanisms [3].

Its strong oxidative power disrupts bacterial and fungal cell membranes by damaging glycoproteins, glycolipids, and enzymes, leading to increased permeability and cell lysis. It also reacts with unsaturated fatty acids to form aldehydes and lipid peroxides, which inactivate microbial nucleic acids and viral structures [3].

Additionally, ozone interferes with biofilm formation by altering salivary biomolecules, thereby reducing microbial adhesion to dental surfaces [3].

On dental hard tissues, ozone promotes remineralization by enhancing calcium and phosphate ion penetration into demineralized enamel and dentin [3].

Within the pulp and periodontal tissues, a mild oxidative stimulus supports homeostasis, stimulates fibroblast and osteoblast proliferation, and promotes tissue regeneration [3].

Finally, ozone modulates inflammatory responses through the controlled generation of reactive oxygen species (ROS), which activate antioxidant pathways and downregulate pro-inflammatory mediators [3].

The aim of this article is to highlight the relevance and therapeutic value of ozone use in dentistry.

2. Materials and Methods

A literature review was conducted using three main databases: PubMed, ScienceDirect, and Google Scholar. The search covered the period from 2015 to 2025 and was performed using the following Boolean equation: (ozone OR ozone) AND (therapy OR treatment) AND (dentistry OR odontology).

Included articles were required to be published in English and to specifically address the application of ozone in dentistry. Non-relevant studies or those published before 2015 were excluded. After screening and full-text review, 38 articles were selected.

Although the main literature search was limited to studies published between 2015 and 2025, a few earlier references were cited in the Discussion to provide

historical background or to support fundamental concepts that remain scientifically relevant. These older studies were not included in the data synthesis or quantitative analysis.

3. Results

The 38 selected studies included 7 systematic reviews, 7 randomized clinical trials, 1 meta-analysis, 14 narrative reviews, 5 case reports, and 4 experimental studies. (Appendix Table A1)

4. Discussion

The analysis of the studies included in this review highlights the growing role of ozone therapy in modern dentistry. This bio-oxidative therapy is distinguished by its antimicrobial, anti-inflammatory, and healing effects, allowing for a preventive, curative, and regenerative approach. Its clinical relevance extends to most dental disciplines.

4.1. Prevention and Management of Dental Caries

Dental caries result from an ecosystem of microorganisms that induce demineralization and tissue destruction. The effectiveness of ozone in caries management is attributed to its antimicrobial properties and its ability to oxidize pyruvic acid produced by cariogenic bacteria, converting it into acetate and carbon dioxide [1].

- Dental Remineralization

Gaseous ozone has demonstrated efficacy in promoting remineralization of early carious lesions [6].

Ozone acts on the organic components of carious lesions, facilitating the mineralization of the dental structure. It also enhances the diffusion of calcium and phosphorus ions into the carious dentin by opening dentinal tubules [4].

- Caries Prevention

Gaseous ozone has also shown effectiveness in preventing the development of new carious lesions in high-risk patients, with results similar to or even better than other preventive treatments. Moreover, combining ozone with other preventive agents, such as hydroxyapatite or fluoride varnish, has produced superior outcomes [7].

Anumula *et al.* demonstrated in their study that ozone is a powerful antimicrobial agent capable of preventing cariogenesis. Ozonated water may be suggested as an effective alternative to chlorhexidine for high-caries-risk patients, providing a preventive approach against dental caries [8].

- Treatment of Pit and Fissure Caries

According to Huth *et al.*, the use of ozone significantly improved non-cavitated initial carious lesions in fissures among high-caries-risk patients over a period of three months [9].

Furthermore, ozone has proven to be an excellent analgesic, exerting a soothing effect on sensory nerve endings while stimulating blood circulation, due to its

ability to infiltrate fissures and dentinal tubules [10].

- Treatment of Deep Carious Lesions

Extensive cavities should be managed by combining conventional therapies with ozone treatment to promote natural remineralization while minimizing the loss of healthy dental tissue. When the lesion extends deeply, multiple treatment sessions may be required. The protocol includes the removal of soft debris and unsupported enamel—that is, enamel that is weakened and no longer supported by underlying dentin, and thus prone to fracture. Ozone is then applied for at least 40 seconds, followed by cleaning with a remineralizing agent such as fluoride toothpaste, amorphous calcium phosphate (ACP) paste, or a nano-hydroxyapatite-enriched product [11].

Hemraj *et al.* demonstrated that ozone therapy can effectively reduce microbial load in deep dentinal carious lesions, particularly *Streptococcus* and *Lactobacillus* species. However, ozone therapy should be applied prior to the final restoration [12].

