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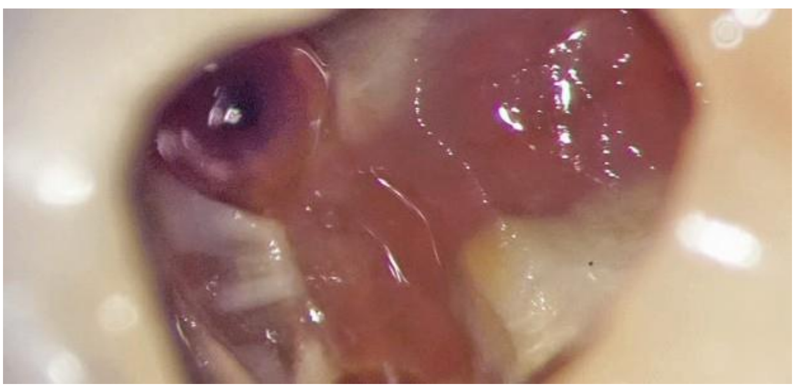

SPECIAL PRINT

Etidronate (Dual Rinse HEDP) for root canal irrigation in clinical use

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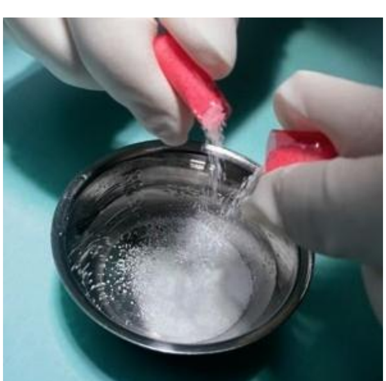

QUINTESSENCE PUBLISHING

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Matthias Zehnder

Keywords

root canal irrigation, chelator, HEDP, HEBP, sodium hypochlorite

Summary

Two steps are essential for a successful root canal treatment: 1) the chemomechanical removal of pulp residues, a possibly existing biofilm, and old filling materials as well as 2) the conditioning of the dentin in order to be able to seal the affected tooth bacteria-proof after endodontic treatment. The most important chemical substance in this context is sodium hypochlorite (NaOCl), which is used in aqueous solution for root canal irrigation. NaOCl has almost all properties necessary for root canal cleaning except a decalcifying effect. This article introduces the Dual Rinse HEDP irrigation additive and explains how to use it. This additive directly gives NaOCl solutions a mild decalcifying component. A combined NaOCl-Dual Rinse HEDP irrigating solution not only simplifies chemical root canal cleaning and dentin conditioning for subsequent root and coronal fillings, but also shortens the time required to reach these goals. After instrumentation of the root canals, the smear layer and inorganic residues (debris) do not have to be removed because continuous calcium complexation inhibits their formation. The dentin is not eroded as in EDTA conditioning, which has a positive effect on the adhesion of adhesive filling materials.

Explanation of terms

The following terms are not always used correctly in the literature and/or have different meanings in German and English. Therefore, a brief clarification of terminology is given here:

- Etidronates are the salts of the etidronic acid, a nitrogen-free bisphosphonate (diphosphonate) having the formula MnHEDP (n ≤ 4), wherein M is mostly sodium.
- Etidronic acid is the trivial name of the (1-Hydroxyethane-1,1-diyl)bis(phosphonic acid).
- HEBP is the German abbreviation for etidronic acid.
- HEDP is short for hydroxyethylidene diphosphonate.

Introductory remarks

If the radicular pulp is irreversibly inflamed or already infected and necrotic, it must be removed at the current state of the art and replaced with a bacteria-proof, alloplastic material. The only exception to this rule is the revascularisation treatment, which is briefly discussed at the end of this article. In any case, however, it is necessary to remove necrotic soft tissue and, if present, biofilm from the affected tooth. In addition to physical means such as root canal instrumentation, irrigation or laser treatment, there are only two clinically approved chemicals that ideally support these measures: Sodium hypochlorite (NaOCl) as an irrigating solution and calcium hydroxide ($Ca(OH)_2$) in suspension as an intermediate dressing. Both agents have a proteolytic effect, dissolving microorganisms and necrotic soft tissue residues[17]. NaOCl acts fast and concentration-dependent, $Ca(OH)_2$ slowly yet continuously[44]. While NaOCl has established itself worldwide, there are still local differences[33] in the use of $Ca(OH)_2$.

