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Review article

EVALUATING THE ROLE OF HEDP-BASED CONTINUOUS CHELATION IN ROOT CANAL DISINFECTION: LITERATURE REVIEW

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ABSTRACT

Aim: This review evaluates the potential of 1-hydroxyethylidene-1,1-diphosphonic acid (HEDP, etidronic acid), including the commercial product Dual Rinse HEDP, as a chelating agent used in combination with sodium hypochlorite (NaOCl) for continuous chelation.

Materials and methods: A narrative literature review was conducted using PubMed/Medline, Scopus, Web of Science and Google Scholar to identify laboratory and clinical studies on HEDP combined with NaOCl for root canal irrigation.

Results: HEDP can be mixed with NaOCl without an immediate loss of available chlorine, although available chlorine decreases over time, depending on the concentration and formulation of the NaOCl solution. Compared with sequential NaOCl/EDTA irrigation, laboratory studies report comparable smear layer removal, less dentin erosion in most studies, more favorable flexural strength and microhardness values, and no detrimental effect on sealer adhesion. The antimicrobial effect of the mixture is attributable mainly to NaOCl, which HEDP does not appear to impair; additional benefits, such as preserved antimicrobial activity in the presence of a smear layer, have been reported in individual *in vitro* studies. Two small randomized clinical trials found no differences from NaOCl alone in postoperative pain, bacterial reduction or periapical inflammatory markers. The evidence is predominantly *in vitro* and *ex vivo*, and protocols vary considerably among studies.

Conclusion: HEDP-based continuous chelation is a promising, simplified alternative to sequential NaOCl/EDTA irrigation. However, the current evidence is derived mainly from laboratory studies, and well-designed clinical trials with long-term outcomes are needed before definitive recommendations can be made.

Keywords: Etidronic Acid, Sodium Hypochlorite, Root Canal Irrigants, Chelating Agents, Smear Layer, Dentin

BACKGROUND

Disinfection of the root canal system is essential for endodontic success and depends on irrigants capable of eliminating resistant biofilms while preserving the periapical tissues. Sodium hypochlorite (NaOCl) remains the gold standard because of its strong antimicrobial and tissue-dissolving properties [1]. It is a nonspecific proteolytic agent used in concentrations of 0.5–6%, acting through saponification of the organic dentin matrix, neutralization of amino acids and release of oxidizing chlorine that inhibits bacterial enzymes [2]. However, NaOCl cannot dissolve inorganic components and therefore cannot remove the smear layer. The smear layer contains organic and inorganic particles, coagulated proteins, pulp tissue, blood cells, bacteria and their by-products; therefore, an additional decalcifying agent is recommended for its effective removal [3]. Ethylenediaminetetraacetic acid (EDTA) in 15–17% concentration is the most commonly used chelator in endodontics. Sequential irrigation with NaOCl and EDTA leads to enlargement of the dentinal tubules and erosion of peritubular and intertubular dentin, with decalcification of the superficial dentin layer (1–5 μm) and the tubular walls (20 μm), which may reduce dentin elasticity and increase the risk of vertical root fracture. While NaOCl dissolves the organic matrix, subsequent EDTA application removes the mineral phase, contributing to further erosion [2]. In addition, EDTA causes an immediate reduction of available chlorine when in contact with NaOCl, which necessitates complex irrigation protocols [4].

Aim:

This review evaluates the potential of HEDP as a chelating agent used in combination with NaOCl for continuous chelation, with particular reference to the commercial product Dual Rinse HEDP.

MATERIALS AND METHODS:

A narrative literature review was conducted using PubMed/Medline, Scopus, Web of Science and Google Scholar. The search covered publications from January 2005 to December 2025 and used combinations of the

terms “etidronic acid”, “etidronate”, “HEDP”, “1-hydroxyethylidene-1,1-diphosphonic acid”, “Dual Rinse”, “continuous chelation”, “sodium hypochlorite” and “root canal irrigation”. English-language in vitro, ex vivo and clinical studies evaluating HEDP combined with NaOCl as an endodontic irrigant were included, together with relevant reviews. Studies on non-endodontic applications of HEDP were excluded, except for background information on its chemistry. The review addresses HEDP-based continuous chelation in general; the commercial product Dual Rinse HEDP is discussed specifically where the cited studies used it. The findings were analyzed descriptively.