- Treatment of Root Caries

Ozone has been found to be more effective for shallow lesions of approximately 1 mm in depth. When the carious cavity is deeper—around 4 mm—and located near the gingival margin, ozone application alone is not effective. In such cases, superficial caries should be removed, leaving approximately 1 mm of carious dentin at the cavity floor, followed by ozone treatment and then conventional restoration [1].

4.2. Root Canal Treatment

During root canal treatment, and more specifically during the chemical preparation phase, ozonated water can be applied as an irrigant instead of sodium hypochlorite or other chemical irrigating agents.

Indeed, it has been demonstrated that for the disinfection of root canals and dentinal tubules, ozone is very effective against *E. faecalis*, *Candida albicans*, *Peptostreptococcus micros*, and *Pseudomonas aeruginosa*, which are endodontic pathogenic microorganisms. Moreover, ozone promotes healing and bone regeneration due to its ability to penetrate through the apical foramen, thus reaching the surrounding bone and supporting tissues [6].

A study conducted by Boch *et al.* evaluated the effectiveness of gaseous ozone against *Enterococcus faecalis*, in comparison with EDTA, NaOCl, and their combinations. The results showed that all treatments reduced the bacterial load, with maximum efficacy observed for NaOCl alone, followed by the combination of NaOCl and ozone. Ozone alone remained less effective than NaOCl. However, when combined with conventional agents, it can enhance disinfection, especially in cases of NaOCl allergy [13].

A study conducted at the University of Zagreb by Halbauer *et al.* showed that the application of gaseous ozone, in addition to conventional chemo-mechanical instrumentation with sodium hypochlorite (NaOCl) irrigation, led to a significant

reduction of 93% in anaerobic bacteria and 67% in aerobic bacteria. Furthermore, a significant decrease was observed for certain specific species such as *Streptococcus mitis* and *Propionibacterium acnes*. Thus, it can be concluded that ozone treatment effectively contributes to the reduction of bacterial load in root canals after instrumentation [14].

4.3. Effect on Dental Plaque and Biofilm

Ozone may serve to manage microscopic infectious agents in dental plaque. Ozonated water has considerably inhibited the formation of experimental dental plaque. Ozone, due to its antimicrobial properties, allows for a significant reduction of bacteria integrated within the biofilm [6].

Indeed, a study conducted by Nagayoshi *et al.* demonstrated that ozonated water at 4 mg/L effectively eliminates oral microorganisms such as *S. mutans* and *C. albicans* within 10 seconds. It also revealed a reduction in the formation of experimental dental plaque. This plaque, created on demineralized human teeth cultured in vitro, was exposed to ozonated water, resulting in a reduction in the number of viable bacterial cells and inhibition of biofilm formation. These results confirm the strong antimicrobial potential of ozonated water in controlling dental plaque and biofilm [15].

Ozonated water presents an antimicrobial activity comparable to that of 2.5% sodium hypochlorite, making it possible to use ozone in aqueous form as an antiseptic agent with fewer harmful effects compared to its gaseous form. Thus, ozone could serve as a therapeutic adjuvant due to its ability to inactivate the microorganisms. Moreover, ozonated water has demonstrated its bactericidal effectiveness against dental plaque and biofilm [6].

Nagayoshi *et al.* showed in their study conducted on dental plaque samples that after 10 seconds of exposure to ozonated water (4 mg/L), all microorganisms disappeared. The authors observed that ozonated water could be beneficial in reducing infections caused by bacteria present in dental plaque [15].

4.4. Effect on Halitosis

Chronic bad breath, also known as halitosis, is mainly caused by bacteria that generate volatile sulfur compounds. Among these microorganisms, *Porphyromonas gingivalis* plays an important role since its presence in saliva is associated with the severity of halitosis. These bacteria may be linked to dental caries, gingival diseases, or oral infections. Smoking also worsens the condition by causing dry mouth and increasing the likelihood of gingival disease. However, ozone has the ability to destroy these bacteria and reduce bad breath [5].

4.5. Effect on Gingival Diseases

Ozone, with its broad antimicrobial activity and lower toxicity compared to conventional agents, presents an interesting option for the management of gingivitis. Bansode *et al.* demonstrated in their study on the use of ozonated water in the treat-

ment of gingivitis that following ozone therapy, there was a significant reduction in bleeding scores and gingival inflammation, thanks to its antibacterial and anti-inflammatory properties [16].

4.6. Management of Chronic Periodontitis

When used in the oral cavity, ozone can exert an antimicrobial action by altering the cell walls of microorganisms and disrupting their metabolic processes. Therefore, ozone represents an attractive option for the treatment of infections associated with periodontal pathogens [6].