In order to ensure the most efficient cleaning of the root canal system and the maximum disinfection time, it is recommended to flood the root canals with NaOCl solution during mechanical preparation[13]. This also reduces mechanical stress on rotating instruments[7]. In addition to a NaOCl solution, which is primarily used for disinfection, decalcifying solutions have also been recommended, which contain chelators, i.e. complexing agents: first ethylenediamine tetraacetate (EDTA)[28] and later citric acid[19]. Historically, the recommended use of these agents is based on histological observations. It was recognized that after mechanical preparation of the canal system and irrigation with a NaOCl solution, a smear layer is formed on instrumented dentin surfaces and inorganic residues (also called debris or "dentin mud") accumulate in non-instrumented areas of the root canal system[16,35]. EDTA and citric acid dissolve these inorganic residues by means of calcium complexation[42], and necrotic and/or infected soft tissue adhering to the canal wall can be washed away more easily[28]. In addition, it was clinically established that such decalcifying agents facilitate the instrumentation of calcified root canals[28]. A frequently cited study has shown that the use of EDTA for root canal irrigation has a positive impact on the clinical outcome of endodontic retreatments[27].

This may be due to the fact that root canal filling materials can be more easily removed from the dentin wall with decalcifying agents than with NaOCl solutions alone. Since EDTA calcium ions are present, the $Ca(OH)_2$ can also be removed from the canal system more easily than with a non-decalcifying solution[34].

Conventional irrigating protocols

The introduction of EDTA and later citric acid into endodontics led to the development of various products based on their chemistry: On the one hand, glycol pastes containing EDTA were marketed[37] and on the other, rinsing solutions were developed which, in addition to decalcifying, also featured a disinfecting effect. However, EDTA-containing glycol compounds do not remove the smear layer and neutralize NaOCl immediately[15], which is clinically unfavorable and makes such products obsolete. Contrary to the opinion propagated by the respective manufacturers, these EDTA-containing pastes also do not reduce the torsional stress on rotary root canal instruments[32].

The first disinfecting and decalcifying solution specially developed for endodontics was REDTA (then Roth Drug Company, Chicago, USA), later marketed under the name EDTAC. Here a quaternary ammonium compound (cetrimide)[21] has been added to EDTA. There are also newer products which pursue this basic concept either on a citric acid-[39] or EDTA basis[9]. However, all these products have a common problem, which is that they are not compatible with NaOCl. The reason for this is that NaOCl reacts immediately with EDTA and even faster and more violently with citric acid[5]. As a result, irrigating protocols had to be defined. Since NaOCl has the clinically most important basic properties for chemical root canal cleaning as described above, such protocols are built around NaOCl. The classical irrigating protocol has thus been to use NaOCl during root canal instrumentation, followed by EDTA or citric acid to remove the smear layer and debris, and then NaOCl again as the final rinse for the final disinfection[42]. This sequence can be shortened by one step, e.g. by adding a disinfectant or antibiotic to the decalcifying final rinse, as is the case with EDTAC. One loses then however the often still necessary unique cleaning effect of the NaOCl after the instrumentation step. In addition, the dentin can be eroded and uncontrollably softened[1].

Dentin conditioning

The conditioning of the dentin for root canal filling and the subsequent coronal restoration are clinically important topics that are not sufficiently considered in the context discussed here. A recent study has shown that, rather contrary to popular belief, leaking root canal fillings can have a fatal effect on clinical results[4]. A thick smear layer on the dentin prevents the adhesion of all dental materials[29,38]. Some decalcification is therefore always desirable if the dentin has been mechanically treated and the root canal system and access cavity are to be tightly filled afterwards. Different materials bind to different elements of dentin (Table 1). It may be assumed that filling materials have been tested on healthy dentin by the respective manufacturers. Dentin is a mixed inorganic-organic substance, which has a crystalline (CaP, mainly hydroxyapatite) and an organic part (mainly collagen type I). With the irrigating protocols described above different results can be obtained. Depending on the final irrigant that is used, the dentin surface will either be deproteinized (NaOCl) or decalcified (strong chelators such as EDTA or citric acid) (Fig. 1).

