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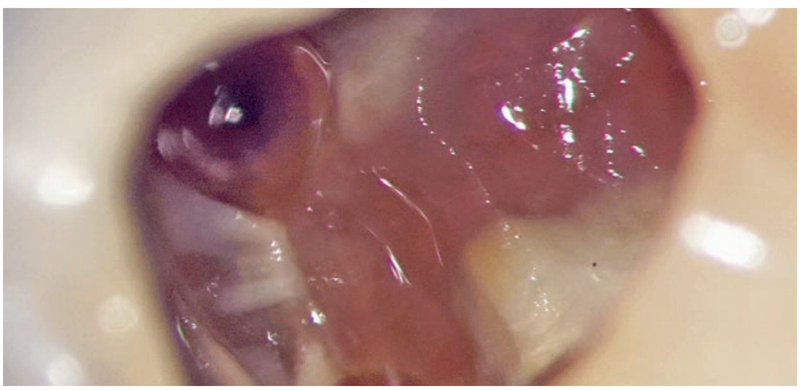

SPECIAL REPRINT

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

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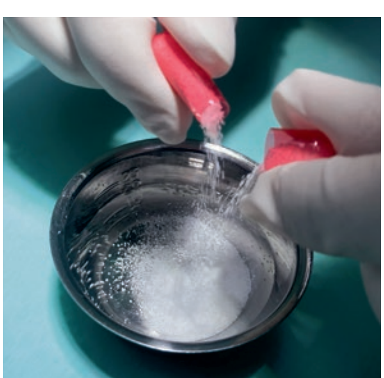

QUINTESSENCE PUBLISHING

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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, biofilm, and old filling materials, as well as 2) dentin conditioning to enable a bacteria-proof seal in the affected tooth after endodontic treatment. The most important chemical substance in this context is sodium hypochlorite (NaOCl), which is used for root canal irrigation as an aqueous solution. NaOCl has almost all properties required for root canal cleaning except a decalcifying effect. This article introduces the Dual Rinse HEDP as an irrigation additive and explains how to use it. This additive directly gives NaOCl solutions a mildly 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 canal, there is no need to remove the smear layer and inorganic residues (debris) because continuous calcium complexation inhibits their formation. In contrast to EDTA conditioning, the dentin does not erode, which has a positive effect on the bond strength of adhesive filling materials.

Clarification of terms

The following terms are not always correctly used 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 etidronic acid, a nitrogen-free bisphosphonate (diphosphonate), abbreviated MnHEDP ($n \leq 4$), wherein M is mostly sodium.
- Etidronic acid is the trivial name for (1-hydroxyethane-1,1-diyl)bis(phosphonic acid).
- HEBP is the German abbreviation for etidronic acid.
- HEDP is the abbreviation for hydroxyethylidene diphosphonate.

Introductory remarks

If the radicular pulp is irreversibly inflamed or already infected and necrotic, it must be removed according to the current state of the art and replaced by a bacteria-proof, alloplastic material. The only exception to this rule is the revascularization treatment, which is briefly discussed at the end of this article. However, in all cases, it is necessary to remove the 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 quickly and is concentration-dependent, $Ca(OH)_2$ acts slowly yet continuously[44]. While NaOCl has established itself worldwide, there are still local differences[33] in the use of $Ca(OH)_2$.

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 rotary 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: the first used was ethylenediamine tetraacetate (EDTA)[28] and the second citric acid[19]. Historically, the recommended use of these agents was based on histological observations. It was recognized that after mechanical preparation of the root canal system and irrigation with a NaOCl solution, a smear layer is formed on instrumented dentin surfaces, and the 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 the 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. Due to the calcium complexation by EDTA, the $Ca(OH)_2$ can also be removed from the canal system more easily compared with the use of 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 especially developed for endodontics was REDTA, previously manufactured by Roth Drug Company (Chicago, USA), and later marketed under the name EDTAC. It contains a quaternary ammonium compound (cetrimide)[21] that has been added to EDTA. There are also newer products that pursue this basic concept, either on a citric acid-[39] or EDTA-basis[9]. However, all these products have the common problem of being incompatible with NaOCl because 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. Thus, the classical irrigating protocol has 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 by adding a disinfectant or antibiotic to the decalcifying final irrigant, as is the case with EDTAC. However, in this case, one loses 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 have not received the attention they deserve. 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]. Therefore, some decalcification is 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 their respective manufacturers. Dentin is a mixed inorganic-organic substance with a crystalline part (CaP, mainly hydroxyapatite) and an organic part (mainly collagen type I). Different results can be obtained with the irrigating protocols described above. Depending on the final irrigant 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]. For example, if an epoxy resin sealant such as AH Plus (Dentsply Sirona, Konstanz, Germany) is used, such erosion has a positive effect on the adhesion and sealability of the root canal filling[25]. However, in the case of the so-called bioceramic sealants (i.e. those based on hydraulic CaSi cements such as MTA), the erosion of dentin is undesirable[8]. Since the pulp chamber and 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]. Therefore, the access cavity should, theoretically, be conditioned with NaOCl or mechanically freshened after the EDTA final rinse and root canal filling have been carried out in order to be able to better close it adhesively.

