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Etidronic acid as a chelating agent in root canal treatment: Review of the literature

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Abstract
Classical irrigating protocol has been to use NaOCl followed by chelating agent. Combination of irrigants is likely to form unwanted by-products. Etidronic acid was suggested as chelating agent that use with NaOCl without adversely effects.The aim of this review is to summarize and discuss the published papers focusing on the different outcomes regarding etidronic acid as a chelator agent.A literature search for relevant published articles on etidronic acid as a chelator agent in the context of endodontics with respect to cleanliness and erosion of dentin, smear layer removal, bond Strength of sealers, biofilm removal, torsional load on rotary instruments, and growth factors release using the most popular electronic databases:The total number of articles that reviewed in this study was 103 but 23 articles met the criteria of this study, Out of 23 studies 3 evaluated the impact of etidronic acid on cleanliness and erosion of dentin, 6 on smear layer removal, 6 on bond strength of sealer, 5 on biofilm removal, 1 on the torsional load on rotary instruments ,and 2 on growth factors release.Etidronic acid can be combined with NaOCl without adversely effect. Continuous chelation protocol benefits RCT since it disinfects the root canal and removes the smear layer. It also improves the bond strength of sealer, reduces the torsional load on rotary instruments, and induces growth factor release.

Keywords: Continuous chelation, Etidronic acid, Irrigation, Root canal, Sequintail chelating, Smear layer

Introduction

Various factors such as proper diagnosis, cleaning with intracanal medicaments, irrigation solutions to remove the necrotic debris, and obturation of the pulpal space followed by final restoration determine the success of endodontic treatment [1]. Due to unusual internal root configurations as lateral and accessory canals, concavities, delta, isthmus, inaccessible fins, cul-de-sacs ….etc, mechanical instrumentation alone can't effectively eliminate the microorganisms from the root canal during root canal therapy [2]. So for the success of endodontic therapy and completely remove all necrotic debris and microorganisms from the root canal chemical agents in combination with instruments should be applied.

Even with the use of manual or rotary instrumentation, instruments only act on the central body of the canal, leaving the complexities of the root canal untouched after completion of the preparation. These areas might harbor tissue debris, microbes and their by-products which might prevent close adaptation of the obturation material and result in persistent inflammation. Irrigation is an essential part of root canal debridement because it allows for cleaning beyond what might be achieved by root canal instrumentation alone [3].

Endodontic irrigants available for disinfecting root canals include sodium hypochlorite (NaOCl), chlorhexidine (CHX), and chelating agents as ethylenediaminetetraacetic acid (EDTA), and citric acid etc. Unfortunately, endodontic irrigants may interact chemically with each other when used in sequence without neutral irrigant as normal saline, since the combination of irrigants is likely to form unwanted by-products which may be toxic or cause allergic reactions [4]. For example the interaction of NaOCl and CHX solution resulted in an orange-brown precipitate called parachloroanaline (PCA) which is suspected to have cytotoxic and carcinogenic effects and impair the good adaptation of obturation materials onto dentinal tubules [5]. As will as NaOCl cannot maintain its antimicrobial property and organic tissue dissolution capacity when used with EDTA, because the free available chlorine tends to decrease due to the interaction between these two irrigants [6].

If CHX is combined with EDTA, it leads to interaction and formation of white precipitate which reduces the efficiency of EDTA solution, [7] while mixing NaOCl and MTAD results in the formation of a yellow precipitate [8]. So there was a need to use different irrigants particularly chelating agents that do not interact with NaOCl or CHX. Different chelating agents as peracetic acid (PAA) and etidronic acid, that do not interact with NaOCl are being investigated.

A 1-hydroxyethylidene-1, 1-bisphosphonate (HEBP), known as etidronic acid or (Dual rins HEDP®) has been suggested as a possible alternative irrigation solution to EDTA. Etidronic acid is a biocompatible decalcifying agent and has previously been reported to achieve smear layer removal when used with NaOCl [9, 10].

