Pesquisa Brasileira em Odontopediatria e Clínica Integrada 2026; 26:e250001
https://doi.org/10.1590/pboci.2026.070
ISSN 1519-0501 / eISSN 1983-4632

ORIGINAL ARTICLE

Application of the 1-Hydroxyethylidene-1,1-Diphosphonic Acid Irrigant in Root Canal Treatment: An Observational Study

Nirvana Khalaf Mansour[1], Nidambur Vasudev Ballal[2]

[1]Private Practice, Suez, Egypt.
[2]Department of Conservative Dentistry and Endodontics, Manipal College of Dental Sciences, Manipal Academy of Higher Education, Manipal, India.

Corresponding author: Nidambur Vasudev Ballal **E-mail:** drballal@yahoo.com

Academic Editor: Alessandro Leite Cavalcanti

Received: January 06, 2025 / **Review:** March 26, 2025 / **Accepted:** September 02, 2025

How to cite: Mansour NK, Ballal NV. Application of the 1-hydroxyethylidene-1,1-diphosphonic acid irrigant in root canal treatment: An observational study. Pesqui Bras Odontopediatria Clín Integr. 2026; 26:e250001. https://doi.org/10.1590/pboci.2026.070

ABSTRACT
Objective: To investigate the radiographic periapical healing after root canal treatment using a novel 1-Hydroxyethylidene-1,1-Diphosphonic acid (Dual Rinse HEDP) irrigant in necrotic teeth with an apical periodontitis. **Material and Methods:** In this clinical study, 65 patients with necrotic molars, premolars, and anterior teeth requiring root canal treatment were enrolled. Before the commencement of the study, all study participants signed informed consent forms individually. Teeth were mechanically prepared with E3 Azure rotary files, irrigated with Dual Rinse HEDP irrigant, and then obturated with a single-cone technique and bio-ceramic sealer. After one year, 50 patients (15 dropped out) were evaluated radiographically for periapical healing using the Periapical Index (PAI) scores. Fisher's Exact test and Friedman's test were used. The significance level was set at 5%. **Results:** After one year, the PAI scores of all patients decreased significantly ($p < 0.001$). Regarding pain, there was a statistically significant decrease in the prevalence of pain after one year of follow-up amongst the different groups of teeth (anteriors, premolars, molars) ($p < 0.001$). **Conclusion:** Dual Rinse HEDP, in conjunction with sodium hypochlorite, can be used as an effective irrigant to promote periapical healing.

Keywords: Dental Pulp Diseases; Endodontics; Periapical Diseases; Smear Layer.

Introduction

One of the most prevalent inflammatory conditions in the mouth is apical periodontitis [1]. The newly diseased and necrotic root canal system due to caries, trauma, and periodontal disease provides an optimal environment for establishing a mixed, primarily anaerobic flora that results in the formation of aggregates and coaggregates, as well as sessile biofilms [2]. The periapical tissues (including the alveolar bone and periodontal ligament that encircle the tooth's root) will be destroyed by microbial byproducts that reach the periapical area, triggering a host defence mechanism involving various cells, intracellular mediators, and humoral antibodies. Healing of apical periodontitis is achieved by chemomechanical methods [3].

Mechanical instrumentation alone is insufficient to eliminate microorganisms effectively, as it cannot reach all areas of the root canal system, such as isthmuses, fins, lateral canals, and apical deltas [4]. It may also lead to the removal of additional dentinal tissue, weakening the tooth structure and rendering it more susceptible to vertical root fracture [5]. Hence, the use of irrigants and antimicrobial agents is essential to complement the mechanical action and ensure a more thorough disinfection. It is crucial for debris removal, tissue breakdown, and disinfection [6]. Its main objective is to reach inaccessible places with mechanical instruments, such as auxiliary canals, isthmuses, and deltas [7].

