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The Use of Ozone Therapy in the Treatment of Radiotherapy- and Chemotherapy-Induced Mucositis: A Systematic Review

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ABSTRACT

Background: Mucositis is a frequent complication of chemo- and/or radiotherapy treatments and causes great pain and discomfort to the affected patient. Ozone therapy is a widely studied treatment in numerous disciplines, first and foremost dermatology; the beneficial effects of this treatment have already been confirmed in this field, particularly in the healing of wounds caused by diabetes. However, there is a shortage of studies on the use of this treatment in the management of radio- and/or chemo-induced mucositis.

Objectives: This review aims to summarise current evidence on the beneficial effects of ozone treatment in the management of chemo- and/or radio-induced mucositis.

Methods: A systematic literature review was carried out on the main databases (Scopus, PubMed and WOS); for each of the included article, the analysis of risk of bias was performed.

Results: Seven articles were included in this systematic review, including six preliminary animal studies and one prospective cohort study. Analysing the variables of the studies, it seems that ozone is associated with a decrease in bacterial load, oedema and inflammatory infiltrate at the level of the lesions and a decrease in thiobarbituric acid reactive substances, indicators of oxidative stress.

Conclusions: The efficacy of ozone for the management of radio- and/or chemo-induced mucositis is still to be confirmed as current evidence provides only two clinical studies. However, beneficial effects were highlighted and deserve to be further investigated.

1 | Introduction

Oral mucositis is a serious complication of chemotherapy and radiotherapy of the head and neck, affecting 40%–80% of treated patients. It initially presents with very painful erythematous lesions that can develop into ulcers [1]. It usually occurs between two and 12 days after the start of chemotherapy or radiotherapy and manifests as an erythematous lesion characterised by atrophy with inflammation of the lamina propria. It progresses to an ulcerated lesion between seven and 14 days later [1–3]. The average duration of the lesions varies between two and 3 weeks

but may persist for longer in severely neutropenic patients [2, 3]. Sonis [4, 5] proposed five phases to divide the pathogenesis of oral mucositis; in the first phase, initiation, there is a loss of proliferative capacity of the basal cells of the epithelium leading to the production of reactive oxygen species (ROS); in the second phase, the response to the primary damage, there is an overregulation of pro-inflammatory cytokines, nitric oxide, ceramide and matrix metalloproteinases, leading to epithelial thinning, tissue damage and cell death, culminating in the destruction of the oral mucosa; in the third phase, signal amplification, some of the molecules present in the previous phase may lead to aggravation and persistence of tissue injury over time through positive or negative feedback; in the fourth phase, ulceration occurs; in this phase, bacterial colonisation of ulcers by *Gram+*, *Gram-*, anaerobic microorganisms begins and bacterial infiltration spreads until it reaches the submucosal connective tissue, causing activation of macrophages leading to further production of pro-inflammatory cytokines, inflammation and pain; and in the final phase, there is epithelial proliferation and differentiation and consequent thickening of the epithelium, resulting in the restoration of the local oral mucosa [4–6].