Since 2005, the number of articles in concerning the interaction of irrigant solutions have grown significantly, and the topic was greatly debated. Therefore, the aim of the present review is to summarize and discuss the published papers focusing on the different outcomes regarding etidronic acid as a chelator agent and a possible alternative irrigation solution to EDTA.

Materials and Methods

A literature search for relevant published articles on etidronic acid as an irrigant solution or a chelator agent in the context of endodontics between April 2009 and April 2025 in all languages using the most popular electronic databases: PubMed, ResearchGate, Web of science, ScienceDirect, Wiley Online Library, and Google Scholar. The search was performed using different keywords (etidronic acid, etidronate, a 1-hydroxyethylidene-1, 1-bisphosphonate or (HEBP), Dual rins HEDP®.

Peer-reviewed studies evaluated the influence of etidronic acid on root canal treatment outcome have been identified through these popular electronic databases. Articles in which keywords do not match the subject of the search, case reports, and non-English language studies have been excluded. After removing duplicates, the remaining papers were retrieved, and their reference lists checked to identify any other articles/textbooks relevant to the topic, which might have provided additional information.

The data have been analyzed, and weighted averages have been determined for each of the following: cleanliness and erosion of root canal walls, smear layer removal and soft tissue-dissolving, bond strength of sealers, removal of biofilm, the effect of etidronic acid on the torsional load on rotary instruments, and growth factors release.

Results

Etidronic acid as chelating agent in root canal treatment has been intensively assessed through the last two decades in dental literature.

A large number of studies have evaluate the toxicity, genotoxic, biocompatibility, and the effect of this irrigant on root canal treatment outcome. Majority of researchesassessed the impact of etidronic acid on smear layer removal and soft tissue-dissolving and bond strength of sealers to dentin and to a lesser extent evaluate the effect of this irrigant solution on cleanliness and erosion of root canal walls, removal of biofilm, the effect of etidronic acid on the torsional load on rotary instruments, and growth factors release.

Different teeth categories were analyzed in these studies, and the sample sizes presented discrepancies and variety in the methodological protocols of the in-vitro studies as electronic scanning microscope (ESM), spectroscopic, push-out test, and optical coherence tomography (OCT).

The total number of articles that reviewed in this study was 103. All of them were peer-reviewed studies and indexed in PubMed, ResearchGate, Web of science, ScienceDirect, Wiley Online Library, and Google Scholar data base.Out of 103 articles 23 met the criteria of this review study, Out of 23 studies 3 evaluated the impact of etidronic acid on cleanliness and erosion of root canal walls, 6 on smear layer removal and soft tissue-dissolving, 6 on bond strength of sealer to root canal dentine, 5 on removal of biofilm, 1 on the torsional load on rotary instruments ,and 2 on growth factors release.

Discussion

The process of endodontic therapy is designed to optimize the cleaning and shaping of the intricate root canal system. An effective way to achieve this is through the use of chemical irrigants. While EDTA and citric acid are commonly used, HEBP (1-hydroxyethylidene-1, 1-bisphosphonate), also known as etidronate or etidronic acid, has emerged as a promising alternative. This is due to its superior efficacy, as it does not react with NaOCl. Additionally, HEBP is a non-toxic substance that has been systematically applied to treat bone diseases [11]. Because of the importance of irrigation of root canals in late decades new irrigation solutions have emerged, and it was necessary to understand the results of this irrigants when interact with another known irrigant as NaOCl and CHX.

It has been shown an orange-brown precipitate called parachloroanaline (PCA) produces when NaOCl and CHX interact with each other, and white precipitate produces when NaOCl and EDTA or CHX and EDTA interact chemically with each other. These precipitates usually negatively affect the properties of irrigants and impair the sealing ability of obturation materials [5, 6]. In general, the irrigation protocols of root canal are built around NaOCl since this irrigant has the clinically most important basic properties for chemical root canal cleaning. Classical irrigating protocol has been to use NaOCl during root canal instrumentation, followed by chelating agent as EDTA or citric acid to remove the smear layer and debris, and then NaOCl again as the final rinse for the final disinfection [12]. This sequence can be shortened by one step by adding a disinfectant or antibiotic to the decalcifying final irrigant but without adverse chemical reactions [13].