In the past, it has been demonstrated that irrigation improves the success rate of root canal therapy, with a more favourable impact on healing [8]. The gold standard for root canal disinfection is sodium hypochlorite (NaOCl), used at concentrations ranging from 1.25% to 6%. It works as a solvent for organic and fatty materials, breaking down fatty acids to produce fatty acid salts (soap) and glycerol (alcohol), which lowers the surface tension of the remaining solution. NaOCl neutralises amino acids, forming a salt and water (neutralisation reaction) [9]. The departure of hydroxyl ions lowers pH. In interaction with organic tissue, hypochlorous acid acts as a solvent, releasing chlorine. This potent oxidant reacts with the amino group to form chloramine, which inhibits bacterial enzymes and disrupts cell metabolism [10]. It is unique among root canal irrigants in that it can dissolve both necrotic and residual essential pulp tissue. In addition, it is the only irrigant that can eliminate biofilms within the root canal area [11]. But when it extends beyond the apex, it irritates the periapical tissues, which eventually causes pain during root canal therapy. It also does not entirely remove the "smear layer" formed during chemomechanical debridement. This smear layer harbours bacteria within the dentinal tubules, inhibits the entry of irrigants and intracanal medications, and thus impairs the sealing ability of obturating materials. Therefore, it ought to be eliminated [12,13]. The most recommended chelating agent for smear layer removal is ethylenediaminetetraacetic acid (EDTA). This standard irrigation technique (NaOCl-EDTA) is known as sequential chelation, the most popular irrigation strategy during root canal treatment.

On the other hand, EDTA has several disadvantages; it can negatively affect the mechanical properties of root dentin [14], cannot eliminate the smear layer in the apical one third [15], can cause dentin erosion [13], is cytotoxic [16], and has detrimental effects on micstructure of hydraulic calcium silicaite cements [17]. Furthermore, it diminishes the active chlorine when combined with NaOCl [18]. Since the sequential use of two or more irrigation solutions during root canal therapy is mandatory, combining a mild chelator with NaOCl is a good substitute for the conventional protocol, in which NaOCl is used first, followed by a potent chelator such as EDTA.

Recently, Dual Rinse HEDP (DR HEDP; Medcem GmbH, Weinfelden, Switzerland) – a preparation that contains 1-hydroxyethylidene-1,1-diphosphonic acid (HEDP) – was approved for use in endodontics. It comes as a capsule that contains 0.9 g of powdered etidronate. To create an all-in-one irrigant [19] that allows doctors to use DR HEDP in a "continuous chelation" method during root canal treatment [20], the powder should be mixed with 10 mL of NaOCl solution before treatment. This method has the benefit of just requiring one irrigant for chemical debridement of the root canal system. According to earlier research, DR HEDP is non-toxic and has antibacterial properties similar to those of NaOCl [21,22]. It also dissolves tissue just as well as NaOCl [23] and enhances the adhesion of sealers and cements to root canal dentin [24,25].

The use of leak-proof, biocompatible obturation materials and techniques that can provide a fluid-tight seal apically, laterally, and coronally, and densely fill the entire root canal system is an essential step in successful root canal treatment after adequate chemomechanical preparation and smear layer removal. Since gutta-percha fails to adhere to canal walls, the use of a sealer during root canal obturation is essential for effective root canal treatment [26]. Calcium silicate-based materials offer several benefits, including outstanding biocompatibility due to their resemblance to biological hydroxyapatite and innate osteoinductive properties. Biocements differ from traditional cement sealers in that they can form a chemical bond with the tooth structure and have adequate radiopacity [27]. Furthermore, these sealers function as resorbable regenerative scaffolds that gradually dissolve when the body regenerates the tissue [28].

To our knowledge, no research has been done on the impact of Dual Rinse HEDP irrigant on periapical healing. Therefore, the objective of the present study was to assess the effect of the Dual Rinse HEDP irrigant on the healing of necrotic teeth with apical periodontitis.