REVIEW RESULTS

The search for alternative decalcifying agents has identified etidronic acid, also known as 1-hydroxyethylidene-1,1-diphosphonic acid (HEDP). HEDP is a non-nitrogenous bisphosphonate containing C–$PO(OH)_2$ groups. It is used in a variety of applications, such as corrosion inhibitors, anti-scaling agents, dispersants in cooling water circulation systems, and builder components in industrial cleaners and household detergents [5]. Dual Rinse HEDP (Medcem GmbH, Switzerland) is a commercial HEDP product supplied in capsules containing 0.9 g of HEDP powder. According to the manufacturer, the powder should be mixed immediately before treatment with 10 mL of NaOCl solution in a sterile autoclavable cup; the mixture remains usable for 1 hour, and the properties of NaOCl remain intact [6]. Alternatively, Dual Rinse HEDP can be mixed with sterile physiological saline (1 capsule per 10 mL) and used as a mild decalcifying solution without proteolytic properties [6].

When added to the NaOCl irrigant, HEDP does not cause an immediate loss of available chlorine [7]; at the same time, it forms complexes with calcium ions, which allows it to act as a chelating agent with a lower erosive potential than EDTA. This simultaneous use of NaOCl and HEDP throughout instrumentation has been termed continuous chelation [8, 9]. It simplifies the irrigation protocol and may shorten the instrumentation time [4].

Recent publications have investigated the efficacy, safety and potential of HEDP to improve endodontic cleaning protocols. The main laboratory and clinical studies are summarized in Table 1, and their findings are discussed below by topic.

Chemical compatibility with NaOCl and clinical handling

The manufacturer’s statement that the properties of NaOCl remain intact [6] should be interpreted in the light of independent studies. HEDP does not cause an immediate loss of available chlorine [7], and no decrease in available chlorine was found within 60 minutes when 9% HEDP was added to 2.5% NaOCl [10]. The ability of NaOCl to dissolve organic tissue is also only minimally affected by HEDP [11]. However, available chlorine decreases progressively over longer periods: after 24 hours, free available chlorine was completely lost and the pH of the mixture decreased by more than three units [12]. Other studies have also reported a time-dependent reduction in available chlorine and pH after the addition of HEDP to NaOCl [13, 14]. The stability of the mixture depends on the concentration and formulation of the NaOCl solution, including proprietary additives [9, 13], and is also likely to be influenced by storage time and temperature.

These findings are not necessarily contradictory. The manufacturer’s claim refers to freshly prepared mixtures used within the recommended period, whereas the reductions in available chlorine reported in the literature are time-dependent and become evident with longer storage. The 1-hour usability period should therefore be regarded as a maximum, and the solution should be prepared immediately before use and discarded if it is not used within this period [9, 13]. Because the extent of chlorine loss differs among NaOCl products, NaOCl solutions that have been tested for compatibility with HEDP should preferably be used.

Smear layer removal and effects on root dentin

In the studies reviewed, smear layer removal, dentin erosion and changes in the mechanical properties of dentin were assessed with different methods and are therefore considered separately. With regard to the smear layer and debris, continuous chelation with NaOCl/HEDP removed or prevented the formation of a smear layer on most instrumented canal walls [15] and reduced, but did not completely prevent, the accumulation of hard-tissue debris during rotary instrumentation [16]. Compared with sequential irrigation with 3% NaOCl and 17% EDTA, an HEDP-containing NaOCl solution resulted in similar canal wall cleanliness, and in both groups more smear layer remained in the apical than in the coronal third [17]. A scoping review of laboratory studies also supported the effectiveness of continuous chelation in removing the smear layer and debris [18].

With regard to dentin erosion, NaOCl combined with HEDP did not cause the decalcification patterns observed after EDTA [15]. In a micro-computed tomography study, HEDP produced erosion depths of approximately 16–20 μm, compared with 32–46 μm for EDTA, with the greatest erosion in the cervical third and only minimal differences at the apical level [19]. In contrast, a scanning electron microscopy study found moderate erosion in 10–26% of the specimens irrigated with either an HEDP-containing NaOCl solution or NaOCl followed by EDTA, without significant differences between the two protocols [17]. The apical third deserves particular attention, because the dentin there is thinner and the canal anatomy is more complex, and because continuous exposure to the mixture throughout instrumentation increases the contact time with the apical dentin walls. Excessive erosion in this region could theoretically contribute to enlargement of the apical foramen and extrusion of the irrigant; however, these concerns are based on laboratory findings and theoretical considerations and have not been confirmed

clinically.