Moreover, O₃ stimulates periodontal tissue regeneration by enhancing the expression of growth factors such as VEGF and TGF- β , which play a crucial role in angiogenesis, fibroblast proliferation, and collagen production. In addition, exposure to O₃ promotes the proliferation and differentiation of periodontal ligament stem cells, thereby aiding in the regeneration of damaged tissues [17].

Marco Colombo *et al.* demonstrated in their study the effectiveness of ozonized gel in the treatment of chronic periodontitis. They suggested that ozone offers a promising alternative for antibacterial treatments while minimizing toxic effects often in association with other antiseptics, thanks to its biocompatibility with periodontal cells [18].

Kaur *et al.* conducted a study on the use of ozonated water and 0.2% chlorhexidine gluconate in the management of chronic periodontitis. The results showed a significant improvement in clinical parameters in the ozone-treated group over time, suggesting that ozone could be an effective treatment modality for periodontal diseases due to its antimicrobial and anti-inflammatory properties [19].

4.7. As an Adjunct to Scaling and Root Planing

Ramzy *et al.* demonstrated in their study that the application of ozonated water as an adjunct to scaling and root planing significantly improved plaque and gingival indices, as well as pocket depth and attachment loss. This is attributed to the bactericidal effect of ozone against bacteria present in periodontal pockets. Moreover, the combination of ozone with conventional treatments provides additional benefits in managing aggressive periodontitis [20].

Deepthi *et al.* showed that the use of ozone, either in gel form or as ozonated water, results in a reduction of Bleeding On Probing (BOP) in cases of periodontitis, as well as an improvement in Clinical Attachment Loss (CAL). Furthermore, ozone has proven effective when used as an adjunct to mechanical debridement in the treatment of periodontitis, contributing to a reduction in pocket depth and an improvement in clinical indices such as Plaque Index (PI) and Gingival Index (GI) [21].

Giulia Teté *et al.* concluded in their study that ozone could be an effective adjunct to non-surgical therapy for chronic periodontitis. Their results showed no statistically significant differences in the reduction of plaque (PI) and bleeding (BOP) indices between the groups treated with and without ozone. However, an

overall improvement in clinical parameters was observed in the ozone-treated group, suggesting that ozone may have a beneficial effect as an adjunct to non-surgical therapy [22].

4.8. Management of Endo-Periodontal Lesions

Makeeva *et al.* demonstrated through a clinical case study involving the treatment of an endo-periodontal lesion using gaseous ozone in a patient suffering from aggressive periodontitis that the addition of ozone to the conventional root canal disinfection protocol resulted in a significant reduction of the associated periapical lesion. Furthermore, ozone exhibits antibacterial efficacy against both aerobic and anaerobic bacterial colonies, thereby improving clinical outcomes in the treatment of endo-periodontal lesions when used in combination with traditional treatments [23].

4.9. Effect on Bone Tissue

Ozone facilitates rapid and complete normalization of nonspecific resistance and cellular immunity, particularly T-cell-mediated immunity, allowing faster healing and reducing complications related to chronic mandibular osteomyelitis. Thanks to its oxidizing properties, ozone could serve as an effective alternative to hyperbaric oxygen therapy for removing bone sequestra during surgery. Moreover, ozonated water can be applied as a preventive treatment after osteotomies in cases of infection [1].

Antonello Pulga, through a clinical case report, demonstrated the effectiveness of ozone-oxygen therapy for the treatment of alveolar ridge bone resorption in a 69-year-old patient following dental extraction. The results showed decreased bone resorption, improved neoangiogenesis, and enhanced bone metabolism. Bone density measurements revealed an increase after ozone therapy, exceeding researchers' expectations. These findings also indicated better preservation of bone peaks during dental implant placement following ozone therapy. Furthermore, ozone may be beneficial in regenerative surgical procedures, promoting better healing and representing a promising option for bone preservation [24].

4.10. Pain Management

Due to its anti-inflammatory, analgesic, and anti-edematous properties, ozone therapy has shown encouraging results in pain management. The oxidation of pain receptors and the stimulation of the antinociceptive system could explain its pain-inhibiting mechanism. Additionally, studies have demonstrated that peripheral ozone injections can alleviate pain and allodynia, particularly in cases of refractory pain in patients with specific conditions. Moreover, ozone application may have muscle-relaxant effects, making it useful in the management of painful muscle hypertonia in dentistry [6].