Material and Methods

Ethical Clearance

The NUB/MRE Ethics Committee No. 05/02/23 approved the study protocol, in accordance with international agreements (Declaration of Helsinki). All study participants provided informed consent after signing the informed consent form.

Sample Size Determination

G*Power version 3.1.9.2, Faul et al. [29], University Kiel, Germany, was used to calculate the sample size. Copyright [c]: 1992–2014. The effect size was 0.35, with alpha [α] and Beta [β] levels of 0.05, i.e., power = 85%, including dropouts. 65 patients who all fulfilled the inclusion and exclusion criteria were included. Figure 1 represents the patient recruitment and allocation process.

Eligibility Criteria

The age range for inclusion was 20 to 65 years, with premolars, molars, and necrotic permanent incisors that required root canal therapy. Individuals who had undergone root canal therapy in the past, smokers, pregnant women, patients with immunocompromised diseases (such as diabetes mellitus, AIDS, hepatitis B, hepatitis C, tuberculosis, and cancer), incompletely formed root apices, weeping canals, internal or external root resorption, or teeth with fractures extending vertically or horizontally below the CEJ were all excluded.

Radiographic Technique

Preoperative diagnostic intra-oral digital periapical radiographs (EzSensor Classic, Size 2, Vatech Inc., Gyeonggi-do, Korea) were obtained to assess the presence of periapical periodontitis using the paralleling technique. Necrosis of the pulp was verified by negative response to cold pulp tests using Ethyl Chloride spray (Endo Ice; Coltene Whaledent Inc., Cuyahoga Falls, OH, USA) on a cotton pellet that was applied to the tooth surface.

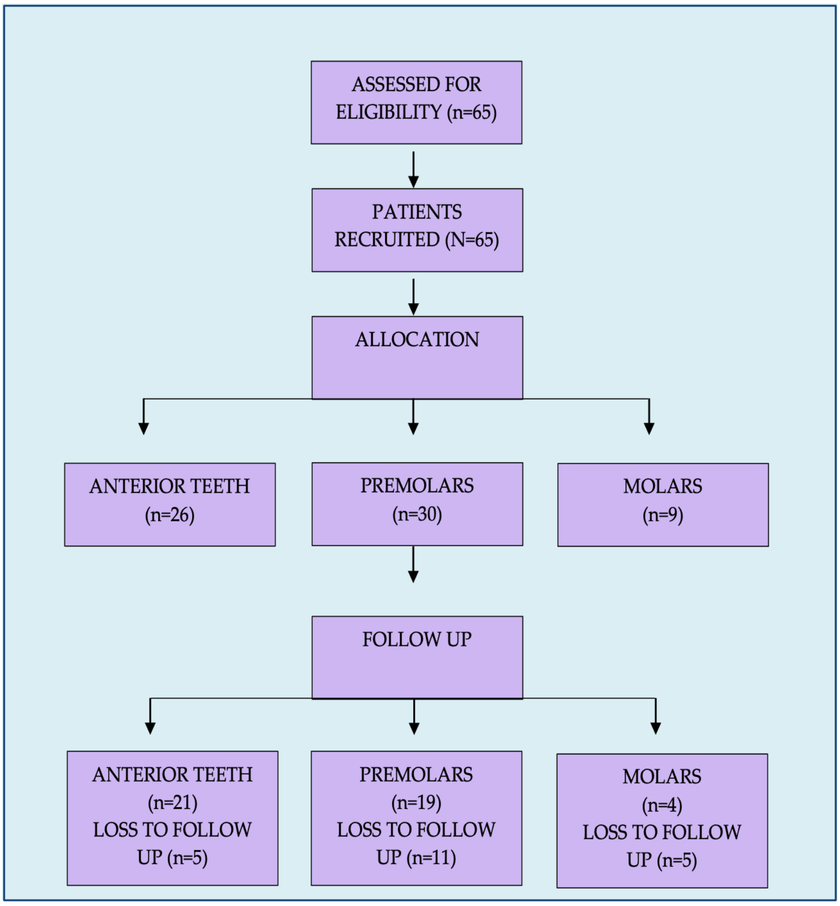


Figure 1. Flow chart of case selection.