Since both EDTA and citric acid not only remove the smear layer, but also erode the dentin and thus expose collagen, their clinical use is not always unproblematic[20]. If, for example, an epoxy resin sealer such as AH-Plus (Dentsply Sirona, Konstanz) is used, such erosion has a positive effect on the adhesion and sealability of the root canal filling[25]. In the case of so-called bioceramic sealers (i.e. those based on hydraulic CaSi cements such as MTA), however, dentin erosion is undesirable[8]. Since the pulp chamber and thus the coronal dentin are also inevitably treated during conditioning of the root canals, the additional problem arises that methacrylate-based dentin adhesives also function poorly on heavily eroded dentin[31]. Treatment with NaOCl can remove eroded dentin and thus improve the adhesion of methacrylate-based adhesives and CaSi-based materials[11,22]. Theoretically, the access cavity should therefore be conditioned with NaOCl or mechanically freshened after the EDTA final rinse and root canal filling has been carried out, in order to be able to close it better adhesively.

Tab. 1 Materials that may come into contact with dentin after the chemical root canal cleaning process and their primary binding sites (*: Examples of materials frequently used in central Europe; there are many other products of each material type with similar chemistry)

Material types	Binding to	Product*
Epoxy resin sealer	Collagen	AH Plus
Bioceramic (CaSi) Sealer	Calcium phosphates	TotalFill BC
Silicone-based sealers	(Purely mechanical sealing)	RoekoSeal
Methacrylates (bonding systems)	Calcium phosphates	OptiBond FL
glass ionomer cements	Calcium phosphates and collagen	Ketac Fil
Hydraulic CaSi cements	Calcium phosphates	ProRoot MTA

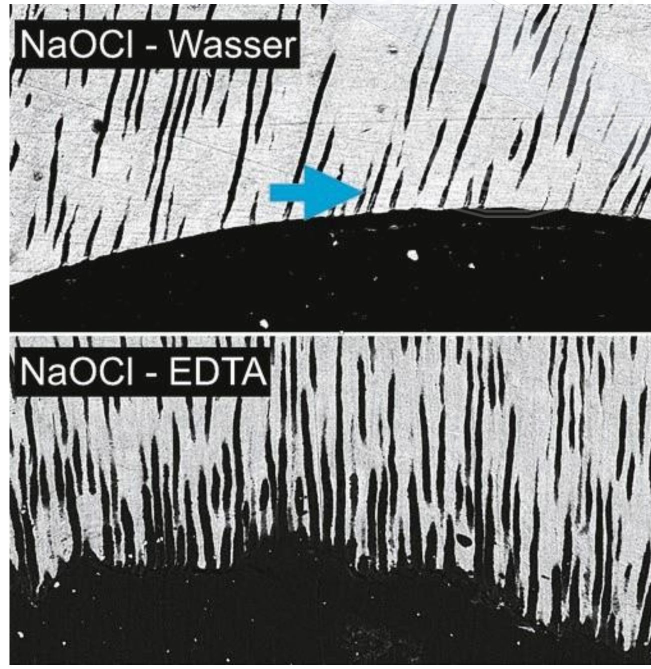

Fig. 1 Previously unpublished images from a study in which root canal walls were embedded, cross-sectioned, and examined by scanning electron microscopy[20]. Extracted premolars were rinsed with 10 mL of a 1% NaOCl solution for 15 minutes during or after mechanical preparation. Afterwards canals were irrigated with water (3 minutes, 5 mL, upper picture) or 17% EDTA (lower picture). In cross-section, the smear layer manifests itself as smear plugs (arrow), i.e. parts of the smear layer which are pressed into the dentinal tubules. In contrast, EDTA erodes the dentin surface (lower image). Non-mineralized dentin components (especially collagen) that interfere with methacrylate-based adhesive systems are exposed in this way.

Why HEDP?

The following question arose from the problems described above: Is there a biocompatible decalcifying agent that can be combined with NaOCl at least for a short time (i.e. for the duration of a treatment) and does not aggressively decalcify the dentin, but leaves it in its natural state (including removal of the smear layer)? This product was found with HEDP[45]. HEDP is used in water and waste water treatment, in detergents and cleaning agents, in cosmetic articles, as a medicinal agent, and to inhibit corrosion and scaling. Like EDTA and citric acid, HEDP is a chelator. It, however, forms somewhat weaker complexes with calcium than the previously mentioned molecules. It is important here that HEDP is used as an additive in the NaOCl irrigating solution and is therefore used during the entire endodontic treatment. Calcium ions are continuously bound so that alternating irrigation schemes are completely eliminated. With this concept, the smear layer and debris are not removed after mechanical root canal preparation, but their formation is prevented[45], and this without decalcification of the canal wall[20]. Studies on extracted human teeth rinsed during root canal preparation with a 1:1 mixture of 5% NaOCl and 18% HEDP (resulting in a combined solution of approximately 2.5% NaOCl and 9% HEDP) have shown that the use of this mixture improves not only the adhesive strength of methacrylate-based adhesives[10] but also that of epoxy resin[26] and CaSi-cement-based materials[24]. In addition, the disinfection of the root canal system can be improved[23] and the torsional load on rotary instruments can be reduced[7].