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 that does not aggressively decalcify the dentin, but leaves it in its natural state (including removal of the smear layer)? This chemical was found in HEDP[45]. HEDP is used in water and wastewater treatment, in detergents and cleaning agents, in cosmetic articles, as a drug, and to inhibit corrosion and scaling. Like EDTA and citric acid, HEDP is a chelator. However, it forms somewhat weaker complexes with calcium than the previously men-

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 type	Binds to	Product*
Epoxy resin sealer	Collagen	AH Plus
Bioceramic (CaSi) sealer	Calcium phosphates	TotalFill BC
Silicone-based sealer	(Purely mechanical sealing)	RoekoSeal
Methacrylates (bonding systems)	Calcium phosphates	OptiBond FL
Glass-ionomer cement	Calcium phosphates and collagen	Ketac Fil
Hydraulic CaSi cement	Calcium phosphates	ProRoot MTA

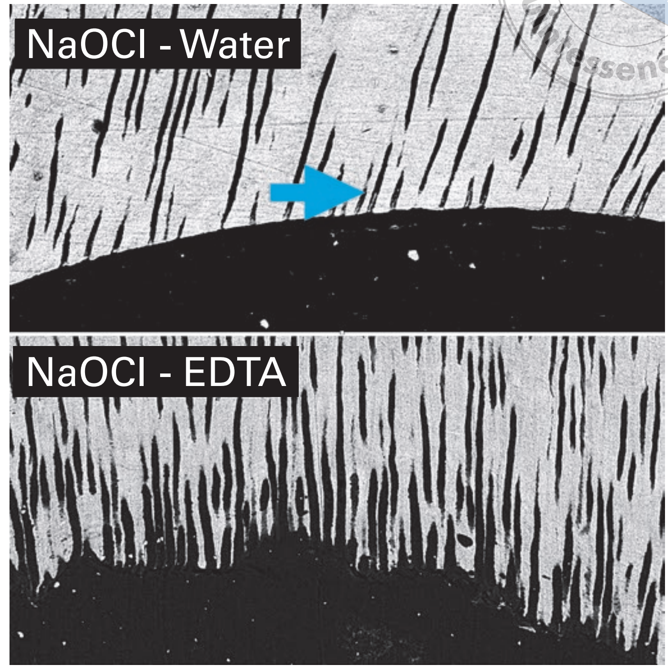

Fig. 1 Previously unpublished images from a study in which root canal walls were embedded, cross-sectioned, and examined by scanning electron microscopy[20]. Extracted premolars were rinsed with 10 ml of a 1 % NaOCl solution for 15 minutes during and after mechanical preparation. Subsequently, the canals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

tioned molecules. HEDP should be used as an additive in the NaOCl irrigating solution and therefore during the entire endodontic treatment. The calcium ions are thus continuously complexed so that the alternating irrigation schemes can be completely eliminated. With this concept, the smear layer and debris are not removed after mechanical root canal preparation, but instead their formation is prevented[45]. This occurs 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 bond 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 reduced[7].

Dual Rinse HEDP

The studies and findings described above led to the development of a commercially viable formulation of HEDP by Dr. Dirk Mohn (Smartodont, Zurich, Switzerland) in cooperation with the author. First tests with two-way syringes with liquid 5 % NaOCl (even in the 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 for the described application. In addition, dentists are using different concentrations 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 a NaOCl solution, the free chlorine in the resulting combined solution is retained in sufficient quantity for the duration of a root canal treatment[6]. The advantage of this is that dentists can continue using 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

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 were 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. A spatula should be used to stir the suspension. 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 rest for a short period and does not require continuous stirring. Once the powder has completely dissolved, the clear combined solution can be drawn into a disposable syringe or other irrigant container and used immediately.

