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Efficacy of Ozone Therapy in the Management of Initial (Non-Cavitated) Dental Caries: A PRISMA-Guided Systematic Review

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Abstract. Background: Initial (non-cavitated) caries is reversible, and minimally invasive strategies aim to arrest or remineralise it before cavitation. Gaseous and aqueous ozone have been proposed as adjuncts or alternatives, but earlier appraisals judged the evidence insufficient. Objective: To synthesise clinical evidence on whether ozone arrests or reverses non-cavitated caries lesions. Methods: PRISMA-guided review with narrative synthesis (SWiM); search conducted on 30 October 2026; effect estimates were recalculated from reported counts where possible. Results: Five clinical studies in initial lesions (occlusal fissure, approximal and white-spot) were synthesised alongside earlier Cochrane, HTA and NICE appraisals. Four reported benefit relative to no ozone or to a remineralising agent alone, and one found ozone comparable to fissure sealant; follow-up was 3–24 months and sample sizes were small. In a white-spot RCT, lesion progression occurred in 3/43 vs 15/43 patients (RR 0.20; 95% CI 0.06–0.64); in an approximal-lesion RCT, remineralisation at one year was 69.3% with nano-hydroxyapatite plus ozone vs 36.5% with nano-hydroxyapatite alone, with relapse after treatment ended. No adverse events were reported in studies that assessed safety. Risk of bias is predominantly high or unclear, and ozone's independent contribution is confounded by co-interventions. Conclusions: Ozone is a plausible, well-tolerated adjunct to remineralisation for initial caries, but evidence does not justify its use as stand-alone therapy; adequately powered, sham-controlled, factorial trials with long follow-up are required.

Keywords: ozone therapy; initial caries; white spot lesion; remineralisation; minimally invasive dentistry; systematic review

1. Introduction

Caries is a dynamic process of demineralisation and remineralisation, and enamel lesions without cavitation can be arrested or reversed. Current non-operative management relies on plaque control, topical fluoride and, where appropriate, pit-and-fissure sealants; the effectiveness of fluoride is established in randomised trials [1]. Chairside adjuncts that do not depend on patient compliance therefore remain of interest, and ozone (O_3) is one of the most debated.

Ozone is a strong oxidant. The proposed rationale is that it damages the cell wall and membrane of cariogenic bacteria, reducing the biofilm burden, and that oxidation of proteins in the demineralised surface favours uptake of remineralising agents and minerals [2]. Appraisals have been sceptical. A Cochrane review of three trials (432 lesions, 137 participants) reported inconsistent effects across measures of caries progression and regression [3]. A health technology assessment found too little evidence from published RCTs to judge effectiveness in occlusal and root caries, noting that very high success rates came mainly from conference abstracts of low reliability [4], and NICE did not recommend HealOzone outside well-designed trials [1]. A 2020 meta-analysis of RCTs, as summarised in a later review, likewise found insufficient evidence to recommend ozone over other strategies, while a 2024 review in primary teeth found ozone comparable with other interventions but with four of seven studies at high risk of bias [2].

Newer controlled trials have since targeted initial lesions specifically, often combining ozone with remineralising agents. This review asks: in patients with non-cavitated caries lesions, does ozone, alone or as an adjunct, arrest or reverse lesions compared with no ozone or conventional non-invasive care?

2. Methods

2.1 Design and reporting

The review followed the PRISMA 2020 statement [5]; because of anticipated clinical and methodological heterogeneity, synthesis without meta-analysis is reported according to the SWiM guideline [6]. The protocol was not prospectively registered.

2.2 Eligibility criteria (PICOS)

Population: humans of any age with non-cavitated caries lesions (white-spot, ICDAS 1–3, enamel lesions on radiographs or laser fluorescence). Intervention: gaseous or aqueous ozone, alone or with remineralising agents. Comparator: no ozone, placebo, remineralising agent alone, sealant or other non-invasive care. Outcomes: lesion arrest, reversal or progression; remineralisation by clinical or instrumental indices; bacterial counts; adverse events. Design: RCTs and controlled clinical studies; in situ studies were considered supportive. Cavitated-lesion and root-caries-only studies, in vitro-only work, case reports and abstracts without a full report were excluded.

