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Efficacy of ozone therapy in dentistry with approach of healing, pain management, and therapeutic outcomes: a systematic review of clinical trials

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Abstract

Ozone therapy has emerged as a promising treatment modality in dentistry due to its antimicrobial and healing properties. This systematic review aimed to evaluate the recent clinical trials on ozone therapy in dentistry and its impact on therapeutic outcomes. A comprehensive literature search was conducted across multiple databases, including Web of Science, PubMed, and Scopus from January 2018 to December 2024, identifying studies that investigated the use of ozone in dental applications. The findings demonstrated that ozone therapy is effective in improving periodontal health, healing soft tissue after dental implant surgery, and reducing postoperative discomfort. The combination of scaling and root planing with gaseous ozone therapy showed superior periodontal response rates. The use of ozone during endodontics procedures resulted in reduced post-treatment pain, while ozonated materials showed promise in the management of dentinal hypersensitivity. However, it is not recommended in restorative dentistry due to potential adverse effects on dentinal bond strength. The findings of this systematic review supported the integration of ozone therapy into dentistry as an adjunctive therapy. More research is needed to elucidate its mechanisms, optimize application techniques, and evaluate long-term outcomes for patient safety and treatment effectiveness.

Keywords Ozone therapy, Dentistry, Periodontal health, Dental implant surgery, Endodontics

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Introduction

Ozone (O_3) is a triatomic molecule that has attracted attention in various fields due to its strong oxidizing properties and effective antimicrobial effect [1, 2]. The use of ozone in dentistry is particularly compelling, as dental practices are continuously seeking innovative solutions to improve oral health outcomes [3, 4]. Given the increasing prevalence of dental diseases worldwide, there is an urgent need to investigate adjunctive therapies such as ozone for more effective treatment and prevention strategies [5, 6].

Ozone has strong oxidizing properties that enable it to effectively disrupt microbial cell walls, thereby reducing microbial load and promoting tissue regeneration [2, 7].

This distinguishes it from traditional antimicrobial agents such as chlorhexidine, hydrogen peroxide and sodium hypochlorite, which, while effective, have limitations in spectrum of action and potential adverse effects [8–10].

Chlorhexidine, a widely used antiseptic in dentistry, is known for its broad-spectrum antimicrobial activity. However, it has been associated with side effects such as tooth staining, altered taste perception, and potential cytotoxicity at higher concentrations [11, 12]. While hydrogen peroxide is the most commonly used oxidant, ozone is emerging as a viable alternative due to its distinct properties, including its ability to penetrate biofilms and provide a broad-spectrum antimicrobial effect [13, 14].

Sodium hypochlorite, commonly used as a root canal irrigator, is effective in eliminating bacteria from root canals but can be irritating to surrounding tissues and has limited efficacy in certain biofilm scenarios [15–17]. In contrast, ozone therapy not only exhibits a broad spectrum of antimicrobial activity against bacteria, viruses, and fungi, but also promotes soft tissue healing by increasing oxygenation, increasing blood flow, and stimulating fibroblast activity. This multifaceted action makes ozone a compelling alternative or complement to traditional agents [18, 19].

Furthermore, the integration of ozone therapy into standard clinical protocols represents a significant advance in dental practice. Its application can be tailored to different clinical scenarios, including periodontal therapy, root canal therapy, and wound healing after surgical interventions [18, 20]. Ozone can be used in various forms, including gaseous ozone, ozonated oils, and ozonated water, allowing for versatile use in various clinical settings [21, 22].

The antibacterial mechanism of ozone primarily involves the oxidation of lipids, proteins, and nucleic acids in bacterial cells, leading to cell lysis. Regarding bleaching ability, the oxidative reactions induced by ozone can effectively break down chromogenic compounds in teeth, resulting in a rapid and efficient bleaching effect [23].

The application of ozone in endodontics offers a promising adjunctive approach for improving disinfection and promoting healing [24]. Research has indicated that ozone can reduce bacterial counts in infected root canals, assist in the disinfection of necrotic pulp tissue, and may enhance the overall success rates of endodontic treatments. Its use is considered a complementary adjunct to traditional endodontic techniques, offering a promising alternative for improving patient outcomes and promoting faster healing [25].

A recent systematic review by Puleio et al. as highlighted that debris extrusion is a primary contributor to postoperative discomfort, particularly during non-surgical endodontic retreatments. This review investigated whether continuous rotating instruments extrude less apical debris compared to reciprocating instruments, concluding that there is no significant difference between the two techniques. This finding revealed the need for strategies that can mitigate the effects of debris extrusion and enhance healing, which is where ozone therapy may play a crucial role [26].

While some studies report positive results on pain management and improvement, others have inconclusive or conflicting results. Furthermore, many trials lack comprehensive analyses of the long-term effects and safety of ozone therapy, leading to uncertainty about its clinical application [13, 27].

This inconsistency represents a significant gap in understanding the efficacy of ozone therapy and its role in a wider range of dental treatments. Given the growing interest in ozone therapy and its potential benefits, there is an urgent need for a systematic review that critically evaluates the current evidence base.

The aim of this systematic review was to comprehensively assess the efficacy of ozone therapy in dentistry, specifically focusing on its effects on healing, pain management, and overall therapeutic outcomes. By combining data from randomized controlled trials (RCTs), this study sought to provide evidence-based insights that could guide dentists in the use of ozone therapy.

Methods

Study design

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review specifically targeted randomized controlled trials (RCTs) that evaluated the efficacy of ozone therapy in dental applications, with a particular focus on its impact on healing outcomes and pain management. The primary research question guiding this study was: "How effective is ozone therapy in improving healing processes and managing pain in dental treatments, as evidenced by clinical trial outcomes?" This question was designed to direct the systematic search and analysis towards specific clinical outcomes associated with ozone therapy.