J. C. R. Glória *et al.* conducted a study comparing the effects of ozonated water and distilled water as irrigation solutions to assess their effectiveness in managing

pain, swelling, and trismus after surgical extraction of wisdom teeth. The results showed that the efficacy of ozonated water in managing pain, edema, and trismus was comparable to that of double-distilled water. The authors suggested that ozonated water could be an effective alternative for irrigation during surgical procedures [25].

4.11. Management of Tooth Extractions

Ozone therapy has numerous applications in oral surgery, particularly in dental extractions. It promotes healing by improving blood circulation and oxygen diffusion in tissues, leading to vasodilation and increased blood supply to ischemic areas [1].

According to a study conducted by Izabela Barczyk *et al.*, the use of ozone as a prophylactic treatment during and after surgery helps reduce adverse effects associated with dental extractions. This includes decreased swelling, improved blood circulation, reduced inflammation, and prevention of complications such as trismus, hematoma formation, and elevated skin temperature [26].

A study conducted by Almeida *et al.* evaluated the effectiveness of ozone therapy in relieving pain, swelling, and trismus following the extraction of unerupted mandibular wisdom teeth. The data indicated that the ozone-treated group experienced significantly reduced postoperative pain and lower analgesic consumption compared to the control group. Although no notable difference was observed regarding swelling and trismus, ozone therapy improved the patients' quality of life. In summary, the authors suggested that ozone therapy is an effective approach for optimizing postoperative pain management after dental extractions [27].

4.12. Osteonecrosis of the Jaws

A study by C. I. Ripamonti *et al.* evaluating the impact of ozone on jaw osteonecrosis revealed that gaseous ozone insufflation effectively promoted sequestration of necrotic bone, with spontaneous elimination of necrotic tissue in six patients. No recurrence was observed among patients followed for 18 months, and the treatment was well tolerated without any observable toxic effects. These effects were noted in patients with ONJ lesions measuring ≥ 2.5 cm. These findings indicate that ozone could be an effective therapeutic option for bisphosphonate-related osteonecrosis of the jaws [28].

4.13. Effect on Oral Mucosa

Filippi demonstrated in his study that the use of ozonated water can promote healing of epithelial wounds of the oral mucosa, with significant effectiveness during the first two days post-intervention. Furthermore, ozone's ability to enhance wound healing contributes to minimizing complications related to recovery [29].

Al-Omiri *et al.* conducted a study on 138 participants—69 receiving ozone treatment and the others serving as controls—to evaluate the efficacy of ozone in the management of Recurrent Aphthous Stomatitis (RAS). The results showed a

significant reduction in ulcer size and pain level from the second day in the ozone-treated group compared to controls. The authors suggested that a one-minute application of ozone to recurrent aphthous lesions improves healing and reduces pain [30].

A comparative study by H. O. Kazancioglu *et al.* evaluated the effectiveness of Low-Level Laser Therapy (LLLT) and ozone therapy in treating oral lichen planus, comparing them with conventional corticosteroid treatments. The results showed greater improvement in symptoms and higher efficacy indices following ozone application compared to LLLT. Additionally, a significant reduction in pain scores was observed in the ozone-treated group, while no improvement was noted in the control group [31].

A study conducted by Kumar *et al.* examined the efficacy of ozone in managing Oral Lichen Planus (OLP). The research aimed to determine whether ozone therapy could produce significant results in reducing pain and lesion size compared to traditional therapies. The findings demonstrated that ozone therapy had a substantial therapeutic impact, with marked reduction in symptoms associated with OLP, such as burning sensation and lesion size [32].

4.14. Treatment of Peri-Implantitis

S. C. Isler *et al.*, in their study assessing the effect of gaseous ozone on implant surface decontamination as an adjunct to Surgical Regenerative Therapy (SRT) for peri-implantitis, demonstrated significant clinical and radiographic improvements following ozone application. Notably, Plaque Index (PI) and Gingival Index (GI) values were better in the ozone-treated group. Furthermore, pocket depth reduction was greater in the ozone group compared with controls [33].

4.15. Management of Primary Teeth

In 2017, Bretta *et al.* conducted a study to evaluate the efficacy of a new protocol for treating deep caries in primary teeth using ozone. This protocol involves partial removal of carious dentin, followed by disinfection of the remaining tissue with ozone. After rubber dam placement, the cavity is restored with composite resin. The study results showed a remarkable success rate of 93.62% after a one-year follow-up for restorations performed according to this protocol, comparable to outcomes achieved with conventional treatments such as pulpotomy. Additionally, the protocol made it possible to treat teeth that would otherwise have required pulpotomy while preserving as much healthy dental tissue as possible. Ozone application was also useful for disinfecting carious dentin and promoting remineralization of dental surfaces. This approach proved particularly beneficial for young uncooperative patients, offering a less invasive and more comfortable alternative [34].