It has been investigated that etidronic acid was a biocompatible decalcifying agent that can be combined with NaOCl during the treatment at least for a short time. This material removed smear layer without adverse effects on dentin since etidronic acid leaves it in its natural state and does not aggressively decalcify it [9]. Etidronic acid is a chelator agent forms somewhat weaker complexes with calcium than that with EDTA and citric acid and when this material mixed with NaOCl the calcium ions are continuously complexed. According to this manner the alternating irrigation schemes can be completely eliminated and the etidronic acid could add to NaOCl during the entire endodontic treatment.With this concept, the smear layer and debris are not removed after mechanical root canal preparation, but instead their formation is prevented [9]. This occurs without decalcification of the canal wall [10].

In the last years, the application of etidronic acid in endodontics has been extensively studied. Some studies focused on the effect of etidronic acid on cleanliness and erosion of root canal walls, smear layer removal and soft tissue-dissolving, while other studies focused on bond strength of resine sealer and CaSi-cement-based sealer, removal of biofilm of enterococcus faecalis and the effect of etidronic acid on the torsional load on rotary instruments and growth factors release.

Cleanliness and erosion of root canal walls

Investigations using microscopic and spectroscopic have revealed that the sequential chelation protocol (NaOCl/EDTA), which is the most commonly used irrigation protocol in root canal treatment, results in widening of the dentinal tubular opening [14] and intertubular tunnelling due to dentin erosion [15]. NaOCl/EDTA results in complete decalcification of the superficial 1−5 μm of intertubular dentin, and up to 20 μm in the dentinal tubular walls [14]. So that the resultant dentin substrate is more brittle than untreated dentin because of erosion of dentine by EDTA [16].

In the study of Rath *et al.* the continuous chelation (NaOCl/HEDP) protocol resulted in a thin, frail layer of exposed collagen on the surface. NaOCl/HEDP resulted in a homogenous organic and inorganic composition of the dentin surface, in contrast to the organic-components rich dentin surface following NaOCl/EDTA treatment [17]. Lottanti *et al.* assessed the effects of EDTA, etidronic and peracetic acid irrigation on human root dentine and the smear layer and included that continuous chelation (1-mixture of 2% NaOCl and 18% EA during and after instrumentation) yielded less calcium ions and eroded the dentine wall less than sequential chelation protocol (1% NaOCl during, 17% EDTA after instrumentation) [10]. While Kfir *et al*. investigated that the continuous chelation protocol did not differ from sequential chelating protocol in terms of cleanliness or the incidence of erosion of the canal wall [18].

Smear layer removal and soft tissue-dissolving

Kuruvilla *et al*. evaluated the ability to remove smear layer using three chelating agents; EDTA, etidronic acid, and maleic acid, the results of this study shewed all irrigants tested, removed smear layer effectively form coronal and middle third.There was no significant difference between etidronic acid and EDTA. At the apical third, all irrigants showed poor smear layer removing property, but maleic acid showed comparatively better results than EDTA and etidronic acid at the apical third [19]. In addition, Hazar investigated that the least reduction in microhardness of canal dentin and lower percentages of the remaining smear layer area were observed when the root canals were irrigated with NaOCl and etidronic acid in continuous pattern [20]. This results were similar to the results of studies conducted by Razumova *et al.* [21], and Aoun *et al*. [22].

On the other hand, few studies revealed equal property of smear layer removal by EDTA and etidronic acid. Lottani *et al*. in their study revealed that both of EDTA and etidronic acid were able to remove or prevent a smear layer [10]. Dual Rinse HEDP or continuous chelation protocol showed similar results to NaOCl/EDTA (sequential chelating protocol) in smear layer and debris removal from root canal as shown in *'Castagnola* study [23]. In another study conducted by Yadav etidronic acid was found inferior than SmearClear and MTAD in removing the smear layer [24].