Search strategy

A systematic search of the literature was performed using multiple databases, including Web of Science, PubMed, and Scopus, for studies published in English from 2018 to 2024. The search terms employed included "Ozone therapy," "Dentistry," "Dental applications," "Healing outcomes," and "Pain management." These terms were

Table 1 Search strategy in the considered databases

Database	Search strategy and possible combination	Number of articles retrieved
Web of Science	(TS = ("Ozone Therapy" OR Ozone) AND TS = ("Dental Therapy" OR Dentistry OR "Oral Health") AND TS = ("Pain Management" OR Healing OR "Therapeutic Outcomes") AND TS = ("Clinical Trials" OR Efficacy))	150
PubMed	(("Ozone Therapy" OR Ozone) AND ("Dental Therapy" OR Dentistry OR "Oral Health") AND ("Pain Management" OR Healing OR "Therapeutic Outcomes") AND ("Clinical Trials" OR Efficacy))	90
Scopus	(TITLE-ABS-KEY("Ozone Therapy" OR Ozone) AND TITLE-ABS-KEY("Dental Therapy" OR Dentistry OR "Oral Health") AND TITLE-ABS-KEY("Pain Management" OR Healing OR "Therapeutic Outcomes") AND TITLE-ABS-KEY("Clinical Trials" OR Efficacy))	62

Table 2 Inclusion and exclusion criteria in the study

Inclusion criteria	Exclusion criteria
Randomized controlled trials (RCTs) published in peer-reviewed journals	Case reports, case series, reviews, meta-analyses, and editorials
Studies that investigate the use of ozone therapy in any form (gas, oil, or water) in dental procedures	Studies that do not specifically focus on ozone therapy or where the ozone therapy intervention is not clearly defined
Studies reporting on at least one of the following outcomes: pain reduction, wound healing, infection control, or overall therapeutic effectiveness	Studies that do not report on pain management, healing outcomes, or other relevant therapeutic outcomes
Studies published from January 2018 to December 2024	Studies published outside the specified date range (January 2018—December 2024)
Articles published in English or with available English translations	Articles not published in English or without available English translations

combined using Boolean operators (AND, OR) to ensure a comprehensive retrieval of relevant literature (Table 1).

Inclusion and exclusion criteria

The inclusion and exclusion criteria in this review have been described in Table 2

Data extraction

Data extraction was performed using a standardized data extraction form. This form was designed to capture essential study characteristics, such as authorship, year of publication, sample size, methodological approach, ozone therapy application, outcome measures, results, and conclusions. Any discrepancies in data extraction were resolved through discussion and consensus [28].

Quality assessment

The quality of the included studies was assessed using the Critical Appraisal Skills Program (CASP) tool, which consists of 10 questions that address key aspects of study quality. These dimensions include the clarity of the research question, appropriateness of the study design, robustness of data collection methods, rigor of data analysis, and consideration of ethical issues (Table 3). For this purpose, Checklist A adapted from CASP was used to evaluate the quality of qualitative and quantitative studies. The questions were answered "yes", "to some extent", "no", and the authors assigned numbers to each answer as "yes = 2", "partially = 1", "no = 0". Scoring was also used to assess the quality of studies. For qualitative and systematic reviews, a total score of 20 was calculated for each article and graded as high quality (score = 20–16), moderate quality (score = 10–15), or low quality (score = 1–9). This grading system was employed to enhance methodological transparency and provide a clear framework for understanding the reliability of the evidence [29].

Table 3 CASP questions to assess the quality of included studies

No.	Question
1	Are the study objectives clearly stated?
2	Is the methodology of study suitable?
3	Is the study design considered correctly?
4	Is the research strategy designed correctly?
5	Have the inclusion criteria been chosen correctly?
6	Is the data extraction correctly chosen?
7	Is the study quality assessment tool considered correctly?
8	Is the synthesis of the data done correctly?
9	Is the interpretation of the data correctly done?
10	Is the results report clearly stated?

Data synthesis

Due to expected heterogeneity among studies, data synthesis was conducted qualitatively. A narrative synthesis

was employed to highlight similarities and differences in study findings, considering variations in study design, outcome measures, and patient populations.

Interpretation of results

Results were interpreted within the context of existing literature, emphasizing their clinical relevance and practical implications for dental practice. The strengths and limitations of the included studies were critically discussed, and recommendations for future research were articulated, specifically addressing identified gaps in the current literature.

Reporting

The findings of this systematic review were reported in alignment with PRISMA guidelines, ensuring comprehensive and transparent presentation of the review process and outcomes (Tables 8 and 9 in Appendices 1 and 2) [30].

Results

Description of the included studies

After conducting a thorough search of the selected databases following the methods outlined in the Methods section, 11 articles were identified from a total of 302 related studies. The included studies consisted of interventional studies (RCTs). The PRISMA flow diagram is presented in Fig. 1, and the characteristics of the studies included in the review are detailed in Table 4.

Quality assessment of the intended studies

This study followed the CASP tool for assessing the quality of the considered studies. The studies included in this study were interventional studies ($n=11$). In general, the results of the qualitative assessment of these studies revealed that 9 studies were of high quality and 2 studies were of moderate quality (Table 5). The included studies were from Italy, Spain, Saudi Arabia, Brazil, Portugal and India. Most of the studies were related to Italy.

Findings of the included studies

The studies reviewed presented strong evidence supporting the advantages of ozone therapy in several dental applications, especially in treating periodontal disease, managing dental implants, performing root canal procedures, and alleviating tooth sensitivity. Key uses of ozone in dentistry identified in these studies are outlined in Table 6. Additionally, a summary of findings from each study is provided in the following table, which includes specific metrics such as reductions in clinical attachment level (CAL), probing pocket depth (PPD), visual analog scale (VAS) pain scores, and early healing scores (EHS) (Table 7). This format offers a clearer understanding of the clinical effectiveness of ozone therapy. The quantitative analysis of the outcomes from these clinical trials indicates that ozone therapy positively influences various dental treatment results, particularly in promoting healing and minimizing pain. Notable decreases in clinical attachment levels, probing pocket depth, and pain scores suggest that ozone therapy may effectively complement various dental procedures, including periodontal treatment and dental implant surgery.

The evaluation of the included studies revealed significant improvements in periodontal parameters for patients receiving scaling and root planing (SRP) combined with gaseous ozone therapy compared to SRP alone. At the 3-month follow-up, there were significant reductions in CAL ($p \leq 0.0001$), PPD ($p \leq 0.0001$), and bleeding on probing (BOP) ($p \leq 0.0001$) for the ozone therapy group [31]. Besides, in a crossover study, sites irrigated with ozonated water showed better wound healing outcomes than those irrigated with saline, with significant differences in EHS on day 1. However, no significant differences were observed on day 5, indicating that while ozone treatment may enhance early healing, its long-term effects require further investigation [43].