With regard to mechanical properties, continuous chelation resulted in higher flexural strength and microhardness of root dentin than sequential chelation with EDTA in an *ex vivo* study [3], and less pronounced changes in dentin after continuous than after sequential chelation have also been reported in other laboratory studies [2]. However, changes in microhardness and flexural strength measured on dentin specimens cannot be directly extrapolated to the fracture resistance of endodontically treated teeth, and their clinical significance remains to be established.

Antimicrobial and antibiofilm activity

The antimicrobial effect of the NaOCl/HEDP mixture is attributable mainly to NaOCl, whereas HEDP itself has limited antibacterial activity. The antibacterial effects of endodontic irrigants are traditionally studied using *Enterococcus faecalis*, as this species is frequently detected in teeth with apical periodontitis. In a biofilm model and in infected dentinal tubules, 2.5% NaOCl with or without 9% HEDP eradicated *E. faecalis* biofilms and showed the greatest antimicrobial effect inside the dentinal tubules, with no significant differences between the two solutions; HEDP alone killed bacteria inside the dentinal tubules but had no significant effect on biofilms [10]. Thus, HEDP did not interfere with the antimicrobial activity of NaOCl. A possible additional contribution of HEDP relates to the smear layer: in infected dentin, the presence of a smear layer significantly reduced the antimicrobial activity of NaOCl alone but not that of the NaOCl/HEDP mixture [20]. An increased dentin disinfection efficacy of NaOCl after the addition of HEDP has also been suggested [21]. Chelators may additionally promote the detachment of biofilms from the root canal walls and bind metal ions that bacteria use as nutrients [18]. However, these results were obtained with different experimental models, bacterial species, concentrations and exposure times, and they cannot be directly extrapolated to the clinical situation.

Adhesion of sealers and tricalcium silicate cements

Continuous chelation with HEDP improved the adhesion of an epoxy resin-based sealer to root dentin [8], and higher bond strength values of endodontic sealers have been reported after irrigation with etidronic acid [22]. In addition, HEDP did not have a detrimental effect on the dislodgement resistance of tricalcium silicate-based cements or on their microstructure [23]. This may be relevant in perforation and resorption repair and in apexification procedures, in which adequate adhesion of the cement to root dentin is essential.

Biocompatibility

Freshly prepared mixtures of HEDP and 2.5% NaOCl were not more cytotoxic to fibroblasts than NaOCl alone, and HEDP alone showed little cytotoxicity and no genotoxicity at the concentrations tested; the cytotoxicity of the mixtures depended on their free available chlorine content [12]. These *in vitro* results suggest that the addition of HEDP does not increase the toxicity of NaOCl, but they do not allow conclusions about tissue reactions *in vivo*.

Clinical evidence

Clinical evidence is limited to a small number of randomized trials with short-term outcomes. In a randomized double-blind trial including 60 patients with asymptomatic apical periodontitis, culture-negative canals were found in 40% of the cases after irrigation with NaOCl alone and in 50% after irrigation with NaOCl/HEDP ($P = 0.60$); postoperative pain was rare in both groups, and the periapical levels of matrix metalloproteinase-9 (MMP-9) decreased significantly after one week, with no difference between the groups [24]. In another randomized clinical trial, 34 patients with necrotic single-canal mandibular premolars were irrigated with 2.5% NaOCl alone or combined with Dual Rinse HEDP. No significant differences were found between the groups in post-instrumentation pain at 6, 12, 24 and 48 hours, in the reduction of the intracanal bacterial load or in periapical MMP-9 levels [25]. The limitations of this trial include the small sample size, the inclusion of a single tooth type and the short observation period. Neither trial assessed long-term periapical healing. Therefore, potential clinical consequences such as apical extrusion of the irrigant or postoperative inflammation remain theoretical considerations based on laboratory data, and the available trials did not show an increase in postoperative pain with the mixture.