Guidelines for the management of these lesions are currently available from the Mucositis Study Group of the Multinational Association for Supportive Care in Cancer and the International Society of Oral Oncology (MASCC/ISOO). These guidelines divide the management of oral mucositis into six areas: nutritional support, pain control, oral decontamination, palliation of dry mouth, management of oral bleeding and therapeutic interventions for oral mucositis. In particular, topical agents, such as sucralfate or systemic analgesia with opioids (morphine is the most commonly used), are used for pain management. For oral decontamination, guidelines recommend the use of fluconazole and good oral hygiene [7]. Despite the treatments currently in use, oral mucositis remains a difficult lesion to manage, with an increased risk of overinfection, feeding difficulties and severe pain [8]. Ozone therapy is widely used in dentistry for the treatment of various lesions and diseases. Three forms of ozone are currently used: ozonised water, ozonised oil and gaseous ozone [9]. Ozonised water and ozonised oil are used to make rinses or as a drinking solution for the treatment of gingivitis, halitosis and other lesions of the hard and soft tissues of the oral cavity; in a study by Butera and coworkers, an ozonised water-based irrigator was used to irrigate sites of peri-implant mucositis, and the results showed a reduction in all clinical indices with subsequent improvement in the 2 months following treatment [10]. A reduction in periodontal indices was also found by Scribante and coworkers [11] in their study using ozonated water as an adjunct treatment for periodontal disease. Ozonised oil, unlike ozonised water, is able to remain in the oral cavity for a longer period of time, resulting in greater tissue penetration [9]; Satapathy and coworkers agree on the beneficial properties of ozonised oil; in their study, they found an acceleration of the healing process of postextraction wounds [12]. Ozone gas, however, is produced by some devices, either in a tank or directly outside the device; these can be equipped with a sealed suction system or without suction [9]. An example of a gaseous ozone generator without an extraction system is the one used in the study by Tasdemir and coworkers (Ozonytron; Bionix, Munich, Germany) [13]. The safest forms of ozone used in dentistry are those in oil and aqueous form, as they allow greater control over the administration procedure without the risk of inhaling gaseous ozone, which can lead to certain side effects, such as rhinitis, cough, headache, nausea and vomiting [9, 14]. Because of its potential harmfulness, the European Union has set a limit for the maximum ozone concentration in the workplace of 0.1 ppm ozone in 8 h or more than 0.3 ppm twice a day for 15 min [15]. Filippi [16] conducted a study on the use of ozone in wound healing, examining three palatal wounds in 30 patients. In this study, patients treated with ozonated water experienced faster wound healing in the first 2 days of treatment than patients in the control group and those treated with water alone. Anzolin and coworkers [17] found in their review that in immunocompromised patients, ozone therapy is able to activate and synthesise interleukins, leukotrienes and prostaglandins, which reduce inflammation and lead to improved healing processes. Given the evidence in the literature of the benefits of ozone therapy in wound healing, treatment of oral lichen planus, treatment of gingivitis, periodontitis, osteonecrosis of the jaw [9] and recurrent aphthous stomatitis [18], the aim of this systematic review was to investigate whether the above benefits are also present in the treatment of radio- and/or chemo-induced mucositis.

2 | Materials and Methods

2.1 | Questions

Does ozone therapy a treatment that can benefit the management of radio- and chemo-induced mucositis? Can it increase the rate of healing of these lesions?

2.2 | Purpose of the Study

Although there are numerous studies in the literature on the effects of ozone therapy as a treatment for various diseases, there are few studies on the use of this treatment in chemo- and radio-induced mucositis. Therefore, the aim of this systematic review was to highlight the benefits of using ozone therapy as a treatment for radio- and/or chemo-induced mucositis.

2.3 | Eligibility Criteria

The following studies were included in this review: (I) type of studies—RCTs, translational studies, longitudinal studies and experimental animal studies; (II) participants—subjects, human and animal, who developed oral and/or gastric mucositis following chemo- and radiotherapy treatments and (III) treatment—ozone therapy treatment, in all its forms (gaseous, ozonised water and ozonised oil). The following studies were excluded: (I) cohort studies, literature reviews and systematic literature reviews; (II) case reports and case series; (III) non-English language articles; (IV) duplicate articles; (V) irrelevant articles and (VI) articles without full text.

2.4 | Research Method

The PICO model was used to search for articles (Table 1): '*p*' the search population includes all subjects, human and nonhuman species, with mucositis, oral or gastrointestinal, induced by radiotherapy and/or chemotherapy. 'I' regarding intervention, all articles that included the use of ozone, in any of its forms, as a therapy for mucositis were included. 'C' for comparison,

TABLE 1 | Summary of the preclinical animal studies included in the review.

