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Major approaches on the use of ozone therapy in endodontics: a concise systematic review

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Abstract

Introduction: Issues related to endodontic treatment are intrinsically linked to the prevention and total control of pulp and periapical infections. The presence of microorganisms is not limited to the endodontic but is also present in the periradicular regions, characterized by an apical biofilm that is strongly adhered to the surface. In this context of decontamination of root and periapical canals, ozone has been highlighted as an important sanitizer. **Objective:** To demonstrate the main experimental and clinical findings of the use of ozone therapy alone and in association with conventional treatments as an antiseptic in the treatment of root canals. **Methods:** The research was carried out from May 2021 to June 2021 and developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar, following the Systematic Review-PRISMA rules. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results:** There is moderate evidence to provide important preliminary information about ozone therapy. As for reducing the microbial load for patients undergoing root canal treatment, ozone therapy has inferior results when compared to conventional chemomechanical techniques using NaOCl. The joint action of these treatments proved to be quite effective. **Conclusion:** Ozone therapy is proving to be a useful new treatment modality that offers great benefits to patients. The strong antimicrobial power of ozone, together with its ability to stimulate the circulatory system and modulate the immune response, makes it a corrective agent of choice in the treatment of various oral infectious diseases. More research is needed to help with its reproducibility, its use should be indicated by the dentist in clinical practice.

Keywords: Endodontic treatment. Ozone therapy. Root canal. Microorganisms. Disinfection.

Introduction

Issues related to endodontic treatment are intrinsically linked to the prevention and total control of pulp infections and periapical regions [1]. In cases of infection, the presence of microorganisms is not limited to the endodontic but is also present in the periradicular regions, characterized by an apical biofilm that is strongly adhered to the cementum surface in teeth with lesions in the periapical region [2].

Therefore, the total elimination of microorganisms from the region of infected root canals has been a great and constant concern in the list of Endodontic treatments, demonstrated by several types of research that, in the end, evaluated the great action of endodontic instruments, the chemical substances used, of the irrigation/aspiration and medication introduced intracanal [3]. The best and safest method to be used to decontaminate the endodontic system canal is judicious and total sanitization since all microorganisms that are present in necrotic root canals cannot be reached by all host defense cells [4].

In this sense, the well-conducted chemical-surgical preparation significantly reduces the predominant microorganisms in the root canal. However, persistent microorganisms survive, not only due to the limitation of endodontic surgery in removing them from anatomical complexities but also due to the presence of some nutrients that are capable of favoring the actual growth of these microorganisms in a residual way, restoring the possibility of contamination of the pulp space and periapical tissues [5,6].

In this context of decontamination of root and periapical canals, ozone has been highlighted as an important sanitizer. Ozone is a natural gas and a very strong and selective oxidizer [7]. Ozone therapy is based on the assumption that ozone (O3) rapidly dissociates into water and releases a reactive form of oxygen that can oxidize cells, thus having antimicrobial efficacy without inducing drug resistance [8]. Ozone acts on glycolipids, glycoproteins, or certain amino acids, which are present in the cytoplasmic membrane of microorganisms [9]. The oxidation process of these unsaturated lipids and proteins generates a quantitative conversion of the olefinic bonds present to reactive species (ozonide) of lipid oxidation products [10]. Ozonides signal and trigger metabolic changes that produce microbicidal effects [8,10].

Also, ozone therapy is being tested as an alternative or co-acting agent to NaOCl. However, some authors have shown that ozone therapy has similar results compared to NaOCl in reducing various species of bacteria [11-13], while others have reported less efficacy [7,8,14].

Also, the action of ozone, directly and indirectly, modulates the relationship of the patient's immune system, thus improving the body's response to the etiological agent. However, it is still necessary to define with scientific evidence the ability of the O3 molecule to stimulate biological effects, encouraging tissue repair, healing, and return of the tooth to its natural function. To all these attributions, it is understood that ozone thus has great potential to be included in endodontic therapy, as it requires and incorporates the two requirements necessary for any substance for endodontic use, such as antimicrobial action par excellence and biocompatibility [3,4].