Root Canal Preparation

Following the injection of a local anesthetic containing articaine HCl (Fullcain Fort Ampul; Onfarma, Samsun, Turkey), a rubber dam was placed to completely isolate the tooth to be treated. Then, moistened cotton with NaOCl (JK Dental Vision, Mansourah, Egypt) was used to disinfect the tooth. In cases of severe tooth structure destruction, composite build-up was performed while replicating normal tooth anatomy. Under a four-fold magnifying dental operating microscope (DOM; Zumax Medical Co., Ltd., Sozhou, China), a straight-line access cavity was created using a sterile Endo access bur (Dentsply Sirona, Charlotte, USA). After that, a periapical radiograph was obtained to confirm the working length measurement obtained with an Apex Locator (Dent Jeosoft, Moscow, Russia). Subsequently, root canal patency was assessed using a 10K manual file (Fanta Dental Materials, Shanghai, China).

The biomechanical preparation was then completed using the V-Blue rotary file system (Perfect Endo, Shenzhen Perfect Medical Instrument, China) to a minimum size 30 taper 4 in molars and premolars, 35 taper 4 in anteriors. The root canal was irrigated with 5ml of Dual Rinse HEDP solution between each instrument change. As directed by the manufacturer, 10 mL of 3% NaOCl was combined with one capsule of Dual Rinse etidronic acid (HEDP) powder (Medcem, GmbH, Vienna, Austria) to create the Dual Rinse HEDP-based solution [14]. For 30 minutes [29], irrigation was performed using a 28-gauge, side-vented needle (Meta Biomed Co, LTD, Cheongju, Korea).

Then the canal was dried with sterile paper points (Meta Biomed Co, LTD, Cheongju, Korea). Bioceramic sealer (Ceraseal, Meta Biomed Co, LTD, Cheongju, Korea) was injected into the root canal, and obturation was performed with gutta-percha cone (4% taper) (Meta Biomed Co, LTD, Cheongju, Korea) that corresponded to the master file applying a single cone technique. Then, at the same visit, the access cavity was restored using composite resin (Coltene Brilliant, Coltène/Whaledent AG, Altstätten, Switzerland). The root canal treatment procedure was performed in a single visit. Patients were assessed clinically (at 24 hours, 72 hours, and 1 year) and radiographically (at 1 year) during follow-up to determine the degree of healing and assess the efficacy of the therapy.

Outcome Measures

Radiographic Assessment of Healing (Primary Outcome Measure)

A digital periapical radiograph was used to evaluate the tooth using the Periapical Index (PAI). The scores ranged from 1 (normal periradicular tissue) to 5 (severe periodontitis with exacerbating features). Based on clinical signs and symptoms and PAI scores, teeth were classified as healed, healing, or diseased [11].

[a] Healed: Radiographic PAI scores of 1 or 2 with clinical normality.

[b] Healing: Clinical normality other than tenderness to percussion accompanied by a reduction in the size of peri-radicular lesion or reduction in PAI score.

[c] Failed: The presence of clinical signs and symptoms accompanied by a radiographic PAI score of 3 or higher, or an increase in the size of peri-radicular lesion, or an increase in PAI score.

As a secondary outcome measure, percussion pain and sinus/pus discharge were assessed. The visual analogue scale (VAS) was employed in this investigation to evaluate postoperative pain. Patients were encouraged to indicate a horizontal scale to describe the level of pain they were experiencing on the day of therapy, three days after therapy, and during a re-evaluation visit (one year following treatment). Each patient was assigned a score of 0-10 [27].