Study	Study design and population	Number of subjects	Comparison groups and pharmacological administration	Tested parameters/analyses conducted	Results
Bayer et al., 2017 [19]	Experimental study on rats	24	Group 1 (Control): No treatment Group 2 (LLLT): Laser treatment for 5 days after the appearance of mucositis Group 3 (Ozone Therapy): Ozone therapy for 5 days after the appearance of mucositis	FGF, PDGF-BB and TGF-β	4 rats in the control group died due to the aggressiveness of the mucositis; from the remaining 25, a 100 μg sample of geniena mucosa was taken, and it was found that FGF, PDGF-BB and TGF-β _were present in all groups. In the laser group, TGF-β_and PDGF-BB showed a nonstatistically significant increase. B-FGF increased in both the ozone and laser groups, but only in the laser group was the increase statistically significant.
Hayashi et al., 2019 [20]	Experimental study on rats	21	Group 1 (Control): No treatment Group 2 (Saline Solution): Treated with physiological saline solution Group 3 (ONBW): Treatment with ozonated water	Grade of mucositis (NCI-CTCAE scale) and oral bacterial count	The baseline grade of mucositis (grade 3 of the modified NCI-CTCAE scale [21] for assessing the degree of chemo-related mucositis in rats) did not worsen in all three groups. In the physiological saline treatment group, there is a slight improvement on day 16. In the ONBW group, there was an improvement in the degree of mucositis on days 11 and 16. The improvement in the degree of mucositis was statistically significant in the ONBW group compared to both the saline group and the control group. There is also an improvement in bacterial counts in all three groups, but the greatest decrease was found in the ONBW group. The difference between the control group and the saline group was statistically significant, as was the difference between the saline group and the ONBW group.

(Continues)

TABLE 1 | (Continued)

Study	Study design and population	Number of subjects	Comparison groups and pharmacological administration	Tested parameters/analyses conducted	Results
Zamora et al., 2008 [22]	Experimental study on rats	36	Group 1 (control) Group 2 (indomethacin [20 mg/kg]) Group 3 (indomethacin and cimetidine [25 mg/kg]) Group 4 (Indo and OSO [4 mg/kg]) Group 5 (Indo and OSO [12 mg/kg]) Group 6 (Indo and OSO [24 mg/kg])	TBARS and SOD	Oral administration of indomethacin led to the occurrence of ulcerated and haemorrhagic lesions of the gastric mucosa with a size of 18.8 ± 0.39 mm2. A statistically significant and dose-dependent decrease in lesion size is seen in rats administered ozonated sunflower oil, 9.5 ± 0.29, 5 ± 3.50 and 2 ± 1.11 mm, respectively. Furthermore, the presence of TBARS in the gastric mucosa was significantly decreased in the OSO and cimetidine groups compared to the indomethacin and control groups. SOD (superoxide dismutase) enzyme activity was found to be decreased in the indomethacin group compared to the control group, whereas a reversal of SOD activity is seen in the cimetidine and OSO groups (12 mg/kg and 24 mg/kg)
Gültekin et al., 2013 [23]	Experimental study on rats	35	Group 1 (Control): Rats are given 17.5 Gy of radiation in the pelvic area Group 2 (Radiation + Saline Solution): Rats are given 17.5 Gy of radiation in the pelvic area and are also given 1 mL of saline solution rectally twice a day from the day of the first radiation Group 3 (Radiation + Ozonated Olive Oil): Rats are given 17.5 Gy of radiation in the pelvic area, plus 1 mL of ozonated olive oil is administered rectally twice a day from the day of the first radiation	Rectal Damage: Clinical outcome scores, macroscopic change scores and scoring of histopathological changes	14 rats (7 in the ozone group and 7 in the saline group) were killed on days 5 and 10 to assess changes in the gastric mucosa. Clinical Outcome Scores: On day 5, an average score of 2.14 in group 2 and 1.71 in group 3; on day 10: 2.71 in group 2 and 2.29 in group 3. Macroscopic Change Scores: On day 5, an average score of 3 in group 2 and 2 in group 3; on day 10: 3.71 in group 2 and 2.57 in group 3. Scoring of Histopathological Changes: On day 5, an average score of 2.29 in group 2 and 1.29 in group 3; on day 10, an average score of 3.29 in group 2 and 1.86 in group 3