Moreover, a study involving patients with necrotic pulp indicated that ultrasonic and sonic activation of ozone during root canal treatment significantly decreased post-treatment pain, as evidenced by lower VAS scores in groups utilizing ozone therapy compared to the control group [33]. Besides, a split-mouth randomized controlled trial showed that Ozonline® treatment resulted in a significant reduction in bacterial counts in periodontal pockets, with the notable eradication of specific pathogens like *Tannerella forsythia* and *Tannerella denticola* [34, 44]. Furthermore, no significant differences in plaque formation or gingival inflammation were observed between groups using ozonated water mouthwash and control mouthwash, with both groups exhibiting similar increases in gingival crevice fluid volume [35].

The evaluation of the included studies also indicated that ozone therapy significantly reduced postoperative inflammation, as indicated by lower C-reactive protein (CRP) levels and lower VAS scores for pain in patients receiving ozone treatment compared to controls. The use of ozonized sunflower oil combined with tea tree oil showed no significant difference in tooth sensitivity compared to potassium nitrate and sodium fluoride, indicating comparable effectiveness in managing sensitivity post-bleaching [45, 46].

Additionally, the studies showed participants experienced less whitening sensitivity when ozone was applied after hydrogen peroxide bleaching, suggesting that ozone can mitigate discomfort associated with bleaching procedures. Additionally, ozonized oils/gels demonstrated

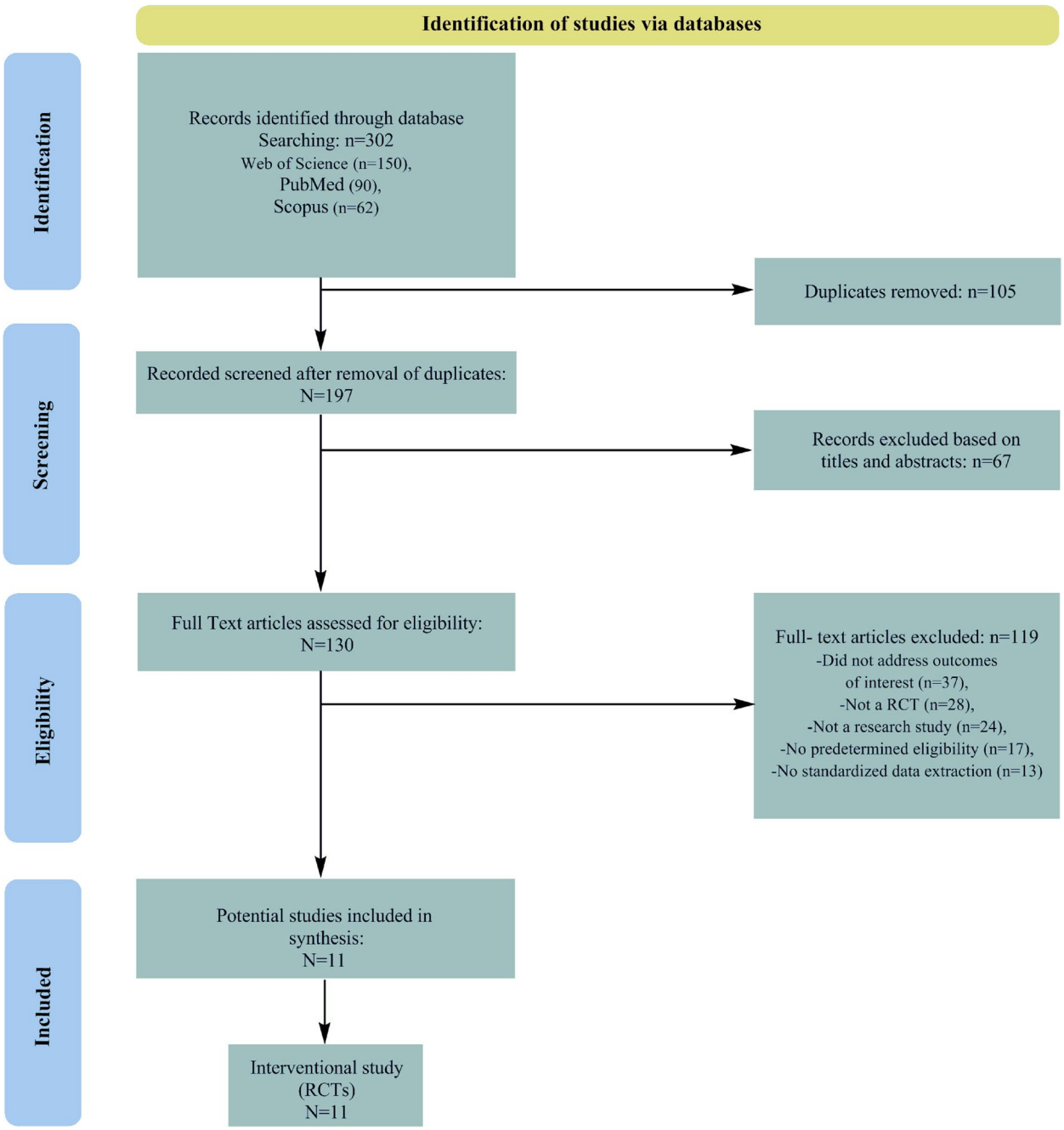

Fig. 1 PRISMA flow diagram

potential as whitening agents for resin composites, showing a moderate effect on color change without significant adverse effects. Based on the studies, ozone treatment effectively reduced bacterial counts from cariogenic bacteria, but it adversely affected dentin bond strength, highlighting the need for cautious application prior to restorative procedures.