The long-cone paralleling technique was used for follow-up radiographs, with a film holder. Pretreatment and one-year follow-up radiographic x-rays of the teeth were created as a PowerPoint presentation (Microsoft® Corporation, Redmond, WA, USA) slide and examined on a computer in a room with poor lighting. Last but not least, the change in periapical radiolucency after a one-year follow-up period was evaluated using the PAI scores of five categories: 1. Normal apical periodontium, 2. Small changes in bone structures 3. Change in bone structure with mineral loss, 4. Periodontitis with a well-defined radiolucent area 5. Severe periodontitis with exacerbating features [13], PAI was determined by two skilled endodontists. In the radiographic assessment, teeth with a PAI score of ≤ 2 and no clinical symptoms were considered "healthy," whereas teeth with a PAI score of ≥ 3 and clinical symptoms were considered "failure." According to intra-observer reliability, the Kappa test value for the PAI score was 0.86 ($p<0.001$).

Statistical Analysis

Using the Kolmogorov-Smirnov test, the data were tested for normality by examining their distribution. Frequencies and percentages were used to portray qualitative data. For comparisons between the two groups (baseline and one-year follow-up), Fisher's Exact test was used. Friedman's test was used to examine the changes in each group over time. The level of significance was set at $p = 0.05$. IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA), was used for statistical analysis.

Results

Table 1 presents the demographic and clinical variables of recruited patients at baseline (N=65) and at the 1-year follow-up (N=50).

Table 1. Demographic and clinical characteristics of participants.

Variables	At Baseline	At One Year Follow-Up
	N	N
Gender		
Male	40	30
Female	25	20
Age (Years)		
10-20	13	13
21-30	10	10
31-40	20	15
41-50	17	10
51-60	5	2
Teeth Type		
Anteriors	26	21
Premolars	30	19
Molars	9	10
Smoking Status		
Smokers	5	3
Non smokers	60	47

Periapical Healing

At baseline and at follow-up (1 year later), there was a highly statistically significant difference in PAI scores (p <0.0001). At baseline, most patients had a score of 3 (41.5%) (Change in bone structure with mineral loss), followed by a score of 4 [27.7%] (Periodontitis with well-defined radiolucent area). Only 10 patients (15.4%) had a score of 2 (small changes in bone structure). The other 10 patients had a score of 5 (Periodontitis with well-defined radiolucent area). After one-year follow-up, most of the patients had a score of 2 (54.0%) (Small changes in bone structure) and a score of 1 (30.0%) (normal apical periodontium), with 15 patients experiencing dropout during the follow-up period (Table 2 and Figure 2).

Table 2. Descriptive statistics and results of periapical healing at different time periods.

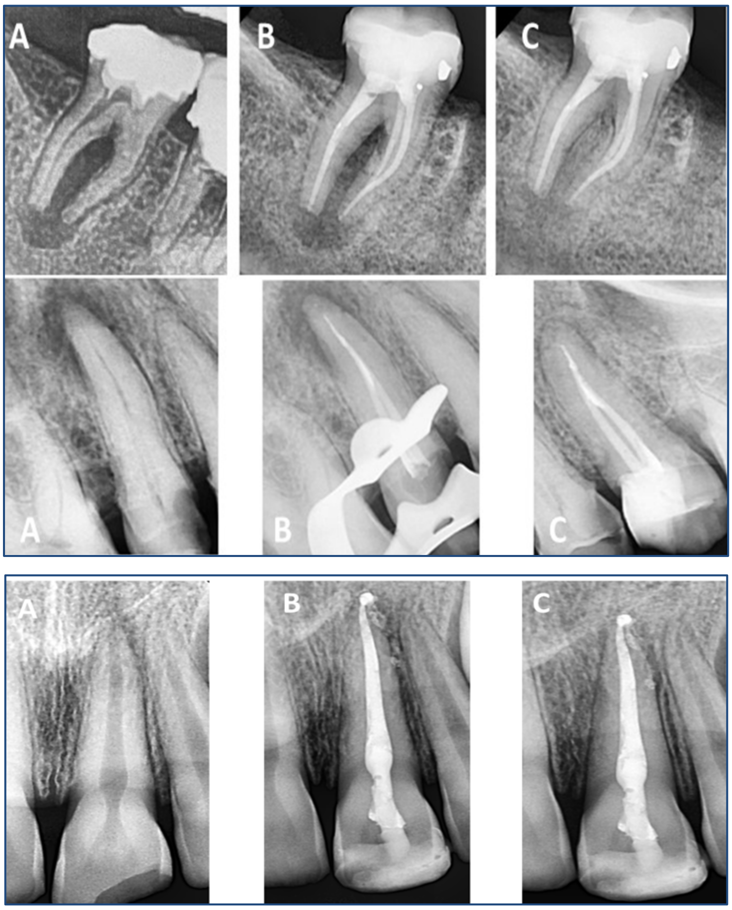
Time Period	N	PAI Score					p-value
		1	2	3	4	5	
		N (%)	N (%)	N (%)	N (%)	N (%)	
Baseline	65	0 (0.0)	10 (15.4)	27 (41.5)	18 (27.7)	10 (15.4)	<0.0001*
Follow-Up [One Year]	50	15 (30.0)	27 (54.0)	8 (16.0)	0 (0.0)	0 (0.0)	