Dual Rinse HEDP

The studies and findings described above led to the development of a commercially viable formulation of HEDP. This was done by Dr. *Dirk Mohn* (smartodont, Zurich, Switzerland) in cooperation with the author. First tests with two-way syringes with liquid 5% NaOCl (even in NaOH stabilized form) in one ampoule and 18% HEDP in the other ampoule showed that NaOCl is too poorly storable to be commercially usable in this form in the described application. In addition, dentists are using different concentrations

Fig. 2a to d Mixing Dual Rinse HEDP with a NaOCl solution in a sterilizable calibrated mixing cup. In the selected example, the contents of two Dual Rinse HEDP capsules are mixed in 20 mL of a 2.5% NaOCl solution, which corresponds to the usual amount and recommended concentration. Depending on the preference, NaOCl can be used in a concentration of up to 5 %; the mixing ratio with Dual Rinse HEDP remains the same.
For mixing it is recommended to stir the suspension with a spatula. This process can take up to 2 minutes and should be performed by a dental assistant at the start of treatment. The suspension can also always rest a little, and it is not necessary to stir all the time. Once the powder has completely dissolved, the clear combined solution can be drawn into a disposable syringe or other irrigant container and used immediately.

of NaOCl solutions. Further experiments have shown that the salt of etidronic acid (etidronate) can simply be used instead of a liquid: Mixed directly into NaOCl solution, the free chlorine in the resulting combined solution is retained in sufficient quantity for the duration of a root canal treatment[6]. This has the advantage that dentists can continue to use their NaOCl solution in their preferred concentration.

These results were later confirmed with the CE-marked and controlled Dual Rinse HEDP product (Medcem, Weinfelden, Switzerland)[46]. A toxicity study showed that Dual Rinse HEDP itself has a very low cytotoxicity and does not increase that of NaOCl. There are also no toxic reaction products between Dual Rinse HEDP and NaOCl[2]. A randomized clinical trial showed that the clinical disinfection effect of 2.5% NaOCl was not worsened by the addition of Dual Rinse HEDP[3]. Postoperative pain and inflammatory mediators in the periapical tissues were not increased by the addition of the product. Studies on extracted teeth also indicated that adding Dual Rinse HEDP to NaOCl increases the adhesion of a CaSi material (Biodentine, Septodont, Paris) to the root canal wall[30], improves disinfection[14] and also maintains the bleaching effect of NaOCl[47]. In contrast to citric acid, the combination of Dual Rinse HEDP with NaOCl had no negative effect on the adhesive strength of a self-etching adhesive (Clearfil SE Bond, Kuraray, Tokyo, Japan) on dentin[18].

Preparation of the combined NaOCl-Dual Rinse HEDP solution

Before starting the clinical application of Dual Rinse HEDP, three limitations should be considered.

The first point concerns the mixing time. The powder should be mixed in a sterile beaker with the NaOCl solution to be used. The Dual Rinse HEDP contained in one capsule per 10 mL of NaOCl solution is used for this purpose (Fig. 2). Depending on how strongly the suspension is stirred (the use of a cement spatula is ideal for this), it takes 1 to 2 minutes for the entire etidronate to dissolve. This time can be perceived as long when one is in the middle of a treatment. It is therefore advisable to mix the amount of NaOCl and Dual Rinse HEDP required in the forthcoming session directly before the start of treatment.

The second point concerns the concentration of NaOCl solutions. With NaOCl above 5%, the mixture with Dual Rinse HEDP becomes critical, as the resulting combined solution becomes too salty and can reprecipitate[2]. According to the author, however, solutions with a NaOCl content above 5 % should not be used as they have a strong caustic effect, damage the collagen network in the dentin, and have no proven clinical advantage over less concentrated solutions[43].