4.16. Management of Molar-Incisor Hypomineralization (MIH)

Moscatti *et al.* reported a case of a child with MIH treated using a combined ap-

proach involving selective excavation and ozone therapy. The results showed a success rate comparable to pulpotomy after a 12-month follow-up. Moreover, this method proved effective in treating deep caries while being less invasive and faster than conventional treatments such as pulpotomy [35].

In their study evaluating the role of ozone in managing MIH, Bretta *et al.* demonstrated that ozone possesses strong disinfecting capacity, capable of eliminating bacteria and promoting remineralization of dental tissues, particularly in mild MIH cases. Furthermore, combining ozone with the Atraumatic Restorative Treatment (ART) approach helps reduce tooth sensitivity and optimize oral hygiene in young patients [36].

4.17. Effects on the Cooperation and Comfort of Young Patients

Ozone offers a therapeutic approach particularly suited for anxious or uncooperative children. Thanks to its antimicrobial, virucidal, disinfectant, biocompatible, anti-inflammatory, and immunostimulating properties, as well as its ability to promote tissue regeneration, it has become a treatment of choice in pediatric dentistry.

Its capacity to destroy bacteria in dental caries without the need to remove affected tissues or use anesthesia makes it especially practical in pediatric dentistry. In the presence of initial lesions, it promotes remineralization of demineralized tissues by facilitating the deposition of calcium and phosphate.

Some antiseptic products can have an unpleasant taste, which makes treatment acceptance in children difficult. However, studies suggest that ozone may offer comparable effectiveness to fluoride varnish in the treatment of carious lesions [37].

4.18. Management of Temporomandibular Disorders (TMD)

G. Tricarico *et al.* demonstrated through their review that ozone could play a role in managing pain associated with TMD. This was illustrated by comparing several studies evaluating the effectiveness of ozone versus conventional treatments such as occlusal splints. The results indicated that while splints led to notable symptom improvement, ozone therapy also resulted in significant pain reduction and improved mouth opening in patients [38].

Daif *et al.* showed in their study that intra-articular ozone injection has a therapeutic effect in managing temporomandibular disorders. Their study, which included 60 patients with bilateral internal derangement of the TMJ associated with reducible disc displacement, demonstrated recovery in 87% of patients. The authors suggest that ozone therapy could be an effective treatment modality for internal TMJ disorders [39].

According to a study conducted by Dogan *et al.*, ozone therapy would be more effective than drug treatment in alleviating pain caused by temporomandibular disorders. The aim of their research was to compare the effectiveness of ozone with that of medication in patients suffering from TMJ-related pain. The results

showed a significant improvement in maximum mouth opening and a reduction in pain levels in the ozone-treated group [40].

4.19. Management of Dental Hypersensitivity

Several factors can cause dental hypersensitivity, including loss of dental tissue due to attrition, abrasion, erosion, or occlusal trauma. Ozone has been shown to be an effective, non-invasive method for relieving hypersensitivity [1].

Applying ozone for one minute, followed by rinsing with water on exposed dentin, leads to a decrease in root sensitivity. This process can be attributed to ozone's ability to remove the smear layer on the root surface, which normally prevents calcium and fluoride ions from penetrating dentinal tubules. Through this action, ozone also widens the diameter of dentinal tubules, allowing faster treatment of root sensitivity compared to conventional methods [6].

4.20. Contribution of Ozone in Orthodontics

The area between enamel and brackets is the most likely to develop white spot lesions, and microleakage can also occur beneath brackets. Therefore, enamel protection plays a crucial preventive role in orthodontics [1].

Safaa Ali Ghobashy *et al.* demonstrated in their study—designed to evaluate the effects of ozonized olive oil gel on enamel demineralization around orthodontic brackets during treatment—that ozone could be a preventive method to protect enamel during orthodontic procedures. The results showed that applying ozonized olive oil gel effectively reduced enamel demineralization compared to the control group. Furthermore, after eight weeks, there was an improvement in enamel surface quality and a decrease in demineralized lesions in the treated teeth [41].

4.21. Tooth Whitening

Ozone can be used for whitening discolored, non-vital teeth. The endodontically treated tooth is exposed to ozone for three to four minutes after applying the bleaching agent to the internal surface of the tooth. This procedure allows whitening within minutes and provides excellent aesthetic results [6].