*Statistically significant.

Pain

The results showed a statistically significant difference in the prevalence of pain amongst the different groups of teeth (anteriors, premolars, molars) at 24 hours and 1 year (p <0.0001). In contrast, there was no statistically significant difference at 72 hours. However, within each group of teeth (anteriors, premolars, and molars), there was a statistically significant change in prevalence of pain (p <0.0001).

At 24 hours after treatment, 11 (42.3%) anterior teeth showed no pain, and 15 (57.7%) showed mild pain; after 1 year, all anterior teeth showed no pain. Regarding Premolars, 5 (16.7%) teeth showed no pain, 20 (66.7%) teeth showed mild pain, and 5 (16.7%) showed moderate pain, but after one year, most of them showed no pain, 19 (63.3%), and only six premolars (20.0%) showed mild pain. In the molars group, 4 (44.4%) molars showed no pain, and 5 (55.6%) showed mild pain. After 1 year, there was no pain in 4 molars and a dropout in 5 molars. There was a decrease in pain prevalence after 1 year (Table 3).



(A) Preoperative radiograph demonstrating periapical lesion; (B) Immediate postoperative radiograph after root canal treatment; (C) Postoperative radiograph after one year follow-up showing satisfactory periapical healing.

Figure 2. Endodontic treatment of necrosed second mandibular right molar (top), second maxillary right premolar (middle), and maxillary left central incisor (bottom).

Table 3. Descriptive statistics and results of Fisher's Exact test for comparison of the prevalence of pain between the groups, and Friedman's test comparing pain at different time periods within each group.

Time Period	Condition	Anteriors N=26	Premolars N=30	Molars N=9	p-value
24 hrs	No Pain	11 (42.3)	5 (16.7)	4 (44.4)	0.04**
	Mild	15 (57.7)	20 (66.7)	5 (55.6)	
	Moderate	0 (0.0)	5 (16.7)	0 (0.0)	
	Sever	0 (0.0)	0 (0.0)	0 (0.0)	
72 hrs	No Pain	14 (53.8)	15 (50.0)	7 (77.8)	0.332
	Mild	12 (46.2)	15 (50.0)	2 (22.2)	
	Moderate	0 (0.0)	0 (0.0)	0 (0.0)	
	Sever	0 (0.0)	0 (0.0)	0 (0.0)	
One Year	No Pain	21 (80.8)	19 (63.3)	4 (44.4)	0.033**
	Mild	0 (0.0)	6 (20.0)	0 (0.0)	
	Moderate	0 (0.0)	0 (0.0)	0 (0.0)	
	Sever	0 (0.0)	0 (0.0)	0 (0.0)	
	Dropout	5 (19.2)	5 (16.7)	5 (55.6)	
	p-value*	<0.001**	<0.001**	<0.001**	

*Friedman's test; **Statistically significant.