2.3 Search, selection and synthesis

Searches were run on 30 October 2026 through web-indexed records (PubMed Central, Cochrane Library, DOAJ-indexed journals, publisher repositories, ClinicalTrials.gov) and by citation chasing of earlier appraisals [1–4], combining the concepts ozone × initial/non-cavitated caries/white-spot lesion/remineralisation. For replication, the corresponding PubMed string is: (ozone[MeSH] OR ozone[tiab] OR ozonated[tiab]) AND ("dental caries"[MeSH] OR "white spot"[tiab] OR "initial caries"[tiab] OR non-cavitated[tiab] OR remineralization[tiab]). Screening and extraction (design, population, intervention, comparator, follow-up, outcomes) were done by one reviewer; formal PRISMA flow counts are therefore not reported. Methodological quality was appraised narratively (randomisation, blinding, comparator, outcome measurement, follow-up, selective reporting) rather than with a scored tool. Where event counts were reported, risk ratios (RR) with 95% confidence intervals (log method) and Fisher exact tests were recalculated by the authors.

3. Results

3.1 Included studies

Five clinical studies in initial lesions were synthesised (Table 1): two on occlusal fissure lesions in permanent molars [7,8], one comparing ozone with fissure sealant [9], and two on white-spot or approximal enamel lesions [10,11]. Supportive evidence comprised an in situ study [12], an RCT on white-spot prevention during orthodontic treatment [13] and a systematic review of white-spot treatment [14]. A further trial of adjunctive ozone with remineralising gel in children is registered (NCT07671651) without results.

Table 1. Clinical studies of ozone in initial caries synthesised in this review.

Study	Design / population	Ozone vs comparator	Follow-up	Main finding

Study	Design / population	Ozone vs comparator	Follow-up	Main finding
Huth et al., 2005 [7]	Split-mouth controlled trial; non-cavitated fissure lesions, permanent molars	HealOzone, single 40-s application vs untreated contralateral lesion	3 mo	More reversal / less progression with ozone in patients with high current caries activity (exploratory analysis)
Atabek & Oztas, 2011 [8]	40 children aged 9–12 y; initial fissure lesions, permanent molars	Ozone 40 s alone, or ozone + remineralising solution, vs paired control teeth	6 mo	Both ozone regimens effective for remineralisation (DIAGNOdent, clinical severity index)
El Meligy & Almushayt, 2023 [9]	50 patients, 100 first permanent molars; active non-cavitated fissure lesions	Ozone (HealOzone, n = 50 teeth) vs fissure sealant (n = 50 teeth)	12 mo	Ozone reported as effective as sealant in managing lesions
Makeeva & Paramonov, 2016 [10]	RCT; 86 athletes aged 17–21 y; white-spot caries (43 + 43)	Professional hygiene + ozone + 15% hydroxyapatite suspension vs no ozone	12 mo	Positive outcome 93.0% vs 65.1%; progression 3/43 vs 15/43
Grocholewicz et al., 2020 [11]	RCT; 92 adults, 546 approximal enamel lesions	nHAP gel (I), ozone (II), nHAP + ozone (III) for 6 mo	1 and 2 y	Remineralised lesions at 1 y: 36.5% (I) vs 69.3% (III); regression of effect by 2 y after treatment stopped

3.2 Occlusal fissure lesions

In a split-mouth trial, a single 40-s gaseous ozone application produced more caries reversal or less progression than untreated contralateral lesions at three months in patients with high current caries activity, although this was an exploratory subgroup finding [7]. In 40 children, ozone alone or followed by a remineralising solution was effective for remineralisation over six months by laser fluorescence and clinical severity scores [8]. Ozone was reported as effective as fissure sealant over 12 months in 100 first permanent molars [9]. These are small, short studies with surrogate endpoints; the earlier Cochrane review, which required allocation concealment and at least six months' outcomes, found inconsistent effects [3], and the HTA reported no benefit in one unpublished trial and no improvement in sealant retention when ozone was added [4].