The studies demonstrated that in patients with generalized periodontitis, ozone therapy as an adjunct treatment resulted in significant improvements in clinical parameters, including reduced gingival index, periodontal attachment loss, and mobility, alongside favorable changes in subgingival flora. Overall, ozone therapy revealed promise in enhancing healing and

Table 4 Characteristics of included studies in this review

Study No.	First author	Year	Country	Title	Study type	Aim	Methods	Results and conclusion	Quality assessment
1	Rapone et al. [31]	2022	Italy	The gaseous ozone therapy as a promising antiseptic adjuvant of periodontal treatment: a randomized controlled clinical trial	Randomized Clinical Trial (RCT)	The evaluation of the effectiveness of gaseous ozone therapy as an adjunct to standard non-surgical periodontal therapy in promoting tissue healing responses in patients with moderate to severe generalized periodontitis	A prospective randomized study was conducted in 90 healthy subjects with a diagnosis of moderate to severe generalized periodontitis. Participants were randomly divided into two groups: Group A received scaling and root planning (SRP) combined with gaseous ozone therapy, while Group B received SRP alone	Results showed significant differences in periodontal parameters between the two groups at the 3-month mark ($p \leq 0.005$). This study indicated that the combination of scaling and root planning with ozone therapy had better clinical outcomes in the treatment of periodontitis compared to standard SRP alone, suggesting that ozone therapy may enhance the therapeutic response in periodontal treatment	18/20
2	Sghaireen et al. [32]	2020	Saudi Arabia	Effect of aqueous ozone solution irrigation on healing after treatment with dental implants: a cross-over randomized controlled clinical trial	Randomized Clinical Trial (RCT)	The determining the effect of local irrigation with ozone (O_3) water solution on soft tissue healing after dental implantation	The recruited patients underwent similar oral surgery (dental implants) on both sides of their upper jaw. Immediately after surgery and after 3 days, one site was randomly irrigated with 10 ml of O_3 water solution, while the other side was irrigated with normal saline	The study revealed that O_3 treatment enhanced soft tissue healing in the immediate postoperative period after dental implantation. However, the lack of a significant difference observed on day 5 suggests that further research is needed to evaluate the long-term clinical outcomes of O3 treatment	17/20

Table 4 (continued)

Study No.	First author	Year	Country	Title	Study type	Aim	Methods	Results and conclusion	Quality assessment
3	Sinha et al. [33]	2021	India	Evaluation of ozone therapy in endodontic treatment of teeth with necrotic pulp and apical periodontitis: a randomized clinical trial	Randomized Clinical Trial (RCT)	The comparison of the effects of different ozone application techniques on the prevalence of post-root canal pain in patients undergoing single-visit root canal treatment	This study included 108 patients with necrotic pulp in single-rooted teeth and apical periodontitis. Patients were randomly assigned to one of five groups. Patient discomfort level was assessed at six different time intervals using a visual analog scale (VAS)	The results showed that VAS scores for pain were highest in the control group and lowest in the NA, MDA, SA, and PUA groups. A statistically significant decrease in VAS scores was observed in the PUA and SA groups compared to the NA, control, and MDA groups. This study concluded that ultrasonic and sonic activation of ozone during a single root canal treatment resulted in less post-root canal pain compared to no ozone treatment	14/20
4	Piva et al. [34]	2020	Italy	The use of ozone therapy for treatment of periodontal disease: A split-mouth, randomized, controlled clinical trial	Randomized Clinical Trial (RCT)	The evaluation of the effectiveness of Ozonline® in the treatment of chronic periodontitis in adult patients	A split-mouth randomized controlled study was conducted in ten patients (5 men and 5 women, 42–73 years old, mean age 55 ± 7 years) with a diagnosis of chronic periodontitis. Microbiological samples were collected from the sites at baseline and again on day 7, for a total of 20 sites (10 sites from the left quadrant treated with Ozonline® and 10 from the right quadrant treated with ultrasonic scaling)	The results showed a significant reduction in bacterial counts in the left quadrant treated with Ozonline® compared to the right quadrant. This study demonstrated the efficacy of Ozonline® in the management of moderate to severe chronic periodontitis, suggesting that this novel treatment can improve patient outcomes by reducing bacterial load in periodontal pockets	16/20

Table 4 (continued)

Study No.	First author	Year	Country	Title	Study type	Aim	Methods	Results and conclusion	Quality assessment
5	Nicolini et al. [35]	2021	Brazil	Efficacy of ozonated water mouthwash on early plaque formation and gingival inflammation: a randomized controlled crossover clinical trial	Randomized Clinical Trial (RCT)	Evaluation of the effect of ozonated water on initial plaque formation and gingivitis	The sample consisted of 42 dental students who were divided into two experimental groups (using ozonated water mouthwash) and a control group (using double-distilled water mouthwash). The plaque-free zone index (PFZI) was used to assess initial sub gingival biofilm formation at 24, 48, 72, and 96 h	The study showed no statistically significant difference in PFZ index conversion scores between the experimental group (19.07) and the control group (19.79) at all tooth surfaces. Ozonated water had no significant effect on supra- and sub gingival biofilm formation or gingivitis	19/20
6	Shekhar et al. [36]	2021	India	An evaluation of the effect of ozone therapy on tissues surrounding dental implants	Randomized Clinical Trial (RCT)	The evaluation of the effect of ozone therapy on inflammation, pain, and wound healing after dental implant surgery	A clinical study was conducted with 60 systematically healthy patients who were divided into two groups: 30 patients treated with ozone (experimental group) and 30 patients who did not receive ozone treatment (control group). Clinical assessments included measurement of C-reactive protein (CRP) levels for inflammation, use of a visual analog scale (VAS) for pain assessment, and assessment of tissue wound healing with the Wound Healing Index (WHI)	The mean tissue healing indices in the experimental group on day 7 (4.23 ± 0.43) and day 14 (4.97 ± 0.18) were significantly higher ($p < 0.01$) compared with the control group (3.07 ± 0.45 and 4.03 ± 0.18, respectively). No adverse events were observed in either group. Ozone therapy accelerates tissue wound healing, minimizes tissue inflammation, and reduces pain after dental implant surgery	18/20

Table 4 (continued)