As a final limitation, NaOCl-Dual Rinse HEDP mixtures should also not be stored heated, not even for a short period of time, as they become unstable as a result and the active chlorine is lost quickly[46]. Aqueous solutions in the root canal system with its high specific surface area almost immediately reach body temperature[36]. A preheating of root canal irrigants is therefore of questionable benefit. Heating NaOCl can be useful, but should be done in the root canal system rather than the container[41].

Clinical procedure

Once the NaOCl-Dual Rinse HEDP solution is mixed and has become clear (Figs. 2a to d), treatment can be started. The combined solution should be applied directly after preparation of the access cavity. Calcium-containing preparations such as Cavit (3M Oral Care, Seefeld) or an already existing Ca(OH)2 dressing can be rinsed out better than with a pure NaOCl solution. As with any root canal treatment, care should be taken to ensure that the pulp cavum is constantly filled with the irrigating solution.

According to the clinical experience of the author, the NaOCl-Dual Rinse HEDP mixture facilitates the detection of calcified canals, because not only the growth lines at the bottom of the pulp cavity are better visible, but also the dentinal tubules (where there never are any root canals!) appear radiantly white. In addition, root filling materials can be rinsed out somewhat more easily than with pure NaOCl (Figs. 3a to f). The HEDP gives the dentin a typical shine and some transparency, which can also be seen after EDTA application.

During canal preparation, it is particularly important that the canals are flooded with the irrigating solution for mechanical cleaning. Soft tissue residues, biofilm and also old root canal filling materials can be better removed in this way. The use of Dual Rinse HEDP offers the advantage that a smear layer and debris accumulation is prevented by flushing calcium-containing hard tissue chips directly out of the instrumented canal. Depending on the complexity of the root canal system, it is important to activate the irrigation solution with sonic or ultrasonic tips. Anatomical file systems can also be used to clean unprepared surfaces. The effect of such instruments is particularly clear in the case of retreatments. HEDP contained in the NaOCl solution can also help here to make the therapy more efficient, since the cleaning step with an EDTA final rinse is omitted[14,40]. For Figures 3a to f, a typical retreatment was chosen as an example, because the cleaning effects of the respective treatment steps are better visible and can be followed up radiologically. In principle, however, exactly the same steps are indicated for primary root canal treatments in order to obtain a clean canal system that is ideally prepared for the subsequent root filling procedure.

The combined NaOCl-Dual Rinse HEDP can therefore be used for all treatment steps, including the final rinse. In addition to the obvious gain in time and the simplicity of this procedure, the use of this concept as opposed to conventional protocols has led to additional clinical benefits.

Fig. 3a Periapical radiograph of a tooth treated alio loco with symptomatic apical periodontitis and insufficient root canal filling. The mesial canals were not sufficiently filled to length and the distal root filling was not sufficiently dense. Filling materials were gutta-percha and an epoxy resin sealer, which experience has shown to be difficult to remove.

Fig. 3b First treatment steps of such a retreatment after preparation of the access cavity and identification of the canal orifices. All steps should always be performed with the irrigant (NaOCl-Dual Rinse HEDP mixture) in the pulp cavity and later in the root canals.
Removal of the filling materials from the coronal root canal half with rotating or reciprocating instru ments, a MicroDebrider (depicted here) and/or *Hedström* files.

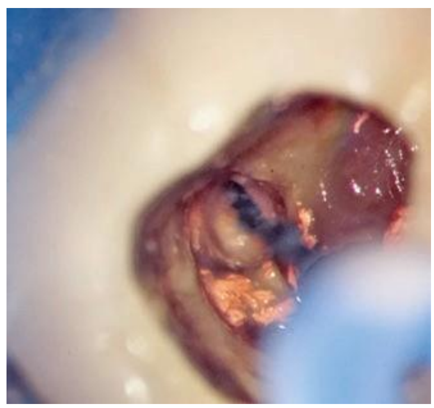

Fig. 3c Lateral cleaning of the canals using an anatomical file (here: XP Shaper, FKG Dentaire, LaChauxdeFonds, Switzerland) and/or ultrasonic tips. Dual Rinse HEDP helps to give the NaOCl solution used for this purpose a mild decalcifying effect. This makes it easier to remove filling materials from the dentin wall. Solvents such as chloroform not permitted for this purpose can thus be avoided.