3.3 White-spot and approximal lesions

In 86 athletes with white-spot lesions, positive outcomes (stabilisation, regression or disappearance) at 12 months were 40/43 (93.0%) with ozone and 28/43 (65.1%) without; progression occurred in 3/43 (7.0%) vs 15/43 (34.9%) [10]. From these counts we calculated RR for a positive outcome of 1.43 (95% CI 1.13–1.80; Fisher p = 0.003) and RR for progression of 0.20 (95% CI 0.06–0.64), an absolute risk reduction of 27.9 percentage points (number needed to treat ≈ 3.6). Blinding is not described in the report, the population is young and athletic, and the ozone arm bundled professional hygiene with ozone and hydroxyapatite. In 92 adults with 546

approximal enamel lesions, remineralisation at one year was seen in 36.5% of lesions with nano-hydroxyapatite (nHAP) gel alone and 69.3% with nHAP plus ozone, the combination performing best; demineralisation recurred by two years after treatment stopped, so benefit was not self-sustaining [11].

3.4 Supportive evidence, safety and cost

In an in situ model, ozonated water plus nHAP gave lower laser-fluorescence scores and deeper remineralisation than nHAP alone or saliva ($P < 0.001$) [12]. In orthodontic patients, groups of 30 receiving fluoride varnish, ozone and octenidine in combination had the lowest percentage with new white-spot lesions [13]; a 2025 systematic review of eight RCTs concluded that ozone combined with fluoride enhanced efficacy compared with single treatments, while calling for long-term studies [14]. No adverse events were reported in the Cochrane-included trials [3], in a 78-participant root-caries trial [15] or in primary-tooth studies [2]. A five-year model estimated that HealOzone added cost over current care for non-cavitated fissure caries (£40.49 vs £24.78), though figures were illustrative [4].

3.5 Appraisal of the evidence

Table 2 summarises features that bear on internal validity. The ozone effect can be isolated in only three studies [7,8,11]; one study bundled ozone with hygiene and hydroxyapatite [10], and one used an active comparator [9]. Participant blinding is impracticable without a sham device, and assessor blinding and allocation concealment were not described in the reports available to us, so selection and detection bias cannot be excluded. Endpoints were largely surrogate (laser fluorescence, clinical indices); only one trial used radiographs [11]. Taking these limitations together with small samples, follow-up of at most two years and probable small-study effects, we judge the overall certainty of evidence for ozone as an adjunct to be low, and very low for ozone as stand-alone therapy (a GRADE-style judgement by the authors, not a formal GRADE assessment).

Table 2. Features bearing on internal validity of the included studies (narrative appraisal).

Study	Ozone effect isolable from co-interventions?	Comparator	Principal endpoint	Sample / follow-up
Huth 2005 [7]	Yes (no remineralising solution)	Untreated contralateral lesion	Clinical caries reversal / progression	Pairs of molars; 3 mo
Atabek 2011 [8]	Partly (ozone-alone arm; second arm adds solution)	Paired untreated teeth	Laser fluorescence (DIAGNOdent); clinical severity index	40 children; 6 mo
El Meligy 2023 [9]	Not applicable (active comparator)	Fissure sealant	Caries status and sealant retention	100 teeth; 12 mo
Makeeva 2016 [10]	No (ozone bundled with hygiene and hydroxyapatite)	No-ozone group	Lesion size, stain intensity, progression	86 patients; 12 mo

Study	Ozone effect isolable from co-interventions?	Comparator	Principal endpoint	Sample / follow-up
Grocholewicz 2020 [11]	Yes (ozone-alone and nHAP-alone arms)	nHAP gel alone; ozone alone	Lesion status on bitewing radiographs	92 patients, 546 lesions; 1 and 2 y

4. Discussion

Earlier syntheses are summarised in Table 3.

Table 3. Earlier systematic appraisals of ozone in caries.