Study No.	First author	Year	Country	Title	Study type	Aim	Methods	Results and conclusion	Quality assessment
7	Schneider et al. [37]	2023	Brazil	Efficacy of ozonized sunflower oil with tea tree oil as desensitizing agents in dental bleaching: randomized and double-blind clinical trial	Randomized Clinical Trial (RCT)	Evaluation of the effectiveness of spearmint oil combined with tea tree oil in controlling dentin sensitivity after bleaching compared to the control group using potassium nitrate and sodium fluoride	A randomized, double-blind, double-blind clinical trial was conducted with participants divided into two experimental groups ($n=29$). The control group received potassium nitrate and sodium fluoride, while the experimental group received ozonated sunflower oil combined with tea tree oil	The results showed that there was no statistically significant difference in sensitivity levels between the experimental and control groups. The study concluded that ozonized oil combined with tea tree oil was as effective as potassium nitrate and sodium fluoride in the control group in reducing tooth sensitivity induced by tooth whitening. Furthermore, neither treatment had any effect on the effect of hydrogen peroxide bleaching	17/20
8	Bin Hassan et al. [38]	2024	Saudi Arabia	Tooth Sensitivity Following Hydrogen Peroxide Bleaching With and Without Ozone: A Randomized Controlled Trial	Randomized Clinical Trial (RCT)	Evaluation of bleaching sensitivity after bleaching using only hydrogen peroxide 38 (H_2O_2) or 38% H_2O_2 and then using ozone	This was a randomized controlled clinical trial involving 80 participants (40 women and 40 men) who were randomly divided into two groups (40 each; 20 women and 20 men). Participants reported tooth sensitivity before and after bleaching using a visual analog scale (VAS) from 0 to 10	Bleaching sensitivity was reported following both bleaching protocols ($p<0.001$). However, participants experienced less bleaching sensitivity when ozone was applied for 60 s after bleaching with 38% H_2O_2 ($p<0.001$). Furthermore, female participants reported greater bleaching sensitivity regardless of the bleaching protocol used ($p<0.05$). Bleaching protocols using 38% hydrogen peroxide were associated with less bleaching sensitivity when ozone application was added after bleaching	20/20

Table 4 (continued)

Study No.	First author	Year	Country	Title	Study type	Aim	Methods	Results and conclusion	Quality assessment
9	Detogni et al. [39]	2023	Brazil	Effect of an Experimental Ozone-based Desensitizing Gel on Tooth Sensitivity and In-office Dental Bleaching	Randomized Clinical Trial (RCT)	The evaluation of bleaching effect (BE), tooth sensitivity (TS), and enamel microstructure after in-office tooth bleaching treatment using a desensitizing trial gel containing ozone (O_3)	The study included forty third molars, divided into two groups (20 each): one group used an ozone-free desensitizing and bleaching agent (OF-B), while the other group used a 16 ppm ozonized desensitizing agent and bleaching agent (O-B). The study was conducted at the Dental Clinic of the Western State University of Paraná from June 2019 to April 2020	Tooth sensitivity in the OF-B group was significantly higher than that in the O-B group. However, no significant difference in bleaching effect was observed between the two groups. The experimental gel containing ozone (O_3) showed potential as a desensitizing agent for clinical use and effectively reduced tooth sensitivity without affecting the color obtained through tooth bleaching or the enamel microstructure	17/20
10	Santos et al. [40]	2024	Portugal	Antibacterial Effect of Ozone on Cariogenic Bacteria and Its Potential Prejudicial Effect on Dentin Bond Strength—An In Vitro Study	Randomized Clinical Trial (RCT)	The evaluation of the antibacterial effect of ozone on caries-causing bacteria and evaluation of its possible adverse effect on dentin bond strength	This study involved exposing a suspension of four cariogenic bacteria (Streptococcus mutans, Streptococcus sobrinus, Lactobacillus casei, and Actinomyces naeslundii) to ozone gas (40 µg/mL) and ozonized water (60 µg/mL) using ozone medical gene. To assess microtensile bond strength (µTBS), 20 human molars were divided into four groups and prepared with Class I cavities	The use of ozone resulted in a significant reduction in bacterial counts, from 10^6 to 10^1 UFC/mL. However, dentin microtensile bond strength (µTBS) was significantly affected by ozone treatment, with ANOVA results showing a p-value of less than 0.001. While ozone shows promising antibacterial activity against cariogenic bacteria, this study demonstrates its detrimental effect on dentin adhesion. Therefore, caution is advised regarding the use of ozone prior to dental restorative treatments	18/20

Table 4 (continued)

Study No.	First author	Year	Country	Title	Study type	Aim	Methods	Results and conclusion	Quality assessment
11	Ramirez-Peña et al. [41]	2022	Spain	Ozone in patients with periodontitis: a clinical and microbiological study	Randomized Clinical Trial (RCT)	The evaluation of the effectiveness of ozone therapy as a complement to mechanical therapy in patients with generalized periodontitis	A total of 32 patients with generalized periodontitis were enrolled in the study. The study used a split-mouth design, in which each patient's mouth was divided into four quadrants. Clinical variables recorded included gingival index, periodontal clinical attachment loss, Miller mobility index, and clinical improvements assessed by visual analog scale (VAS)	After four weeks of treatment, the ozone-treated quadrants showed a statistically significant reduction in gingival index and improvement in clinical adhesion ($p<0.0001$). A significant difference was also observed in the qualitative study of the subgingival flora ($p<0.0001$). The overall results of the trial support the conclusion that ozone therapy is effective and well tolerated as an adjunctive treatment in cases of generalized chronic periodontitis	17/20

Table 5 Quality assessment of interventional studies applied from CASP (Checklist A)

No.	References	Question										Score Max = 20
		1	2	3	4	5	6	7	8	9	10	
1	**Rapone et al.**	2	2	1	2	1	2	2	2	2	2	18/20
2	**Sghaireen et al.**	2	2	2	1	2	2	1	2	1	2	17/20
3	**Sinha et al.**	1	1	1	1	2	2	1	1	2	2	14/20
4	**Piva et al.**	2	2	2	1	2	2	2	1	1	1	16/20
5	**Nicolini et al.**	2	2	2	2	2	2	2	1	2	2	1920
6	**Shekhar et al.**	2	2	1	2	2	2	2	2	1	2	18/20
7	**Schneider et al.**	2	2	2	1	2	1	2	1	2	2	17/20
8	**Bin Hassan et al.**	2	2	2	2	2	2	2	2	2	2	20/20
9	**Detogni et al.**	2	2	1	1	2	2	2	2	1	2	17/20
10	**Santos et al.**	2	2	2	2	2	2	1	1	2	2	18/20
11	**Ramirez-Peña et al.**	1	2	2	2	2	2	2	1	2	1	17/20

1- Aims of the study are clearly stated

2- Qualitative methodology is appropriate

3- Research design is appropriate to address the aims of the research

4- Recruitment strategy is appropriate to the aims of the research

5- The data is collected in a way that it addresses the research issue

6- The relationship between researcher and participants are adequately considered

7- Ethical issues have been taken into consideration

8- The data analysis is sufficiently rigorous

9- The findings are clearly stated

10- The value of the research is discussed

Scores: 0 = No, 1 = Partially, 2 = Yes

Table 6 Some key applications of ozone in dentistry in the included studies [42]