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 and NaOCl had no negative effect on the bond 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 limitation concerns the mixing time. The powder should be mixed in a sterile container 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 stirring), it takes 1 to 2 minutes for the entire etidronate to dissolve. This duration can be perceived as long when one is in the middle of a treatment. Therefore, it is advisable to mix the amount of NaOCl and Dual Rinse HEDP required in the forthcoming session directly before the start of treatment.

The second limitation concerns the concentration of NaOCl solutions. By using concentrations above 5 % NaOCl, the mixture with Dual Rinse HEDP becomes critical, as the resulting combined solution becomes too salty and can reprecipitate[2]. However, according to the author, 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, the NaOCl-Dual Rinse HEDP mixture should not be stored heated, not even for a short period of time, as it becomes unstable as a result and the active chlorine is quickly lost[46]. Aqueous solutions in the root canal system with its high specific surface area almost immediately reach body temperature[36]. Therefore, the preheating of root canal irrigants is 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), the treatment can be started. The combined solution should be applied directly after the preparation of the access cavity. Calcium-containing preparations such as Cavit (3M Oral Care, Seefeld, Germany) or an already existing $Ca(OH)_2$ dressing can be better rinsed out 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, not only because the growth lines at the bottom of the pulp cavity are more visible, but also due to the fact that the dentinal tubules 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, biofilms, and also old root canal filling materials can be better removed 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. The HEDP contained in the NaOCl solution can also help to make the therapy more efficient, since the cleaning step with an EDTA final rinse is omitted[14,40]. Figures 3a to f show an example of a typical retreatment, where the cleaning effect of the respective treatment steps are better visible and can be followed up radiologically. However, in principle, 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.

Therefore, the combined NaOCl-Dual Rinse HEDP can 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. 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 after 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 is used. The question 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 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 should be renewed and left to act passively until no bubble formation is observed anymore. 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 revasculariza-

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 has been shown to be difficult to remove.

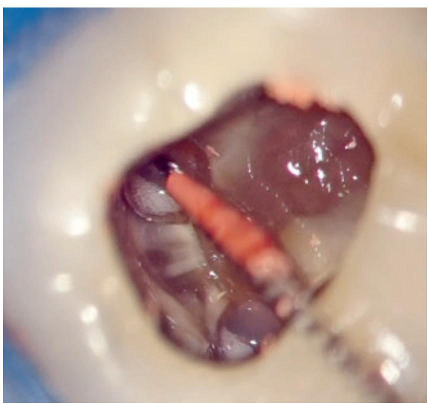

Fig. 3b First treatment steps of a retreatment after preparation of the access cavity and identification of the canal orifices. All steps should always be performed with the irrigant (NaOCl-Dual Rinse HEDP mixture) in the pulp cavity and later in the root canals. Removal of the filling materials from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

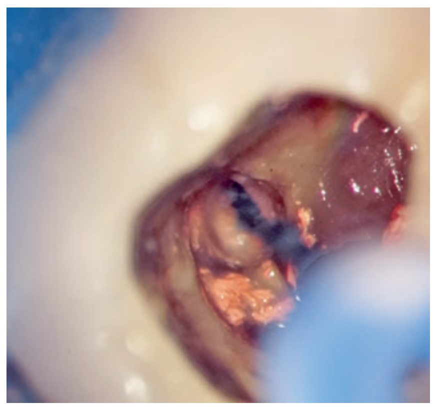

Fig. 3c Lateral cleaning of the canals using an anatomical file (here the XP Shaper file was used [FKG Dentaire, LaChauxdeFonds, Switzerland]) and/or ultrasonic tips. The Dual Rinse HEDP gives a mild decalcifying effect to the NaOCl solution used for this purpose. This makes it easier to remove filling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

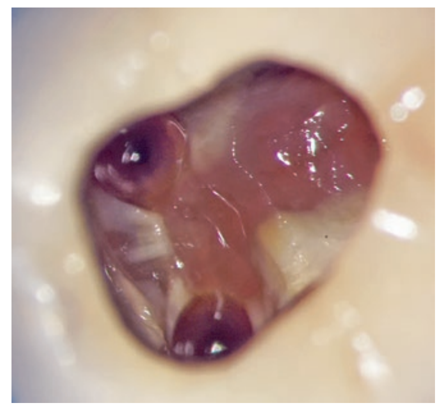

Fig. 3d Pulp cavity after chemomechanical cleaning with the above instruments and the NaOCl-Dual Rinse HEDP mixture as the single irrigating solution. In this way, the root canal system can be chemomechanically prepared without having to abstain from the disinfectant, cleansing, and bleaching effect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

tion treatment of teeth with incomplete root development, in which bleeding is induced and pluripotent cells are attracted from the periapex. In this case, 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.