Bond strength of sealer to root canal dentine

Chelating agents as EDTA and citric acid not only remove the smear layer but also erode the dentin and thus expose collagen. This erosion has a positive effect on the adhesion and sealability of resin based sealers as epoxy resin and methacrylate based sealers, while the erosion of dentin is undesirable in the case of bioceramic sealers (i.e. those based on hydraulic calcium silicate cements such as MTA) [13, 25]. In addition, the heavily erosion of dentine in root canal and pulp chamber during conditioning of the root canals negatively affects the adhesion and function of methacrylate-based dentin adhesives, so it is necessary to irrigate the root canal system with NaOCl after the EDTA final rinse since NaOCl can remove eroded dentin and thus improve the adhesion of methacrylate-based adhesives and calcium silicate-based materials [26, 27].

Many studies using push-out test have shown good outcomes in bond strength of root canal sealers when NaOCl combined with etidronic acid in continuous chelation protocol. This mixture improves the bond strength of epoxy resin sealer as AH plus [28, 29, 30] and CaSi-cement-based materials [20, 30, 31.32,]. Since etidronic acid is a biocompatible decalcifying agent that can be combined with NaOCl during root canal treatment for a short time, does not aggressively decalcify the dentin, and leaves it in its natural state including removal of the smear layer [13].

Removal of biofilm and antibacterial effects

A biofilm is defined as a highly organized structure consisting of bacterial cells enmeshed in a self-produced extracellular polymeric matrix attached on a surface of tooth root. It has been confirmed that biofilm has a main role in the development and perpetuation of apical periodontitis [33].

The microorganisms of biofilms in the root canal are highly resistant to root canal therapy procedures as root canal instrumentation and intracanal medicaments used as disinfecting agents. The complex and unpredictable nature of root canal anatomy and the multi-species biofilms complicated eradication of the microbial biomasses from there [34].

Anyway, root canal preparation aims to enlarging the root canal with instruments and cleaning the space using chemical disinfectants to kill the microbiota within the root canal system, including disruption of the microbial biofilm. It has been shown that NaOCl is able to kill the biofilm microorganisms and breaks down the biofilm polymeric matrix in the highest concentrations, but the limitation of the static NaOCl administration is that the reactive components of NaOCl are progressively deactivated when in contact with organic substrate, such as the biofilm particularly if working lifespan of NaOCl increases [35]. The addition of etidronic acid to NaOCl could increase the antibiofilm potency of the irrigant, whilst maintaining the benefits of continuous chelation. Several in-vitro studies conducted to assess the the potency of continuous chelation against microbial biofilms using scanning electronic microscope (SEM) or optical coherence tomography (OCT) which provides quantitative measurements of biofilm removal or disruption. Borges *et al.* investigated that continuous chelation (mixing etidronic acid with NaOCl) caused a delay in the antibiofilm action of the NaOCl without compromising its antibiofilm efficacy [35]. All irrigants used in *'Castagnola* study including Dual Rinse HEDP or continuous chelation protocol have antimicrobial activity and reduced the number of *E. faecalis* and *C. albicans* [23]. Wright revealed that etidronate mixtures with sodium hypochlorite were equally as effective against *Enterococcus faecalis* biofilms as sodium hypochlorite of the same concentration. While the mixtures showed no additional benefits [36]. Morago *et al.* conducted a research to evaluate the impact of smear layer on the antimicrobial activity of a NaOCl and etidronic acid irrigating solution in infected dentin. In this study the smear layer has important influence on antimicrobial activity of NaOCl alone or with etidronic acid.The presence of the smear layer reduced the antimicrobial activity of 2.5% NaOCl. The combination of 2.5% NaOCl/9% etidronic acid exerted antimicrobial activity that was not reduced by the smear layer [37]. On the contrary, Arias-Moliz *et al*. showed in their study that NaOCl solution killed 100% of the *E. faecalis* biofilms and showed the highest antimicrobial activity inside dentinal tubules, while the etidronic acid alone killed bacteria inside dentinal tubules but did not present any significant effect against *E. faecalis* biofilms, and the mixture of NaOCl with etidronic acid has no effect on the ability of NaOCl to kill *E. faecalis* grown in biofilms and inside dentinal tubules [38].