Therefore, the present study aimed, through a systematic review, to demonstrate the main experimental and clinical findings of the use of ozone therapy alone and in association with conventional treatments such as antiseptic in the treatment of root canals.

Methods

Study Design

The rules of the Systematic Review-PRISMA Platform (Transparent reporting of systematic reviews and meta-analysis-HTTP://www.prisma-statement.org/) were followed [15].

Data sources and research strategy

The search strategies for this systematic review were based on the keywords (MeSH Terms): "Endodontic treatment. Ozone therapy. Root canal. Microorganisms. Disinfection". The research was carried out from May 2021 to June 2021 and developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar. Also, a combination of the keywords with the booleans "OR", "AND", and the operator "NOT" were used to target the scientific articles of interest.

Study Quality and Bias Risk

The quality of the studies was based on the GRADE instrument [16] and the risk of bias was analyzed according to the Cochrane instrument [17]. Two independent reviewers carried out research and study selection. Data extraction was performed by reviewer 1 and fully reviewed by reviewer 2. A third investigator decided on some conflicting points and made the final decision to choose the articles.

Results and Discussion

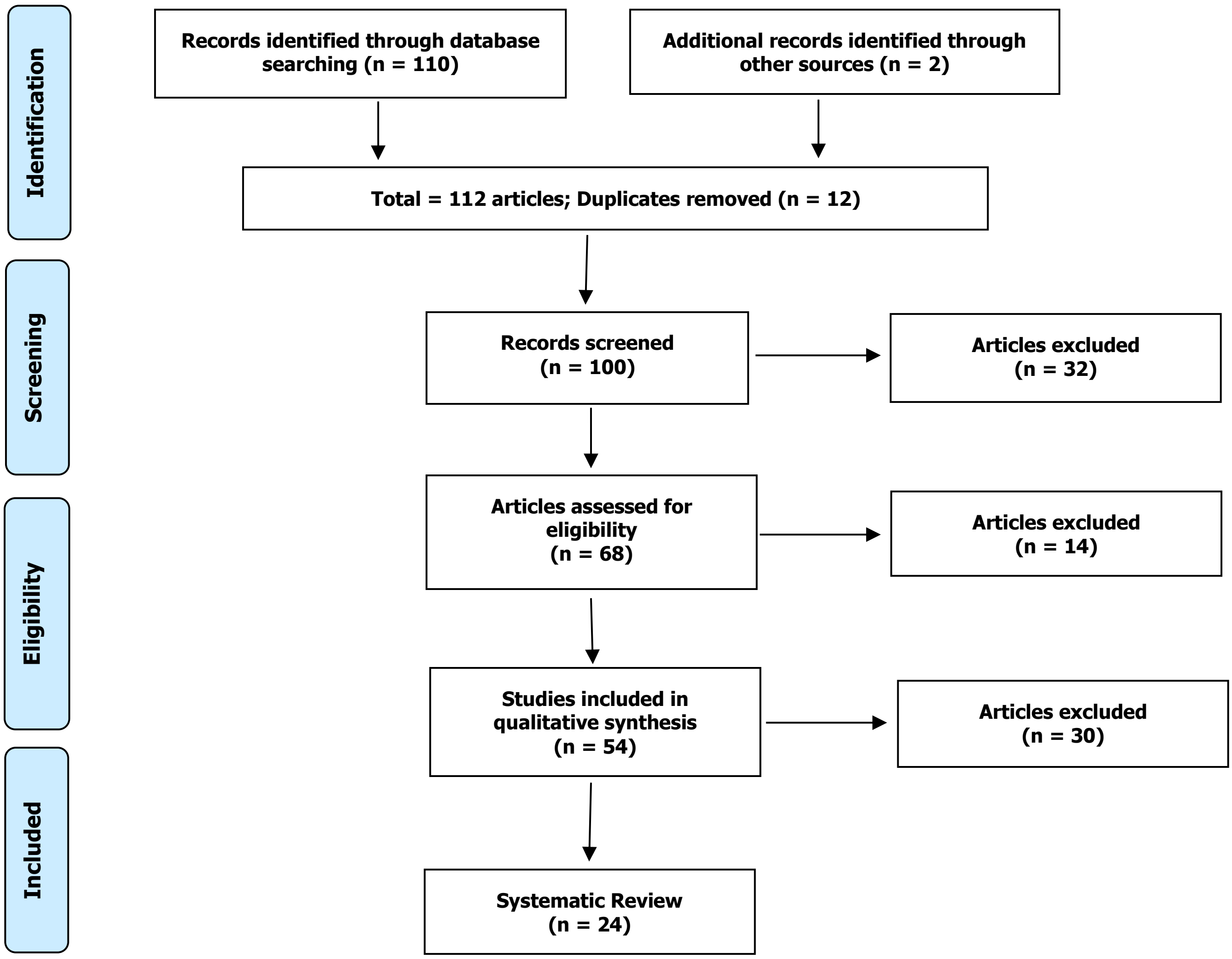
A total of 112 articles were found on the ozone therapy in endodontics. Initially, duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing articles that did not include the theme of this article. A total of 54 articles were evaluated in full and 24 were included and evaluated in the present study (**Figure 1**).