Synthesis	Scope	Evidence base	Conclusion
Rickard et al., 2004 [3]	Ozone for caries; RCTs with ≥6-mo outcomes	3 trials; 432 lesions; 137 participants	Inconsistent effects; more rigorous evidence needed
Brazzelli et al., 2006 [4]; NICE TA92 [1]	HealOzone for occlusal and root caries	Ten RCTs incl. abstracts and theses	Insufficient evidence; not recommended outside well-designed RCTs
Veneri et al., 2024 [2]	Caries in primary teeth	7 studies from 215 records; 4 at high risk of bias	Comparable to other interventions; no adverse effects; no meta-analysis possible
Lamorgese et al., 2025 [14]	White-spot lesions; combined treatments	8 RCTs from 1185 articles	Combined strategies, incl. ozone + fluoride, superior to single treatments

Recent controlled studies point in a consistent direction: ozone, particularly when combined with a remineralising agent, was associated with more lesion regression or less progression than the comparator in four of five studies, and was comparable to sealant in the fifth. This does not contradict the older null appraisals. Those reviews applied strict criteria (allocation concealment, outcomes at six months or longer) to heterogeneous early trials, many reported only as abstracts or theses [3,4], whereas the present evidence concerns different lesion types, mostly adjunctive designs and surrogate endpoints.

Three issues limit inference. First, confounding by co-interventions: in most positive studies ozone was layered on hydroxyapatite, remineralising solutions, fluoride or professional hygiene [8,10,11,14], so the effect attributable to ozone alone is unknown; only factorial or ozone-only versus sham-ozone arms can isolate it. Second, mechanism: antibacterial action is the usual explanation, yet a study of non-cavitated occlusal lesions found that 40 s of ozone did not significantly reduce viable bacteria in infected dentine [16]. It is therefore plausible, though unproven, that benefit arises from oxidative conditioning that enhances mineral uptake rather than from disinfection. Third, durability: relapse after treatment ceased [11] implies that ozone does not replace behavioural control and maintenance remineralisation.

Methodologically, the evidence base is weak: small samples, follow-up of 3–24 months, laser fluorescence or visual scores as endpoints, limited reporting of blinding and allocation concealment (blinding gas delivery is intrinsically difficult without a sham device), split-mouth designs with possible carry-over, and probable publication bias favouring positive trials. Standardised dosing is lacking (device, exposure time, repeat applications). Limitations of this review itself include single-

reviewer screening, a search conducted through web-indexed records rather than exported bibliographic databases, no registered protocol, no formal risk-of-bias instrument and no meta-analysis; it should be read as a PRISMA-guided structured synthesis, not a replacement for a registered, dual-reviewer review.

The magnitude of the reported effects deserves cautious reading. In the three-arm trial, nHAP alone remineralised 36.5% of lesions at one year, so adding ozone corresponded to an increment of roughly 33 percentage points [11]; in the white-spot trial the absolute difference in progression was 27.9 percentage points [10]. Effects of this size from small, single-centre trials warrant independent replication before they are treated as established. Subgroup signals are also worth testing prospectively: the benefit in high-caries-activity patients [7], the orthodontic setting where white-spot prevention is the goal [13,14], and young or poorly cooperative children for whom a rapid, non-invasive, well-accepted procedure may be the only feasible option [2].

For practice, established measures (fluoride, sealants, sound hygiene) remain first-line [1]. Ozone may be considered a low-risk adjunct where chairside remineralisation support is wanted, with realistic expectations and recall. Future trials should register protocols, use ICDAS/radiographic or quantitative light-induced fluorescence endpoints at ≥24 months, adopt sham-controlled factorial designs, report device settings, and adopt a core outcome set so that meta-analysis becomes feasible.

5. Conclusion

Current evidence suggests that ozone is a safe and potentially useful adjunct to remineralisation of initial caries, with consistent but low-certainty benefit in small, short trials. Evidence is insufficient to support ozone as stand-alone treatment or to establish cost-effectiveness. Rigorous multi-centre sham-controlled trials are needed.

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