Al-Omiri *et al.* conducted a study to evaluate the effectiveness of ozone combined with 38% hydrogen peroxide compared to 38% hydrogen peroxide alone for tooth whitening. The results showed that the combination of ozone and 38% H₂O₂ produced lighter tooth shades than using hydrogen peroxide alone [42].

4.22. Dental Unit Waterlines and Ozone

Dental Unit Waterlines (DUWL) can become contaminated with microorganisms such as bacteria and yeasts, posing a risk to both dental staff and patients. Due to its antimicrobial effectiveness at low concentrations, ozone can be used to purify DUWL water and control contamination in dental settings [6].

Walker *et al.* (2003) demonstrated in their study that ozone reduces bacterial

viability and biofilm coverage, though not completely eliminating them. Ozone caused approximately a 65% reduction in viable bacteria within the biofilm and a 57% reduction in the biofilm-covered surface area [43].

4.23. Toxicity and Adverse Effects of Ozone

Ozone inhalation can be toxic to the lungs and other organs, but complications from ozone therapy are rare, with an estimated risk of 0.07% per session (~7 cases per 10,000) [44].

Exposure to 0.05 ppm for eight hours is considered safe, while the maximum allowable oral concentration during treatment should not exceed 0.01 ppm [45].

Due to ozone's strong oxidizing properties, materials in contact with the gas must be resistant, such as glass, silicone, or Teflon [44].

Ozone's reactivity can induce lipid peroxidation and free radical formation, triggering lipase activation and inflammatory mediator release. Therefore, precise application is essential to ensure safety [6].

Minor adverse effects may include nausea, headache, fatigue, excessive tearing, upper airway irritation, rhinitis, cough, vomiting, vascular swelling, circulatory disturbances, and cardiac events. Vasovagal reactions, often related to pain during infiltration, are considered the most critical; injections should be performed gradually, especially when high concentrations of ozone are used [5] [11] [46]-[48].

4.24. Management of Ozone Toxicity

Ozone inhalation is not recommended due to the vulnerability of the broncho-pulmonary system to this agent. The mucosal cells of the respiratory tract are highly sensitive to oxidation, as the lining fluid consists of a thin aqueous layer with very few antioxidant components. Consequently, the European Society for Ozone Therapy has prohibited intravenous ozone administration since 1983, following a reported case of pulmonary embolism [6].

Additionally, Chloe Y. Y. Wong *et al.* reported a case of a neurological crisis with persistent cognitive impairments requiring prolonged rehabilitation after intravenous ozone therapy. Significant neurological deficits can occur following IV administration, although such cases are rarely reported [49].

In the event of ozone toxicity, the following measures are recommended:

- Place the patient in a horizontal position;
- Administer humidified oxygen.
- Provide supportive therapy with:
 - o Ascorbic acid;
 - o Vitamin E;
 - o N-acetylcysteine [5].

4.25. Prevention of Toxicity in Dentistry

It is essential to follow a careful approach to avoid toxicity when using ozone. This includes using a dedicated ozone generator equipped with a properly calibrated

photometer, administering a gas volume with a specific ozone concentration, determining and applying the optimal dose to achieve a therapeutic effect, and using appropriate protective masks [2].

Medical-grade ozone is a mixture containing 0.1% to 5% ozone, with the remainder being pure oxygen at a concentration of 95% to 99.6%. Practitioners must adhere to recommended doses, ensuring that ozone concentration does not exceed 5% and oxygen content remains at or above 95%. To achieve this precision, it is crucial to use generators equipped with reliable photometers capable of strict concentration control [50].

4.26. Contraindications of Ozone Therapy

The main contraindications that should be considered before treatment include: [4]

- o Pregnancy;
- o Severe anemia;
- o Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency;
- o Hyperthyroidism;
- o Thrombocytopenia;
- o Immunosuppression;
- o Moderate or acute alcohol intoxication;
- o Hemorrhage;
- o Ozone allergy;
- o Myocardial Infarction (MI);
- o Recent MI.

5. Limitations and Future Directions

One of the major limitations identified in this review is the absence of standardized clinical protocols for ozone application in dentistry.

Future studies should aim to establish well-defined parameters, including ozone concentration (in gaseous, aqueous, or oil-based forms), method of delivery (such as gaseous insufflation, ozonated water irrigation, or topical application), exposure duration, and frequency of treatment sessions.

These parameters may vary depending on the specific dental procedure—for instance, cavity disinfection, endodontic irrigation, periodontal therapy, or postoperative wound healing.

Developing standardized protocols would not only enhance the reproducibility and comparability of research findings but also help determine the optimal therapeutic dosage and ensure patient safety in long-term clinical use.