Considering the Cochrane Tool for Risk of Bias, the Overall Assessment in 4 Studies with a High Risk of Bias and 2 Studies with Uncertain Risk. The domains that presented the highest risk of bias were related to the number of participants in each study addressed, and the uncertain risk was related to the safety and efficacy of the Ozone Therapy. Also, there was an absence of the source of funding in 3 studies and 2 studies did not disclose information about the conflict of interest statement.

Through the evaluation of selected studies, it was found that ozone was first suggested for root canal treatment because of its reported high antimicrobial action [12,18]. A significant decrease in oral cell cytotoxicity was observed with ozone gas compared to 2.25% NaOCl and 2% chlorhexidine gluconate [19,20]. Furthermore, aqueous ozone (up to 20 mg mL-1) was not toxic to oral cells [12,18,20].

Despite significantly reducing bacterial levels, ozone when used alone is not capable of producing results similar to NaOCl [7,8,11,14,18]. Ozone has shown comparable results to NaOCl solution in vitro studies with higher concentrations [12] or periods of use [21],

Figure 1. Flow Chart of Study Eligibility.



especially when associated with PUI [11], NaOCl [7], or chlorhexidine gluconate [21]. Still, studies show that ozone is associated with lower bacterial load reductions than NaOCl [7,8,11,14,18].

A systematic review study revealed that the antimicrobial effect of ozone is strongly associated with the application protocol used, such as dose, time, and correlation with the use of complementary sources of disinfection. Also, ozone has different antimicrobial effects according to groups of bacteria (Gram-positive and Gram-negative). Since the structure of Gram-negative bacteria contains lipopolysaccharides (LPS) and phospholipids in the membrane, this group appears more susceptible to ozone [22].

In this respect, higher concentrations and longer periods of ozone application allow better disinfection results. Furthermore, better results are also found when using ultrasound, NaOCl, or chlorhexidine associated with ozone therapy [7,11,21].

Also, a study analyzed whether irrigation with sodium hypochlorite, chlorhexidine, and ozone gas, alone or in combination, were effective against *Enterococcus faecalis* and *Candida albicans*. A total of 220 recently extracted single-leg teeth were inoculated with *Candida albicans* and *Enterococcus faecalis*. The formulations tested were sodium hypochlorite at 1, 3 and 5%, chlorhexidine at 0.2% and 2%, and ozone gas applied for different periods. The combination of 5% sodium hypochlorite and 2% chlorhexidine with gaseous ozone was also evaluated. Sodium hypochlorite, chlorhexidine, and ozone gas alone were ineffective in eliminating the microorganisms. The association of 2% chlorhexidine followed by ozone gas for 24 seconds promoted the complete elimination of *Candida albicans* and *Enterococcus faecalis* [21].