(Continues)

TABLE 1 | (Continued)

Study	Study design and population	Number of subjects	Comparison groups and pharmacological administration	Tested parameters/analyses conducted	Results
Zamora et al., 2007 [24]	Experimental study on rats	30	Group 1 (Control): No treatment Group 2: Ethanol (1 mL/200 g) Group 3: Sunflower oil (0.12 mg/kg) and ethanol Group 4: OSO (4 mg/kg) and ethanol Group 5: OSO (12 mg/kg) and ethanol Group 6: OSO (24 mg/kg) and ethanol Ozonated sunflower oil was administered once a day for 4 days via an intragastric cannula in different doses according to the groups; this was the case in groups 4, 5 and 6. In group 3, ozonated sunflower oil was administered orally preventatively (before ethanol administration).	SOD, CAT, GSH-Px and TBARS, ulcer size expressed in terms of the ulcer index (UI, square millimetres)	The administration of ethanol led to the genesis of gastric ulcers with a size of 115.75 ± 20.29 mm2. In group 3, the ulcer size was almost the same as in group 2 (115 ± 11.62) In groups 4, 5 and 6, there was a statistically significant decrease in ulcer size; in relation to increasing dose of OSO administered, there were increasing decreases: group 4 18.5 ± 5.65, group 5 7 ± 5.45 and group 6 3 ± 2.27. There is no statistically significant decrease in TBARS levels in the gastric mucosa. Furthermore, it is noted that in rats treated with OSO before ethanol administration (especially in those given higher doses), the activity of the antioxidant enzymes SOD and GSH-Px undergoes a significant reversal. In contrast, the activity of the CAT enzyme does not change significantly in any group
Kesik et al., 2009 [25]	Experimental study on rats	20	Sham Group: 4 rats Treatment Group: 8 rats with methotrexate + ozone therapy Control Group: 8 methotrexate-only rats Ozone gas administration performed with OZONOSAN Photonik 1014 ozone generator (Hansler GmbH, Nordring 8, Iffezheim, Germany) immediately at a dose of 0.72 mg/kg intraperitoneally for 15 days, once daily. Then, methotrexate was administered the day after the end of the 15 applications.	SOD, GSH-Px and MDA in intestine, liver and kidney	Two rats in the methotrexate group died before reaching the end of the study (25%), MDA levels were significantly higher in the methotrexate group than in the other two groups, and MDA levels in the treatment group were similar to those in the sham group, attesting to the protective function of ozone. Histologically, it can be seen that in the treatment group, there is less inflammatory cell infiltrate and less oedema, and the intestinal villi and epithelium morphology are better preserved in the treatment group than in the methotrexate group.

Note: MDA, malondialdehyde; TBARS, thiobarbituric acid reactive substances.
Abbreviations: FGF = fibroblast growth factor, PDGF-BB = platelet-derived growth factor-BB, ONBW = ozone nanobubble water.

articles were included if they had at least one control group or at least one additional comparison group. 'O' for outcomes, the expected outcome was an improvement in radio- and/or chemo-induced mucositis following ozone treatment.

2.5 | Research

Articles were searched using the PubMed, Scopus and WOS databases. The keywords used were the following: 'Ozone AND Mucositis'; 'Ozonated AND Mucositis'; 'Ozone AND Head and neck'; 'Ozone therapy AND Mucositis'; 'Ozone therapy AND Colonic'; 'Ozone AND Oral mucosa'; 'Ozone AND Oral AND Mucosa'; 'Ozone AND Large bowel'; 'Ozone AND Pharynx'; 'Ozone AND Oropharynx'; 'Ozone therapy AND Colon'; 'Ozone AND Therapy AND Colon'; 'Ozonated AND Head and neck'; 'Ozonated AND Head and neck'; 'Ozonated AND Mucositis'; 'Ozonated AND Oral mucosa'; 'Ozonated AND Oral mucosa'; 'Ozonated AND Large bowel'; 'Ozonated AND Large bowel'; 'Ozonated AND Pharynx'; 'Ozonated AND Pharynx'; 'Ozonated AND Oropharynx'; 'Ozonated AND Oropharynx'; 'Ozone AND Chemotherapy AND Mucosa'; 'Ozonetherapy AND Radiotherapy'.