Conclusion

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

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

Fig. 3f Radiograph conducted after root canal filling and adhesive closure of the access cavity. The 1-year follow-up examination radiograph was not available at the time of publication of this article.

treated in a single 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 as well as 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. Nevertheless, it may be the most simple method to obtain good results in this context.

Literature

1. ArandaGarcia AJ, Kuga MC, ChavézAndrade GM et al. Effect of final irrigation protocols on microhardness and erosion of root canal dentin. Microsc Res Tech 2013;76:10791083.
2. Ballal NV, Das S, Rao BSS, Zehnder M, Mohn D. Chemical, cytotoxic and genotoxic analysis of etidronate in sodium hypochlorite solution. Int Endod J 2019;52:1228-1234.
3. Ballal NV, Gandhi P, Shenoy PA et al. Safety assessment of an etidronate in a sodium hypochlorite solution: randomized doubleblind trial. Int Endod J 2019;52:1274-1282.
4. Barborka BJ, Woodmansey KF, Glickman GN, Schneiderman E, He J. Longterm clinical outcome of teeth obturated with Resilon. J Endod 2017;43: 556560.
5. Baumgartner JC, Ibay AC. The chemical reactions of irrigants used for root canal debridement. J Endod 1987;13:4751.
6. Biel P, Mohn D, Attin T, Zehnder M. Interactions between the tetrasodium salts of EDTA and 1hydroxyethane 1,1diphosphonic acid with sodium hypochlorite irrigants. J Endod 2017;43:657661.
7. Boessler C, Peter's OA, Zehnder M. Impact of lubricant parameters on rotary instrument torque and force. J Endod 2007; 33:280283.
8. Carvalho NK, Prado MC, Senna PM et al. Do smear-layer removal agents affect the pushout bond strength of calcium silicatebased endodontic sealers? Int Endod J 2017;50:612619.
9. Dai L, Khechen K, Khan S et al. The effect of QMix, an experimental antibacterial root canal irrigant, on removal of canal wall smear layer and debris. J Endod 2011;37:80-84.
10. DeDeus G, Souza EM, Marins JR, Reis C, Paciornik S, Zehnder M. Smear layer dissolution by peracetic acid of low concentration. Int Endod J 2011;44: 485490.
11. Deari S, Wegehaupt FJ, Tauböck TT, Attin T. Influence

of different pretreatments on the microtensile bond strength to eroded dentin. J Adhes Dent 2017;19:147155.