A randomized trial analyzing the efficacy of ozone or NaOCl/Chlorhexidine disinfection protocol was compared in root canal treatment of apical periodontitis. A total of 60 permanent teeth were randomly allocated. Ozone gas (32 g m-3) or NaOCl (3%) was applied, followed by dressing at an interval of 1 week ($Ca(OH)_2$). There were no significant differences between success rates between the ozone and NaOCl groups after 6/12 months. The most commonly found bacterial genera were *Streptococcus spp.*, *Parvimonas spp.*, and *Prevotella spp.* Therefore, the ozone gas and NaOCl/chlorhexidine gluconate protocols used here showed no difference in bacterial reduction in the sampled areas of root canals [13].

Besides, a study evaluated the post-disinfection of the space using different irrigants. A total of 40 single-rooted mandibular premolars were collected and disinfected. The samples from group 1 were submitted to photoactivated disinfection, group 2 irrigated with ethanol-based propolis, group 3 disinfected with ozone, and group 4 irrigated with 2.25% NaOCl and 17% EDTA. Each sample was cut in 1 mm of coronal, middle, and apical and subjected to pushout bond strength (PBS) using a universal testing machine. The highest PBS at all three levels was found in group 4, channel disinfected with 2.5% NaOCl with 17% EDTA. Whereas, the lowest PBS was observed in group 1. In the intergroup comparison, the prosthetic space disinfected with propolis extract showed no significant difference compared to group 4 disinfected with 2.5% NaOCl with 17% EDTA and in all three levels. The intra-group comparison in all experimental groups showed no significant difference observed in the coronal and middle thirds of group 1, group 2, and group 3, respectively ($p>0.05$) [23].

Finally, a study evaluated the effectiveness of irrigation of periodontal pockets with ozonized water and 0.2% chlorhexidine gluconate as an adjunct to scaling and root planning in the management of chronic periodontitis. A total of 20 patients aged 30-60 years with chronic periodontitis were included. Irrigation was performed after 2 weeks of scaling and root planing on the same day with ozonized water and 0.2% chlorhexidine gluconate for two and a half minutes. Both groups showed improvement in clinical parameters. When the comparison was made between the two groups, the ozonized water showed a slightly better improvement than the chlorhexidine group. Therefore, subgingival irrigation with ozonized water is beneficial over conventional therapeutic modalities. Ozonized water restricts the formation of dental plaque and reduces the number of subgingival pathogens, thus treating periodontal diseases [24].

Bias and limitations

Important biases and limitations were found, which can be identified as the variability between studies regarding methodologies, such as the ozone application protocol and NaOCl concentrations (1–5.25%). Also, failure in the equivalence of parameters between control and experimental groups [11,13], limited sample size with the absence of sample calculation [7,8,12,18,21], relevant lack of information on group distributions, and the presentation of results [12,18].

Conclusion

It is concluded that ozone treatments can have numerous benefits in treatments related to different areas of dentistry, such as surgery, dentistry, and, mainly, as discussed in this work, in endodontic treatments when used in precise concentration. But, its contraindications cannot be neglected. The professional must be aware of the correct handling, be updated, and be prepared for its use. In this sense, more research is needed to help with its reproducibility, its use should be indicated by the dentist in clinical practice. There is moderate evidence to provide important preliminary information about ozone therapy. As for reducing the microbial load for patients undergoing root canal treatment, ozone therapy has inferior results when compared to conventional chemomechanical techniques using NaOCl. The joint action of these treatments proved to be quite effective.

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Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.