From this search, 1716 articles were found; of these, 1185 were excluded because they were duplicates, 26 because they were not in English, 50 because there was no full text, and finally, after reading the titles, a further 437 were discarded because they were not relevant to the topic under examination. A total of 1698 articles were eliminated from this first phase. Of the 18 remaining articles, the abstract was read; these included 9 literature reviews and 1 case report, which were excluded. Of the 1716 articles found, only 7 could be included in this study; these were 6 preliminary animal studies and 1 prospective cohort study (Figure 1).

The present protocol was registered on the Open Science Framework platform (registration link: https://doi.org/10.17605/OSF.IO/8A3DS).

3 | Results

3.1 | Article Analysis

In total, these studies evaluated 166 animal (rat) and 123 human models. Two studies used ozonised water, three used ozonised oil and two treated volunteers with gaseous ozone. The following indices were evaluated in these studies: FGF levels, PDGF-BB levels, FGF-β levels, B-FGF levels, degree of mucositis, degree of pain (VAS scale), bacterial count, thiobarbituric acid reactive substances (TBARS) levels, superoxide dismutase (SOD) enzyme activity, GSH-Px enzyme activity, malondialdehyde (MDA)

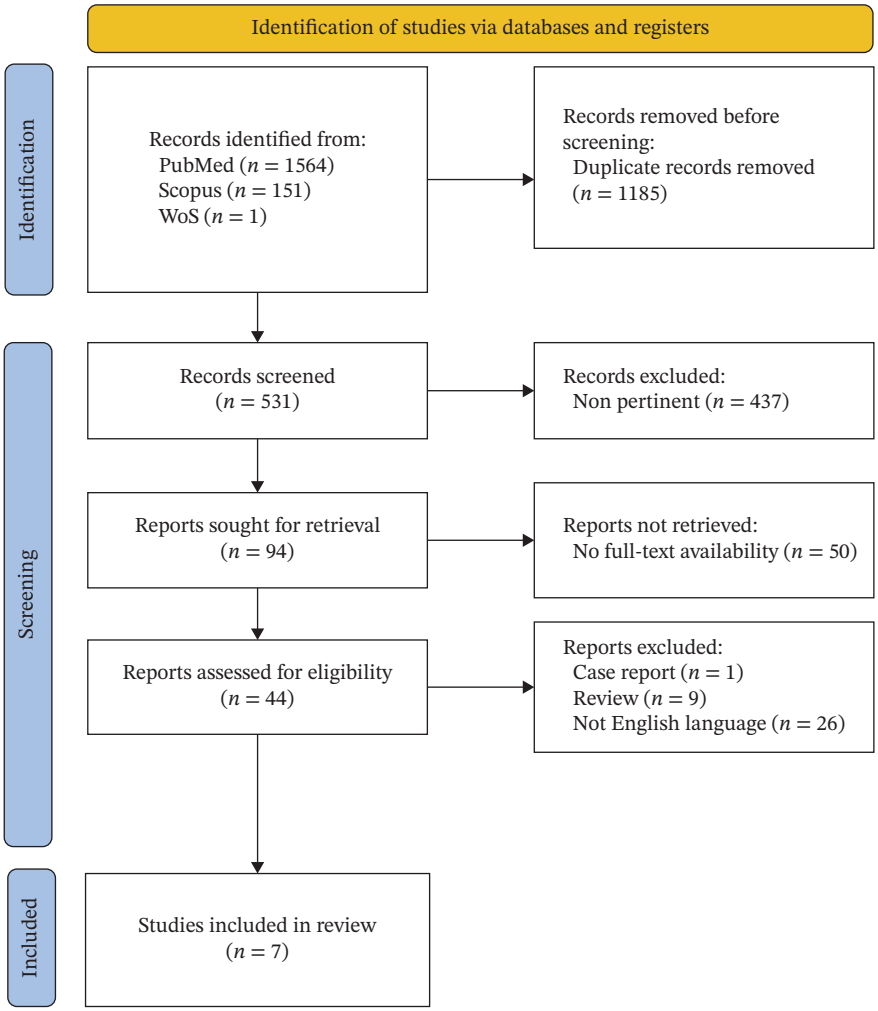

FIGURE 1 | Flow chart of the included studies.

levels, intestinal villus morphology and gastric mucosal epithelial structure (see Table 2).

From their analysis, it appears that in the groups treated with ozone, whether gas, oil or water, there is an increase in FGF-β levels [19], a more rapid improvement in lesion size [20, 22–26] and in the degree of pain as measured by the VAS scale [22, 23, 25], a decrease in the inflammatory infiltrate and oedema in the intestinal tissue and a reduction in tissue damage [25]. In the two studies [22, 24] evaluating the activity of the enzymes SOD and GSH-Px, there is a statistically significant reversal of their activity in the ozone-treated groups compared to the other groups. TBARS levels were reduced in the ozone-treated and cimetidine-treated groups [25]. In the analysis of intestinal tissue, similar MDA levels were found in the ozone therapy group and the sham group, while in the analysis of kidney and liver tissue, although the MDA levels were reduced, the lesions found in the treatment and control groups were similar [25], which attests to the protective function of ozone in the intestinal mucosa, while in the kidneys and liver, the protective function of ozone is present but partial due to the accumulation of the drug (methotrexate) in these organs. Finally, histopathological analysis shows that the morphology of the epithelium of the gastric mucosa and the intestinal villi is better preserved in the groups receiving ozone therapy [25].