Application	Description
Cavity Treatment	Ozone can be used to treat early carious lesions. It helps in remineralizing the enamel and can potentially halt the progression of cavities by eliminating bacteria responsible for decay
Root Canal Treatment	Ozone can be employed during root canal procedures to disinfect the root canal system. Its gas or aqueous forms can be used to eradicate bacteria and reduce the risk of reinfection
Periodontal Therapy	Ozone therapy may serve as an adjunct in the treatment of periodontal disease. It can help reduce bacterial load in periodontal pockets, promote healing, and decrease inflammation
Antimicrobial Rinses	Ozone-infused water or gas can be used as an oral rinse to reduce oral bacterial load and improve overall oral hygiene. This application can be particularly beneficial for patients with compromised immune systems or those undergoing certain dental procedures
Wound Healing	Ozone has been shown to promote faster healing of oral soft tissue wounds, such as after tooth extractions or surgeries, by enhancing blood flow and reducing inflammation
Treatment of Oral Infections	Ozone can be used to treat various oral infections, including herpetic lesions and candidiasis, due to its broad-spectrum antimicrobial properties
Desensitizing Agent	Ozone has been studied for its ability to reduce tooth sensitivity, acting on exposed dentin surfaces by occluding the tubules or through other mechanisms
Prevention of Odontogenic Infections	Ozone therapy can be used to sterilize instruments and surfaces in the dental clinic, which helps in preventing cross-contamination and the spread of infections
Enhancement of Dental Materials	Ozone may be utilized in combination with dental materials to enhance their antimicrobial properties and improve the longevity of restorations
Whitening Procedures	Some dental practices integrate ozone therapy into professional teeth whitening treatments to enhance the effectiveness and minimize potential side effects, such as sensitivity

Table 7 Quantitative synthesis of the outcomes in the included studies

Study Reference	Outcome Measure	Ozone Treatment Group Results	Control Group Results	Statistical Significance (*p*-value)
Rapone et al.	CAL (mm)	Reduction from baseline (mean)	Not reported	≤ 0.0001
	PPD (mm)	Reduction from baseline (mean)	Not reported	≤ 0.0001
	Bleeding on Probing (BOP)	Significant improvement	Not reported	≤ 0.0001
Sghaireen et al.	Early Healing Score (EHS)	Significant improvement on day 1	Lower scores on day 1	Not reported
		No significant difference on day 5		Not significant
Sinha et al.	Pain Score (VAS)	Lowest in PUA and SA groups	Highest in control group	*P* < 0.001
Piva et al.	Bacterial Load (CFU)	38% reduction in Fusobacterium nucleatum	Not reported	Not reported
Nicolini et al.	PFZ Index	19.07 (ozonated water)	19.79 (control)	Not significant
Shekhar et al.	CRP (mg/dL)	0.10 (ozonated water)	0.63 (control)	*p* < 0.001
	Pain Score (VAS)	3.50 ± 0.63 (day 7)	37.70 ± 4.17 (day 7)	*p* < 0.001
	Wound Healing Index (WHI)	4.23 ± 0.43 (day 7)	3.07 ± 0.45 (day 7)	*p* < 0.01
Schneider et al.	Sensitivity Levels	No significant difference	No significant difference	Not significant
Bin Hassan et al.	VAS (Sensitivity)	Less sensitivity with ozone	Higher sensitivity without ozone	*p* < 0.001
Detogni et al.	VAS (Tooth Sensitivity)	Lower sensitivity with ozone	Higher sensitivity without ozone	Not reported
Santos et al.	Bacterial Counts (CFU/mL)	Reduction from 10^6 to 10^1	Not reported	*p* < 0.001
	Microtensile Bond Strength (μTBS)	Significantly affected by ozone	Not reported	*p* < 0.001
Ramirez-Peña et al.	Gingival Index	Significant reduction	Not reported	*p* < 0.0001
	Clinical Attachment Level	Significant improvement	Not reported	*p* < 0.0001
	Mobility Index	Reduced by 70–86%	Not reported	*p* < 0.0001
	VAS (Overall Improvement)	Clinically significant	Not reported	*p* < 0.0001

treatment outcomes across various dental applications, although some studies indicated the necessity of further research to optimize its use and understand its long-term effects [41].

Discussion

The systematic review of clinical trials evaluating the efficacy of ozone therapy in dentistry reveals a promising adjunctive treatment modality across various dental applications. The reviewed studies collectively highlight the multifaceted benefits of ozone therapy, particularly in the management of periodontal disease, root canal treatment, dental implants, and sensitivity associated with bleaching procedures.

Ozone therapy, a treatment method using ozone gas, has attracted increasing attention in the field of dentistry due to its potential applications in improving treatment outcomes and results [33, 37, 40]. Ozone is a natural gas composed of three oxygen atoms and has potent antimicrobial, anti-inflammatory, and wound healing properties. In recent years, ozone therapy has been investigated for its effectiveness in various dental procedures, including periodontal treatment [47].

In dentistry, both gaseous and solution forms of ozone have been investigated for therapeutic applications [48, 49]. The unique properties of ozone enable it to act effectively against a wide range of microbial pathogens, including bacteria, viruses, and fungi, making it a valuable tool in the prevention and treatment of oral diseases [50]. In the treatment of periodontal disease, ozonated water is used in irrigation during periodontal procedures to reduce bacterial load and heal inflamed tissues. Ozone therapy can also be integrated into root canal treatments [51].

The use of ozonated water in cleaning and disinfecting root canals helps to eliminate bacteria and can increase the success of root canal treatments. Additionally, ozone has been shown to promote healing at oral surgical sites and wounds, stimulate tissue regeneration, and improve overall healing outcomes [52]. For topical treatments, ozonated oils and gels can be applied to oral lesions or infected areas, providing sustained release of ozone and facilitating healing while maintaining antimicrobial efficacy [53].

The findings revealed the important role of ozone therapy as a complementary approach in periodontal treatment. The results demonstrated that when combined with conventional methods such as SRP, ozone therapy leads to significant improvements in clinical parameters, including reductions in CAL and PPD. These findings showed that ozone therapy may effectively address the inflammatory processes underlying

periodontal disease, thereby enhancing healing and pain management.