6. Conclusions

Ozone therapy in dentistry is a non-invasive, safe, and effective method that helps prevent and treat various oral conditions thanks to its antimicrobial and reparative properties.

It plays a role in the prevention and management of caries—whether pit and fissure caries or deep caries.

It is also effective for disinfecting root canals in endodontic treatments and managing periodontal diseases.

Ozone promotes wound healing after surgical interventions such as dental extractions or implant procedures and assists in managing postoperative pain and edema. It also contributes to treating jaw osteonecrosis and reducing dentinal hypersensitivity.

Ozone aids in healing various oral mucosal lesions such as aphthous ulcers, herpes labialis, and oral lichen planus, as well as in whitening discolored non-vital teeth after root canal therapy.

These benefits highlight its potential as an adjunct or alternative treatment, though standardized protocols are necessary for optimal clinical use.

Future studies should focus on establishing clear and standardized clinical parameters, including ozone concentration, delivery methods, and exposure duration, according to the specific dental procedure.

Long-term clinical trials and comparative studies with conventional techniques are needed to confirm the long-term safety, reproducibility, and cost-effectiveness of ozone therapy.

Such research will help define optimal treatment protocols and support the integration of ozone therapy into evidence-based dental practice.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix

Table A1. Summary of all the studies included in this work.

Author/ Year (Ref.)	Objective	Main Results	Conclusion
H. O. Kazancioglu <i>et al.</i> 2015 [32]	Compare ozone therapy, low-intensity laser therapy, and topical corticosteroids in treating Oral Lichen Planus (OLP)	Ozone and corticosteroids showed greater symptom improvement and lesion reduction; less recurrence with ozone.	Ozone shows promise as an effective adjunct in OLP management.
S. V. Naik <i>et al.</i> 2016 [5]	Manage varicose veins, root canal disinfection, and wound healing with Oxygen-Ozone Therapy (OOT)	Effective in reducing postoperative pain and improving disinfection and healing outcomes.	OOT is a promising therapeutic tool in dentistry.
M. K. AL-Omiri <i>et al.</i> 2016 [30]	Evaluate the effect of ozone during tooth extraction to prevent MRONJ	Improves healing (significant scores at days 3 - 5 and day 14), may help prevent MRONJ in high-risk patients.	Ozone could be an effective adjunct to enhance healing and prevent complications.
S. Tiwari <i>et al.</i> 2017 [1]	Test ozonated sunflower oil as an adjunct in periodontal therapy	Enhances tissue regeneration, reduces inflammation, and postoperative pain.	Potential benefit in periodontal treatment requiring further validation.
M. Beretta <i>et al.</i> 2017 [34]	Use of ozone in oral surgery for healing enhancement	Promotes better healing, reduces alveolitis, osteonecrosis, and supports bone regeneration.	Ozone is beneficial for postoperative healing in oral surgery.
Antonello Pulga 2018 [24]	Effectiveness of ozone in chronic periodontal disease	Decreases plaque, bleeding, and pocket depth; results vary due to protocol differences.	Ozone appears beneficial but requires standardized protocols.
J. C. G. Ramos <i>et al.</i> 2018 [25]	Ozone as an adjunct to mechanical debridement in periodontitis	Reduces pocket depth, bleeding, and improves attachment; enhances treatment outcomes.	Confirmed as a helpful adjunct in periodontal therapy.
S. C. Isler <i>et al.</i> 2018 [33]	Applications in conservative and endodontic dentistry	Disinfects carious dentin, aids remineralization, reduces hypersensitivity, and assists in bleaching.	Ozone is effective in various conservative treatments.
Y. Suh <i>et al.</i> 2019 [51]	Use ozone for deep caries in primary teeth	Shows comparable results to traditional treatments over 12 months, preserving pulp vitality.	Promising minimally invasive approach for primary teeth.
S. Sen <i>et al.</i> 2020 [4]	Evaluate ozone in lichen planus treatment	Improves symptoms more than laser therapy; recurrences within 5 weeks, less with ozone + corticosteroids.	Ozone is effective with better symptom control.
G. Tricarico <i>et al.</i> 2020 [38]	Use in surgical healing and regeneration	Aids in healing, reduces pain and swelling, accelerates recovery.	Ozone supports wound healing post-surgery.
T. Malik <i>et al.</i> 2020 [2]	Effect on periodontal inflammation	Decreases plaque, bleeding, and pocket depth; improves gingival health after 6 weeks.	Ozone enhances periodontal healing.