3.2 | Bias Risk Assessment

The Cochrane risk-of-bias tool (RoB2) [29] was used to assess the risk of bias in studies (risk of bias), while the Robvis (visualisation tool) [29] was used to create the bias table. Only one study was found to be at low risk; the others were found to be at moderate risk; and no study was found to be at high risk. The overall level of risk of bias of the studies analysed thus results as moderate risk (Figure 2).

4 | Discussion

Ozone therapy is being studied in several areas of medicine. In a review by Ye and coworkers [30], it is shown that ozone therapy has beneficial effects due to its disinfectant and systemic antibacterial and antiviral effects. Furthermore, ozone is claimed to improve tissue hypoxia by regulating the expression of hypoxia-inducible transcription factor alpha (HIF-α) and activating vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) [30]. Ozone applied to diabetic wounds can activate the enzyme SOD, reduce oxidative stress and accelerate wound healing [30]. According to other authors, ozone has antimicrobial, anti-inflammatory and immunostimulant properties, which is why it appears to be effective in many areas, including oral lesions, wound healing, caries management, gingivitis, periodontitis, halitosis, denture stomatitis and recurrent aphthous stomatitis [18, 31]. Ozone therapy has also shown beneficial effects in the treatment of oral lichen planus as adjunct to corticosteroid with respect to corticosteroids alone, colleagues [32]. A recent systematic review [33] showed the beneficial effect of ozone in reducing perceived pain after tissue injury if compared with placebo and with equal effect with corticosteroid and low-level laser therapy. The study by Priya and coworkers [34] also seems to confirm the efficacy of ozone in reducing the healing time; this study shows that the application of topical ozone in the form of an oil aided the healing of a surgical wound. With regard to the treatment of periodontitis and peri-implantitis, some authors [35, 36] have investigated the efficacy of an ozone gel for the treatment of peri-implant mucositis showing comparable effects to 1% chlorhexidine gel. In periodontal setting [36–38], comparable results of ozone with respect to chlorhexidine gel were found.

Ozone is also able to act on the periodontal ligament by promoting the proliferation of ligament cells and the synthesis of type I collagen fibres, thereby increasing the regenerative capacity of the periodontal tissue [39].