Physical properties and areas of conflicting evidence

HEDP reduces the pH of NaOCl and increases the surface tension and viscosity of the solution [13, 21], which theoretically may limit its penetration into areas that are difficult to reach, such as the apical third, isthmuses and dentinal tubules. Nevertheless, an increased dentin disinfection efficacy has been reported despite the higher surface tension [21]. Heating decreases the viscosity of NaOCl and improves its flow properties, and the tissue-dissolving ability of NaOCl combined with Dual Rinse HEDP has been evaluated at different temperatures [26]; however, the effect of heating on the chemical stability of the mixture requires further investigation.

The available studies provide differing results in several areas. Some laboratory studies report less dentin erosion with HEDP than with EDTA [15, 19], whereas others found no differences [17]; the stability of available chlorine varies with time, concentration and formulation [10, 12, 13]; and potential additional antimicrobial benefits of HEDP were observed only under specific experimental conditions [20, 21]. These differences are likely explained by differences in study design, irrigant concentrations, exposure times, activation methods and outcome measures, which limit direct comparison between studies.

Table 1. Summary of the main studies on HEDP combined with NaOCl included in the review

Study	Type of study / model	Irrigants compared	Main findings
Lottanti et al. [15]	*Ex vivo*, human roots; SEM, calcium elution	NaOCl + HEDP vs NaOCl → EDTA or peracetic acid	Smear layer removed or prevented with all decalcifying protocols; no dentin decalcification with NaOCl + HEDP, typical demineralization with EDTA.
Paqué et al. [16]	*Ex vivo*, mandibular molars; micro-CT	2.5% NaOCl vs 2.5% NaOCl + 9% HEDP	Less hard-tissue debris with HEDP (3.8 vs 5.5 vol%), but debris not eliminated.
Arias-Moliz et al. [10]	*In vitro*, *E. faecalis* biofilm and infected dentinal tubules	2.5% NaOCl, 9% HEDP, NaOCl + HEDP	Both NaOCl solutions eradicated biofilms; HEDP did not impair NaOCl; no loss of available chlorine within 60 min.
Morago et al. [20]	*In vitro*, infected dentin with/without smear layer; CLSM	2.5% NaOCl vs 2.5% NaOCl + 9% HEDP	Smear layer reduced the activity of NaOCl alone but not of NaOCl + HEDP
Ballal et al. [12]	*In vitro*, chemical analysis and fibroblast assays	Fresh and 24-h-old NaOCl + HEDP vs NaOCl and HEDP alone	Complete loss of free available chlorine after 24 h; fresh mixture not more cytotoxic than NaOCl; no genotoxicity of HEDP
Kfir et al. [17]	*Ex vivo*, single-rooted teeth; SEM	3% NaOCl + HEDP vs 3% NaOCl → 17% EDTA	No differences in smear layer, debris or erosion; more smear layer apically in both groups
Zarean et al. [19]	*Ex vivo*, premolars; micro-CT	NaOCl → HEDP vs NaOCl → EDTA (ultrasonic activation)	Erosion approx. 16–20 μm with HEDP vs 32–46 μm with EDTA; greatest in the cervical third
Ballal et al. [3]	*Ex vivo*, root dentin; mechanical testing	Continuous vs sequential chelation	Higher flexural strength and microhardness with continuous chelation
Ballal et al. [24]	RCT, 60 patients with asymptomatic apical periodontitis	NaOCl vs NaOCl + HEDP	Culture-negative canals 40% vs 50% (P = 0.60); no differences in postoperative pain or MMP-9
Abdel-Hamid et al. [25]	RCT, 34 patients with necrotic mandibular premolars	2.5% NaOCl vs 2.5% NaOCl + Dual Rinse HEDP	No differences in pain (6–48 h), bacterial reduction or MMP-9

SEM – scanning electron microscopy; micro-CT – micro-computed tomography; CLSM – confocal laser scanning microscopy; RCT – randomized clinical trial; MMP-9 – matrix metalloproteinase-9; → – followed by.

CONCLUSION

The available evidence indicates that HEDP can be combined with NaOCl for continuous chelation, providing smear layer removal comparable to that of sequential NaOCl/EDTA irrigation, with less dentin erosion in most laboratory studies and without impairing the antimicrobial activity of NaOCl. Because available chlorine decreases over time, the mixture should be prepared immediately before use.

However, the evidence is derived mainly from *in vitro* and *ex vivo* studies, and the few randomized clinical trials have small samples and short-term outcomes. Well-designed clinical trials evaluating long-term periapical healing, as well as standardization of concentrations and irrigation protocols, are needed before definitive clinical recommendations can be made.

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