As an adjunctive therapy, ozone has been investigated for its potential benefits in the management of oral diseases, particularly periodontal conditions. Periodontal disease, characterized by inflammatory destruction of tooth-supporting structures, poses significant challenges in clinical practice and requires effective interventions for pain management and healing [54]. Traditional treatments, such as SRP, have long been the cornerstone of periodontal treatment. However, the integration of ozone therapy into these conventional approaches may enhance clinical outcomes and improve patient comfort. The antimicrobial properties of ozone play a significant role in these treatment outcomes [55].

By targeting pathogenic bacteria in the subgingival environment, ozone therapy can help restore a balanced microbial flora, which is essential for periodontal health. Previous research supports the idea that the oxidative properties of ozone can disrupt bacterial cell walls, leading to a reduction in microbial burden and inflammation [56]. This is consistent with the extracted findings, where significant improvements in periodontal parameters were observed after treatment. Furthermore, the integration of ozone therapy into standard periodontal protocols may not only improve clinical outcomes but also improve patient comfort during and after the procedure [57]. Reducing inflammation and pain associated with ozone therapy can lead to a more positive patient experience and encourage compliance with treatment recommendations and aftercare [58].

Moreover, the findings from the reviewed clinical trials indicated the potential of ozone therapy to improve early outcomes in dental patients, as demonstrated by significant differences in EHS following the use of ozonated water [59]. This initial increase in healing may be attributed to the antimicrobial properties of ozone, which can effectively reduce bacterial load and create a more favorable environment for tissue regeneration [60]. However, the lack of sustained benefits in long-term healing outcomes prompts cautious interpretation of these results. While ozone therapy may provide an effective short-term solution, its long-term efficacy is not clearly established, highlighting an important gap in the current literature [61].

Recent clinical trials have showed the ability of ozone to promote early healing, particularly through the use of ozonated water during procedures such as dental surgeries and periodontal treatments [42, 47, 62]. The importance of EHS in assessing the effectiveness of therapeutic interventions emphasizes the importance of timely healing in dental patients. However, while initial results appear promising, the question of the long-term effectiveness of ozone therapy remains controversial [63].

The lack of significant differences in treatment outcomes at later follow-up points suggests that the initial benefits obtained through ozone application may diminish over time. This phenomenon raises important questions about the biological mechanisms underlying ozone therapy and its role in chronic conditions frequently encountered in dentistry [59]. It is essential to investigate whether the transient benefits observed in initial healing can translate into sustained improvements in long-term patient outcomes. Furthermore, the variability in study designs, sample sizes, and follow-up durations in the reviewed trials complicates the ability to draw definitive conclusions about the overall effectiveness of ozone therapy.

The findings also provided the potential of ozone therapy as a valuable tool in dental practice, particularly in the management of postoperative pain associated with root canal treatments. The significant reduction in VAS scores among patients receiving ozone therapy suggests that it can increase patient comfort during recovery and thus improve overall treatment outcomes [64].

Ozone has been investigated as an adjunct therapy in various dental procedures, including endodontics and restorative dentistry. Its antibacterial capabilities make it an attractive option for root canal disinfection, potentially reducing the risk of postoperative complications [65]. However, while the analgesic effects of ozone therapy are increasingly recognized, concerns have emerged regarding its impact on the mechanical properties of dental materials, particularly dentin bond strength [66]. While its antibacterial properties can effectively reduce microbial load and promote healing, the negative impact on dentin bond strength raises questions about the integrity of restorative procedures following the use of ozone. This trade-off emphasizes the necessity of a balanced and careful approach when integrating ozone therapy into clinical protocols [67].

The findings also demonstrated ozone therapy's efficacy in mitigating sensitivity associated with bleaching procedures. Participants reported less discomfort when ozone was applied following hydrogen peroxide treatments, suggesting its potential as a valuable adjunct for improving patient experience during esthetic procedures [60]. However, the comparable effectiveness of ozonized oils and gels to traditional sensitivity management agents like potassium nitrate emphasizes the need for further investigation into the optimal formulations and application protocols for achieving the best therapeutic outcomes.

Teeth whitening procedures have become increasingly common in modern dentistry, with many patients seeking brighter smiles through various bleaching

techniques. However, a common side effect associated with these procedures is tooth sensitivity, which can be uncomfortable and prevent patients from pursuing or completing whitening treatments [68]. Tooth sensitivity occurs when the protective layer of tooth enamel is damaged, exposing the underlying dentin and pulp to external stimuli that result in pain or discomfort during or after bleaching [69].

Recent advances in dental treatments have led to the discovery of ozone therapy as a potential adjunct treatment to reduce sensitivity associated with tooth bleaching. Ozone, a natural molecule, has strong antimicrobial properties and is known for its ability to enhance healing and reduce inflammation [25]. In the field of dentistry, ozone therapy has been used for a variety of applications, including caries management, periodontal treatment, and even roots canal therapy. Its potential role in reducing sensitivity during and after bleaching procedures has attracted the attention of dental professionals [70].

Variation in application techniques across the studies demonstrated significant challenges in interpreting the efficacy of ozone therapy. Different ozone concentrations, delivery methods (e.g., gas versus ozonated water), and treatment durations were observed, leading to inconsistent results [71]. This variation not only complicates the establishment of standardized protocols but also raises questions about the reproducibility of results across different clinical settings. Besides, many of the evaluated studies lacked long-term follow-up data, which is critical in assessing the persistence of ozone therapy effects. Most studies reported results at relatively short intervals, leaving a gap in knowledge about the longevity of the observed benefits [72, 73].

In addition to these methodological concerns, practical challenges also arise when considering the integration of ozone therapy into routine dental practice. The cost implications of adopting ozone therapy, including the purchase of necessary equipment and staff training, may be a barrier for many dentists [74].

While ozone therapy has shown promise in terms of enhancing treatment outcomes, the economic feasibility of its implementation needs to be fully evaluated. It is essential for future studies to focus not only on clinical efficacy, but also to assess cost-effectiveness and return on investment for dental practices [75].

Additionally, practical challenges such as patient acceptance and understanding of ozone therapy need to be considered. Dentists may encounter resistance from patients who are unfamiliar with ozone therapy or are skeptical of its effectiveness. Therefore, effective communication strategies and educational initiatives are crucial to inform patients about the benefits and safety of ozone therapy, thereby creating a more receptive environment for its inclusion in dental treatment plans [76, 77].

The standardization of application techniques, long-term follow-up studies, and comprehensive cost–benefit analyses are essential steps toward establishing ozone therapy as a mainstream treatment modality in dentistry. By addressing these critical areas, the clinical relevance of ozone therapy can be increased and patients can be better served.