The studies included in the present review [19, 20, 22–26] provide converging experimental and clinical evidence supporting the potential therapeutic role of ozone and ozone-derived products (ozonated water and ozonated oils) in the management of mucositis and inflammatory mucosal injuries, mainly through antioxidant, anti-inflammatory and cytoprotective mechanisms.

TABLE 2 | Summary of the clinical studies included in the review.

Title	Type of study	Number of subjects	Comparison groups and pharmacological administration	Tested parameters/analyses conducted	Results
Ghorbani et al., 2021 [26]	Prospective cohort study	93	Group 1: Rinses with 15 mL of ozonated water with a concentration of 20–50 ppm for 1 minute both before and after radiotherapy; if mucositis develops, standard treatment is added. Group 2: Rinses with 15 mL of ozonated water with a concentration of 20–50 ppm for 3 minutes both before and after radiotherapy, after which the same water should not be spat out but swallowed. If mucositis develops, standard treatment is added. Group 3: Standard therapy, so rinses with saline solution and with diphenhydramine, pilocarpine and antibiotics.	Ulcer size (RTOG scale) [27] and VAS scale [28]	

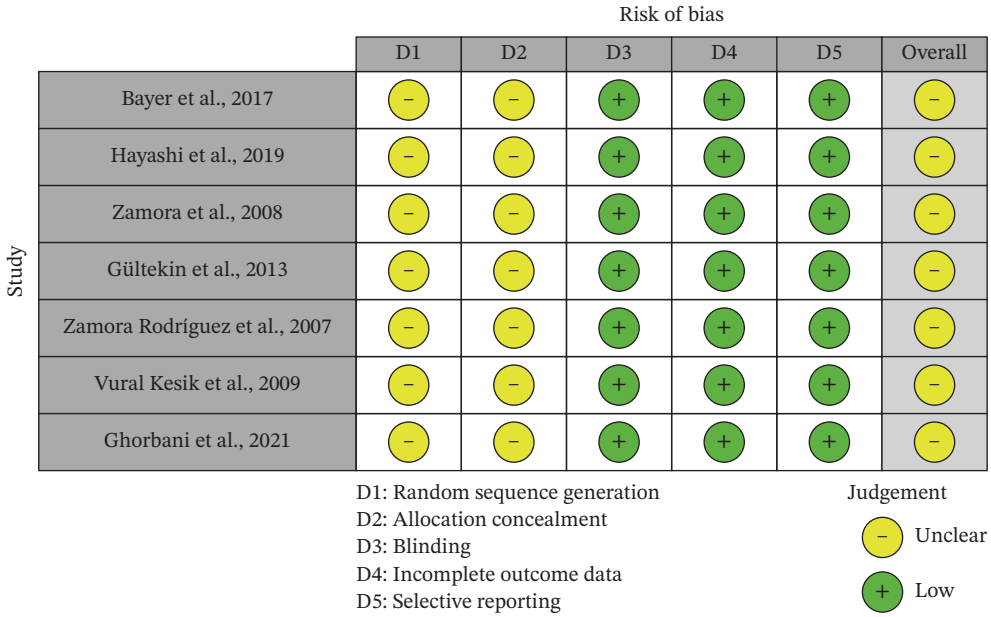

FIGURE 2 | Bias table.

In experimental models of oral mucositis, Bayer et al. [19] demonstrated that ozone treatment significantly reduced the severity of mucosal lesions, with outcomes comparable to those achieved with laser therapy. This finding is clinically relevant, as it suggests that ozone may represent a noninvasive and potentially cost-effective alternative treatment. Similarly, Hayashi et al. [20] reported that ozone nanobubble water attenuated chemotherapy-induced mucositis by preserving epithelial integrity and reducing inflammatory responses. The use of nanobubble technology appears particularly advantageous, as it improves ozone stability in aqueous solutions and enhances tissue interaction.