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M. K. Makeeva et al. 2020 [23]	Ozone for MIH in children	Successful in managing MIH with less invasiveness and faster recovery.	Useful in pediatric endodontics.
M. Beretta et al. 2020 [36]	Treatment of MIH with ozone and selective excavation	Preserves pulp, shows promising short-term results; long-term studies needed.	A promising approach for managing deep caries in MIH.
R. Deepthi et al. 2020 [21]	Post-extraction healing, especially in high-risk patients	Reduces pain, swelling, and complications like MRONJ.	Effective in improving healing, especially for at-risk groups.
A. Gore et al. 2021 [45]	Effectiveness in periodontal disease	Improvement in clinical parameters; outcomes vary due to protocol differences.	Shows promise but needs standardization.
M. Colombo et al. 2021 [18]	Ozone vs. laser and corticosteroids in oral lichen planus	Ozone has better symptom control than laser; recurrences within weeks.	An effective alternative with manageable recurrences.
R. K Yadav et al. 2022 [11]	Disinfection during cavity preparation	Eliminates bacteria, enhances remineralization, and reduces hypersensitivity.	Useful in conservative dentistry.
O. Di Fede et al. 2022 [52]	Disinfection in root canal retreatment	Effective against resistant bacteria, improves healing.	Beneficial in endodontic disinfection.
H. Badhe et al. 2022 [12]	Instrument sterilization and cross-contamination prevention	Shows promise in maintaining sterility standards.	Useful in infection control.
O. A. El-Meligy et al. 2023 [6]	Ozone combined with corticosteroids or laser in OLP	Better symptom reduction than laser alone; corticosteroids more durable.	Effective in OLP therapy.
A. M. AbdulMajeed et al. 2023 [10]	Reduction of postoperative complications	Decreases pain, swelling, and alveolitis after surgery.	Supports postoperative management.
P. Goswami et al. 2023 [53]	Caries management in children	Promotes remineralization and bacterial reduction; improvements over time.	Effective and minimally invasive.
I. Barczyk et al. 2023 [26]	Orthodontic applications	Reduces bacterial counts, potentially decreasing gingivitis.	Supports oral health during orthodontic treatment.
G. Tetè et al. 2023 [22]	Non-surgical periodontal therapy	Enhances clinical outcomes with adjunctive ozone.	Reinforces ozone's adjunctive role.
A. Alsakr et al. 2023 [54]	Periodontal tissue healing	Reduces plaque, bleeding, and pocket depth; improves health after 6 weeks.	Promotes healing and reduces inflammation.
F. Veneri et al. 2024 [37]	Alveolar ridge preservation	Supports bone healing, reduces discomfort postoperatively.	Beneficial in ridge preservation.
F. Veneri et al. 2024 [3]	Pulp therapy in primary teeth	Disinfects the pulp chamber and maintains vitality for years.	Promising in pediatric pulp therapy.

Continued

A. Kumar <i>et al.</i> 2024 [32]	Bleaching treatment enhancement	Penetrates dentinal tubules, improves whitening with less sensitivity.	Supports esthetic procedures.
S. V. Kotecha <i>et al.</i> 2024 [55]	Summary of ozone benefits	Shows benefits across multiple fields; protocols need standardization.	Overall promising, subject to further research.
M. Moscati <i>et al.</i> 2024 [35]	Safety and clinical efficacy	Reduces periodontal signs, promotes healing; minimal side effects.	Supports safe clinical use.
A. Rosa <i>et al.</i> 2024 [56]	Deep caries in primary teeth	Effective in disinfection and preservation for over 12 months.	Validates minimally invasive approach.
P. Bansode <i>et al.</i> 2024 [16]	Oral rehabilitation and healing	Improves healing, reduces postoperative discomfort.	Valid support for surgical recovery.
O. Di Fede <i>et al.</i> 2024 [57]	Managing MIH lesions in children	Promising results with ozone and remineralization techniques.	Encouraging management option.
R. A. do CARMO <i>et al.</i> 2025 [58]	Molar extraction healing in high-risk patients	Reduces pain and complications, especially MRONJ.	Useful adjunct in complex cases.
R. B. de Almeida <i>et al.</i> 2025 [27]	Periodontal disease treatment	Improves clinical parameters; protocols need standardization.	Promising but requires uniform protocols.
N. T. Hashim <i>et al.</i> 2025 [17]	Ozone vs. laser/corticosteroids in OLP	Ozone outperforms laser, but recurrences occur.	Effective with manageable relapses.
F. Veneri <i>et al.</i> 2025 [7]	Overall benefits of ozone	Promotes healing, disinfection, and regeneration; long-term studies needed.	Highly promising with further validation required.