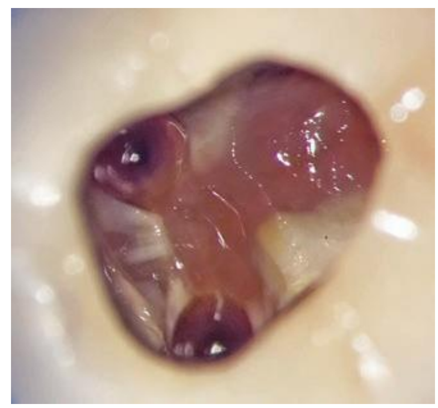

Fig. 3d Pulp cavity after chemomechanical cleaning with the above instruments and the NaOCl-Dual Rinse HEDP mixture as the single irrigating solution. In this way, the root canal system can be chemomechanically prepared without having to abstain from the disinfectant, cleansing and bleaching effect of NaOCl. EDTA irrigation is no longer required

The advantages of this method include better hemostasis when there is a perforation (as opposed to EDTA), and the maintenance of the bleaching effect of NaOCl in blood-stained dentin[47]. It is often forgotten that chelators such as EDTA, citric acid and HEDP without NaOCl have an anticoagulant effect and can, for example, prolong internal bleeding in the periapical tissues during accidental over-irrigation.

However, if HEDP is mixed with NaOCl, the proteolytic effect of NaOCl predominates, and at least with perforations it bleeds less than if EDTA was used. The questions as to whether this is also the case with accidental over-irrigation cannot be answered at present, as no corresponding clinical reports are available.

A useful test to determine whether the root canal system has been cleaned sufficiently is the

Fig. 3e Periapical radiograph to check this cleaning after insertion of the (non-radiopaque) calcium hydroxide dressing and temporary closure of the access cavity (rubber dam already removed)

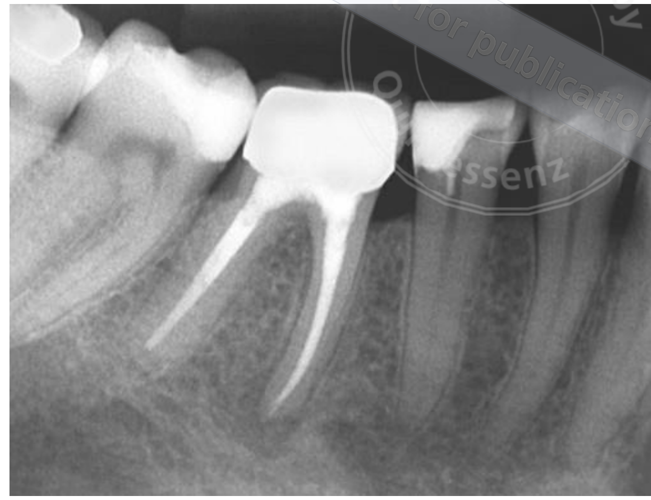

Fig. 3f X-ray after root canal filling and adhesive closure of the access cavity. The picture for the radiographic follow-up examination after 1 year was not available at the time of the completion of this article.

so-called champagne test. If bubbles still rise in the NaOCl-containing solution when it is passively introduced into the fully instrumented root canal system, the irrigating solution has to be renewed and activated and/or can be renewed and left to act passively. The bubbles arise from the reaction of organic molecules in the root canal with the OCl^- (hypochlorite) ions. This test works just as well with combined NaOCl-Dual Rinse HEDP solutions as with pure NaOCl solutions.

After successful treatment and final rinsing, the canal system can be dried with paper points and either an interim dressing or the root canal filling can be placed. The only exception is the revascularization treatment of teeth with incomplete root development, in which bleeding is induced and pluripotent cells are attracted from the periapex. Here it is recommended to irrigate with a purely decalcifying solution at the end, such as 17% EDTA, 10% citric acid or 18% HEDP [12]. To obtain 18% HEDP, it is possible to dissolve the content of one capsule of Dual Rinse HEDP in 5 mL (instead of 10 mL as with NaOCl) of sterile saline solution and use it as a final rinsing agent.

Bottom line

In summary, it can be stated that a combined NaOCl-Dual Rinse HEDP solution actually results in a chemical combination with which almost all cases can be treated in sole application without having to worry about dentin conditioning. The duration and amount of irrigation depends on the complexity of the root canal anatomy to be treated and also on the degree of infection.

Author’s statement

The irrigation concept described here is based on the author's many years of clinical and experimental involvement with the subject. However, it should not be claimed in any way that the method presented here is the only way to clean root canals chemically.It may neverthless be the most simple method to obtain good results in this context.

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