12. Deniz Sungur D, Aksel H, Ozturk S, Yılmaz Z, Ulubayram K. Effect of dentine conditioning with phytic acid or etidronic acid on growth factor release, dental pulp stem cell migration and viability. Int Endod J 2019;52: 838846.
13. Gazzaneo I, Vieira GCS, Pérez AR et al. Root canal disinfection by single and multipleinstrument systems: Effects of sodium hypochlorite volume, concentration, and retention time. J Endod 2019;45:736741.
14. Giardino L, Del Fabbro M, Morra M et al. Dual Rinse® HEDP increases the surface tension of NaOCl but may increase its dentin disinfection efficacy. Odontology 2019; 107:521-529.
15. Girard S, Paque F, Badertscher M, Sener B, Zehnder M. Assessment of a geltype chelating preparation containing 1hydroxyethylidene1, 1bisphosphonate. Int Endod J 2005;38:810816.
16. Gwinnett AJ. Smear layer: morphological considerations. Oper Dent Suppl 1984;3:212.
17. Hasselgren G, Olsson B, Cvek M. Effects of calcium hydroxide and sodium hypochlorite on the dissolution of necrotic porcine muscle tissue. J Endod 1988;14:125127.
18. Kaki GD, Recen D, Baser Kolcu MI, Güvenç P. Effect of Dual Rinse HEDP root canal irrigation solution on coronal dentin adhesion. Med J SDU 2018;25:412419.
19. Loel DA. Use of acid cleanser in endodontic therapy. J Am Dent Assoc 1975;90:148151.
20. Lottanti S, Gautschi H, Sener B, Zehnder M. Effects of ethylene diaminetetraacetic, etidronic and peracetic acid irrigation on human root dentine and the smear layer. Int Endod J 2009; 42:335343.
21. McComb D, Smith DC. A preliminary scanning electron microscopic study of root canals after endodontic procedures. J Endod 1975;1:238-242.
22. Meraji N, Nekoofar MH, Yazdi KA, Sharifian MR, Fakhari N, Camilleri J. Bonding to caries affected dentine. Dent Mater 2018;34:e236e245.
23. Morago A, OrdinolaZapata R, FerrerLuque CM, Baca P, Ruiz-Linares M, AriasMoliz MT. Influence of smear layer on the antimicrobial activity of a sodium hypochlorite/etidronic acid irrigating solution in infected dentin. J Endod 2016;42: 16471650.
24. Neelakantan P, Nandagopala M, Shemesh H, Wesselink P. The effect of root dentin conditioning protocols on the pushout bond strength of three calcium silicate sealers. Int J Adhes Adhes 2015; 60:104108.
25. Neelakantan P, Subbarao C, Subbarao CV, DeDeus G, Zehnder M. The impact of root dentine conditioning on sealing ability and pushout bond strength of an epoxy resin root canal sealer. Int Endod J 2011;44:491498.
26. Neelakantan P, Varughese AA, Sharma S, Subbarao CV, Zehnder M, DeDeus G. Continuous chelation irrigation improves the adhesion of epoxy resinbased root canal sealer to root dentine. Int Endod J 2012; 45:10971102.
27. Ng YL, Mann V, Gulabivala K. A prospective study of the factors affecting outcomes of nonsurgical root canal treatment: part 1: periapical health. Int Endod J 2011;44:583609.
28. Nygaard Östby B. Chelation in root canal therapy. Odontol Tidskr 1957;65:311.
29. Pashley DH, Carvalho RM. Dentine permeability and dentine adhesion. J Dent 1997;25: 355372.
30. Paulson L, Ballal NV, Bhagat A. Effect of root dentin conditioning on the pushout bond strength of biodentine. J Endod 2018;44:11861190.
31. Perdigão J, Eiriksson S, Rosa BT, Lopes M, Gomes G. Effect of calcium removal on dentin bond strengths. Quintessence Int 2001;32:142146.
32. Peters OA, Boessler C, Zehnder M. Effect of liquid and pastetype lubricants on torque values during simulated rotary root canal instrumentation. Int Endod J 2005;38:223229.
33. Qualtrough AJ, Whitworth JM, Dummer PM. Preclinical endodontology: an international comparison. Int Endod J 1999;32: 406414.
34. Rödig T, Vogel S, Zapf A, Hülsmann M. Efficacy of different irrigants in the removal of calcium hydroxide from root canals. Int Endod J 2010;43: 519527.
35. Schilder H. Cleaning and shaping the root canal. Dent Clin North Am 1974;18:269296.
36. Sonntag D, Raab WH, Martin E, Keppel R. Intracanal use of heated rinsing solutions: A pilot study. Quintessence Int 2017;48:281285.
37. Stewart GG, Kapsimalas P, Rappaport H. EDTA and urea peroxide for root canal preparation. J Am Dent Assoc 1969;78:335338.
38. Tay FR, Smales RJ, Ngo H, Wei SH, Pashley DH. Effect of different conditioning protocols on adhesion of a GIC to dentin. J Adhes Dent 2001;3:153167.
39. Torabinejad M, Khademi AA, Babagoli J et al. A new solution for the removal of the smear layer. J Endod 2003;29:170175.
40. Ulusoy ÖI, Savur IG, Alaçam T, Çelik B. The effectiveness of various irrigation protocols on organic tissue removal from

simulated internal resorption defects. Int Endod J 2018;51:10301036.
41. Wright PP, Kahler B, Walsh LJ. The effect of heating to intracanal temperature on the stability of sodium hypochlorite admixed with etidronate or EDTA for continuous chelation. J Endod 2019;45:5761.
42. Yamada RS, Armas A, Goldman M, Lin PS. A scanning electron microscopic comparison of a high volume final flush with several irrigating solutions: Part 3. J Endod 1983;9:137142.
43. Zehnder M. Root canal irrigants. J Endod 2006;32:389-398.
44. Zehnder M, Grawehr M, Hasselgren G, Waltimo T. Tissuedissolution capacity and dentindisinfecting potential of calcium hydroxide mixed with irrigating solutions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96:608613.
45. Zehnder M, Schmidlin P, Sener B, Waltimo T. Chelation in root canal therapy reconsidered. J Endod 2005;31:817820.
46. Zollinger A, Mohn D, Zeltner M, Zehnder M. Shortterm storage stability of NaOCl solutions when combined with Dual Rinse HEDP. Int Endod J 2018;51:691696.
47. Zollinger A, Attin T, Mohn, D, Zehnder M. Effects of endodontic irrigants on blood and bloodstained dentin. Heliyon 2019;5:e01794.

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