The effect of etidronic acid on the torsional load on rotary instruments

Lubricants are commonly used in the biomechanical preparation of root canals to suspend and emulsify debris generated by the mechanical action of hand and rotary files [39]. While paste-type lubricants and aqueous lubricants are available for use, there is a lack of studies in the literature documenting the effects of these lubricants on file fracture, obturation quality, and postoperative pain. Peters *et al*. evaluated the effect of liquid and paste-type lubricants on torque values during rotary root canal instrumentation and revealed that lubrication appeared to be advantageous. Aqueous solutions generally performed better than the paste-type product [40]. Boessler *et al*. assessed the effect of NaOCl and a etidronic acid in aqueous and gel-type form on maximum torque, full torsional load, and maximum force values, this study showed that using etidronic acid reduced the torsional load on rotary instruments. In addition, an aqueous lubricant was more beneficial than a gel-type counterpart since the paste-type lubricants showed significantly more torque accumulation during root-canal instrumentation than the aqueous irrigants [41].

Effects of etidronic acid on the release of growth factors

Regenerative endodontics is a biological procedure designed to replace the diseased, missing, and traumatized tissue including dentin and root structures as well as cells of pulp-dentin complex [42]. Stem cells, growth factors (GFs) are essential to successful regenerative endodontics procedures. However, the researcheson GFs, unlike that of stem cells are limited [43, 44]. The GFs usually embed in the extracellular matrix of dentin, they are definitive for the migration, proliferation, and differentiation of dental pulp stem cells (DPSCs) [45, 46]. Dentin matrix can demineralize after applying dental materials, acids, or chelating agents. This leads to solubilization and exposure of matrix-bound growth factors [47].

Irrigants can alter dentin structure so they can influence stem cell proliferation and migration. The type of irrigation solution such as chelating agents has paramount role in GFs release since this agents demineralize the dentin matrix and induce the release of GFs [48]. It has been suggested EDTA as final step in sequential irrigation protocol because EDTA serves the dual purpose of eliminate the negative effects of NaOCl and release GFs from the dentin matrix [49, 50]. Another materials, such as citric acid, phytic acid, phosphoric acid, and maleic acid, have been tested for their effectiveness in releasing GFs in regenerative endodontics [44, 51, 52, 53]. Etidronic acid is also used in endodontics due to its chelating properties, which do not adversely affect NaOCl. Researches on its use as a final irrigation agent to release GFs in regenerative endodontics are limited [51]. Sungor *et al*. assessed the effect of dentine conditioning using etidronic acid in comparison to EDTA and phytic acid on growth factor release, dental pulp stem cells migration and viability. They concluded that etidronic acid and phytic acid were effective as EDTA in growth factor release and stem cells migration, while etidronic acid in this study did not induce cell proliferation [51].

Another study conducted by Mumcu *et al*. evaluated EDTA and etidronic acid with different irrigant activation techniques on the release of growth factors from dentin. The results of this study showed that the both used chelating agents were able to release growth factors from the dentin which enhanced by using irrigant activation techniques [54].

Conclusion

- Etidronic acid is a biocompatible decalcifying agent that can be combined with NaOCl during root canal treatment without adversely effect, so it could be a promising alternative chelating agent in endodontic irrigation protocols.
- Mixing NaOCl with etidronic acid which is called continuous chelation protocol benefits root canal treatment since it disinfects the root canal, dissolves organic matter and removes the smear layer.
- Continuous chelation protocol improves the bond strength of resin-based sealer as well as CaSi-cement-based sealer. In addition, it reduces the torsional load on rotary instruments.
- Etidronic acid can be effective as EDTA in growth factor release and stem cells migration.

Conflict of Interest

Not available.

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