Strengths of the study

This systematic review included a wide range of clinical trials, providing an overview of the current state of research on ozone therapy in dentistry. This can help to understand its effectiveness and applications. By focusing on clinical trials, this study was based on evidence-based research, which can help clinicians make informed decisions about implementing ozone therapy in their practice. Furthermore, by highlighting the positive effects of ozone therapy, this study may encourage further exploration of innovative treatment approaches that could improve patient care and outcomes.

Limitations of the study

Variations in ozone application techniques, concentrations, and treatment duration across studies can make generalization of findings challenging. Furthermore, different studies may have used different criteria to assess treatment outcomes, complicating comparisons and pooling of results. In addition, factors such as patient demographics, underlying health conditions, and concomitant therapies may have influenced the results, making it difficult to isolate the effects of ozone therapy.

Conclusion

This systematic review of clinical trials on ozone therapy in dentistry revealed its effectiveness as a promising adjunctive therapy in a wide range of dental applications. The findings obtained from the evaluated studies consistently demonstrated significant improvements in clinical parameters, including reductions in CAL, PPD, and pain scores, particularly in periodontal disease management, root canal treatments, and postoperative care. Ozone therapy was found to improve early healing and reduce post-treatment discomfort, indicating its potential to improve patient outcomes. Considerable evidence from various studies has been presented demonstrating the positive effects of ozone therapy on healing and pain management. For example, combining SRP with gaseous ozone therapy resulted in significant improvements compared to standard treatment alone. Similarly, its application in root canal procedures significantly reduced post-treatment pain and inflammation, suggesting that ozone therapy could be essential for

enhancing patient comfort and recovery. Despite promising results, some studies have shown limitations and the need for further research to establish long-term effects and optimize treatment protocols involving ozone therapy. While the antibacterial properties of ozone were evident, caution is warranted due to its potential impact on dentin bond strength, which requires careful consideration in restorative dentistry. Ozone therapy appears to be a valuable tool in modern dentistry, offering advances in the treatment and management of pain in a variety of modalities. Continued research into its applications and mechanisms is essential to fully understand its therapeutic potential and ensure its safe integration into clinical practice.

Appendix 1

Table 8 PRISMA_2020_Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			**Yes**
Title	1	Identify the report as a systematic review	**Yes**
ABSTRACT			**Yes**
Abstract	2	See the PRISMA 2020 for Abstracts checklist	**Yes**
INTRODUCTION			**Yes**
Rationale	3	Describe the rationale for the review in the context of existing knowledge	**Yes**
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses	**Yes**
METHODS			**Yes**
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses	**Yes**
Information sources	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted	**Yes**
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used	**Yes**
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process	**Yes**
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process	**Yes**
Data items	10 a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect	**Yes**
	10 b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information	**Yes**
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process	**No**

Section and Topic	Item #	Checklist item	Reported (Yes/No)
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results	**No**
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5))	**Yes**
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions	**Yes**
	13 c	Describe any methods used to tabulate or visually display results of individual studies and syntheses	**Yes**
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used	**Yes**
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression)	**Yes**
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results	**Yes**
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases)	**No**
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome	**Yes**
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram	**Yes**
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded	**Yes**
Study characteristics	17	Cite each included study and present its characteristics	**Yes**
Risk of bias in studies	18	Present assessments of risk of bias for each included study	**No**
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots	**Yes**
Results of syntheses	20a	For each synthesis, briefly summaries the characteristics and risk of bias among contributing studies	**Yes**
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect	**Yes**
	20c	Present results of all investigations of possible causes of heterogeneity among study results	**Yes**
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results	**Yes**
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed	**No**

Section and Topic	Item #	Checklist item	Reported (Yes/No)
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed	**Yes**
DISCUSSION			**Yes**
Discussion	23a	Provide a general interpretation of the results in the context of other evidence	**Yes**
	23b	Discuss any limitations of the evidence included in the review	**Yes**
	23c	Discuss any limitations of the review processes used	**Yes**
	23d	Discuss implications of the results for practice, policy, and future research	**Yes**
OTHER INFORMATION			**Yes**
Registration of protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered	**No**
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared	**No**
	24c	Describe and explain any amendments to information provided at registration or in the protocol	**No**
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review	**Yes**
Competing interests	26	Declare any competing interests of review authors	**Yes**
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review	**Yes**

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372:n71. https://doi.org/10.1136/bmj.n71

Appendix 2

Table 9 PRISMA_2020_Abstract_Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			**Yes**
Title	1	Identify the report as a systematic review	**Yes**
BACKGROUND			**Yes**
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses	**Yes**
METHODS			**Yes**
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review	**Yes**
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched	**Yes**
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies	**No**
Synthesis of results	6	Specify the methods used to present and synthesize results	**Yes**
RESULTS			**Yes**
Included studies	7	Give the total number of included studies and participants and summaries relevant characteristics of studies	**Yes**
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favored)	**Yes**
DISCUSSION			**Yes**
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision)	**Yes**
Interpretation	10	Provide a general interpretation of the results and important implications	**Yes**

Section and Topic	Item #	Checklist item	Reported (Yes/No)
OTHER			**Yes**
Funding	11	Specify the primary source of funding for the review	**Yes**
Registration	12	Provide the register name and registration number	**No**

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic Reviews: BMJ 2021; 372:n71. https://doi.org/10.1136/bmj.n71

Abbreviations

PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCTs	Randomized controlled trials
CASP	Critical Appraisal Skills Program
SRP	Scaling and root planning
VAS	Visual analog scale
PFZI	Plaque-free zone index
CRP	C-reactive protein
WHI	Wound Healing Index
BE	Bleaching effect
TS	Tooth sensitivity
μTBS	Microtensile bond strength
CAL	Clinical attachment level
PPD	Probing pocket depth
EHS	Early healing scores
SRP	Scaling and root planning
BOP	Bleeding on probing

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Authors' contributions
M.R., A.K., T.K., and F.G. conceived the study idea and led the conceptualization. T.A., S.A., and F.H. created the study protocol and wrote the original draft. M.N. and S.A. contributed to the data analysis/interpretation and manuscript preparation. M.R., M.N., and S.A. led the review and editing. A.S. and M.N. interpreted the results. All authors reviewed the manuscript.

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Declarations

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