A consistent finding across gastrointestinal experimental models [22, 24, 25] is the central role of oxidative stress modulation. Zamora et al. [22, 24] demonstrated that ozonised vegetable oils, particularly ozonised sunflower oil, significantly reduced oxidative damage induced by indomethacin and ethanol. This protective effect was associated with increased activity of endogenous antioxidant enzymes, such as SOD and catalase, along with reduced lipid peroxidation. These results support the concept that ozone, despite being a strong oxidant, induces an adaptive response by activating endogenous antioxidant defence systems.

Comparable protective effects were observed by Gültekin et al. [23] in a rat model of acute radiation proctitis, where ozonated olive oil significantly decreased inflammation, oedema and histopathological damage of the rectal mucosa. In this context, ozone appears to act not only as a modulator of oxidative stress but also as a regulator of radiation-induced inflammatory cascades, a mechanism of particular relevance for oncological patients.

Kesik et al. [25] further expanded this evidence by showing that ozone administration ameliorated methotrexate-induced intestinal injury in rats. The observed reductions in apoptosis and structural mucosal damage reinforce the hypothesis that ozone exerts a systemic cytoprotective effect, potentially supporting its use as an adjunctive therapy in chemotherapy-related toxicity.

From a clinical perspective, the study by Ghorbani et al. [26] represents an initial translational attempt, reporting reduced severity of oral mucositis and pain in head and neck cancer patients treated with ozonated water during radiotherapy. However, the cross-sectional design and the lack of randomisation substantially limit the strength of these findings, underscoring the need for well-designed randomised controlled trials.

Overall, the analysed studies demonstrate substantial biological consistency in the effects of ozone on mucosal tissues, regardless of anatomical site. Nevertheless, significant methodological limitations remain, including heterogeneity in ozone concentration, delivery protocols and treatment duration, which currently hinder direct comparison across studies and the establishment of standardised clinical guidelines.

In conclusion, existing evidence suggests that ozone and ozone-based therapies may represent a promising strategy for the management of mucositis and inflammatory mucosal injuries, particularly in oncological settings. Further controlled clinical trials are required to define optimal dosages, safety profiles and long-term clinical benefits compared with conventional therapeutic approaches as considered in current trends [40, 41].

5 | Conclusions

Despite the limited number of trials in the literature, ozone therapy appears to be a promising treatment, with benefits seen in all the studies analysed. Considering that the majority of the studies included in this review were animal studies, further research on human populations is needed to provide higher evidence.

Clinical Relevance: The objective of this systematic review was to evaluate the existing literature on the efficacy of ozone therapy in

the management of mucositis induced by radiation and chemotherapy. Although only a limited number of studies are currently available, the findings suggest that ozone therapy may be effective in reducing inflammatory symptoms, improving the quality of life of cancer patients, and preventing treatment interruptions caused by adverse effects. Consistent with evidence from previously published studies on periodontal and implant patients, ozone therapy appears to represent a promising supportive strategy. Its proactive use could provide valuable benefits for cancer patients undergoing oncological treatments.

Author Contributions

Conceptualisation, Andrea Scribante, Andrea Butera and Marco Zecca; software, Andrea Scribante and Maurizio Pascadopoli; validation, Andrea Scribante, Andrea Butera, Marco Zecca and Silvia Rosso; formal analysis, Maurizio Pascadopoli, Marco Monticone and Andrea Scribante; investigation, Gaia Soressi, and Maurizio Pascadopoli; resources, Andrea Butera; data curation, Andrea Scribante, Maurizio Pascadopoli and Gaia Soressi; writing–original draft preparation, Gaia Soressi and Maurizio Pascadopoli; writing–review and editing, Andrea Scribante, Andrea Butera and Maurizio Pascadopoli; visualisation, Andrea Butera and Anna Maria Grugnetti; supervision, Andrea Scribante, Marco Monticone and Anna Maria Grugnetti; project administration, Andrea Scribante and Andrea Butera.

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Ethics Statement

The authors have nothing to report.

Consent

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data are available upon motivated request to the corresponding authors.

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