Discussion

The current clinical study evaluated the efficacy of a novel 1-Hydroxyethylidene-1,1-Diphosphonic acid (Dual Rinse HEDP) when mixed with NaOCl for periapical healing of necrotic teeth with apical periodontitis.

The results revealed that Dual Rinse HEDP, in conjunction with sodium hypochlorite, promoted satisfactory periapical healing. Dual Rinse etidronic acid, a potent chelating agent, plays a crucial role in root canal treatment by effectively removing smear layer and debris from the root canal system. This enhances the ability of disinfectants and medicaments to penetrate deeper into the canal, ensuring thorough cleaning and disinfection. Additionally, etidronic acid promotes better adhesion of obturation materials and improves the overall success rate of endodontic treatments. Its use in combination with an irrigant solution provides an optimal environment for successful root canal therapy, ultimately leading to improved treatment outcomes and long-term success in the management of periapical lesions.

The parallel technique with film holders was used in the current investigation to acquire baseline and follow-up radiographs. In 1986, PAI scoring was developed as a basis for epidemiological research, including Orstavik's periapical periodontitis index [3]. This scoring system, based on the correlation between histologic diagnosis and radiographic findings, is highly accurate, repeatable, and objective. One potential limitation, though, is sensitivity to observer variance. To address this problem, two calibrated, blinded endodontists evaluated each radiograph separately in the current experiment. Periapical radiographs were obtained from 50 patients by the end of the one-year follow-up period to assess the outcomes of the current study. None of these patients displayed any symptoms of discomfort, oedema, sinus congestion, loss of function, or other issues.

Strindberg's [30] criteria state that the presence or absence of periapical periodontitis affects the success rate of endodontic therapy, which is dependent on several factors, such as chemomechanical preparation, root canal system disinfection, intracanal medicaments, root canal sealers, and the apical extent of obturation.

To fight microorganisms effectively and permanently, the irrigants used in chemomechanical preparations must diffuse throughout dentinal tubules. They should also be biocompatible with periapical tissues and be able to remove the smear layer without harming dentin or the sealing ability [31]. Ideally, they should be able to destroy bacterial endotoxins and degrade organic molecules [32]. *E. faecalis* is a facultatively anaerobic, Gram-positive coccus primarily prevalent in asymptomatic cases of primary endodontic infections and unsuccessful endodontic cases. Dentine discs were contaminated with *E. faecalis* and *C. albicans* biofilms to investigate the variable irrigating solutions, Triton, Dual Rinse HEDP, and a dual-step irrigation procedure that involved NaOCl followed by EDTA, according to a study by Castagnola et al. [33]. The fact that all tested irrigating solutions eliminated 100% of *E. faecalis*, and that SEM evaluation verified the absence of bacteria or the presence of trace amounts not detected by colony-forming unit analysis, may be responsible for the satisfactory periapical healing outcomes observed in the present study. This antimicrobial effect appears similar to that of a protocol including NaOCl followed by a final rinse with EDTA [34]. Research by Lottanti et al. 2009 [35], Ballal et al. [21], and lvarez-Sagües et al. [36] has shown that 5.25% NaOCl alone can effectively remove infectious pathogens and prevent biofilm formation. However, NaOCl alone is not always effective, and chelating agents [EDTA or HEDP] are needed to remove the root-associated biofilm. Also, Arias-Moliz and Camilleri [35] compared the antimicrobial activity of 2.5% NaOCl and 2.5% NaOCl + 9% HEBP, reporting that both solutions killed 100% of the *E. faecalis* biofilms, in agreement with Giardino et al. [36], who had reported that Dual Rinse HEDP kills *E. faecalis* more efficiently than NaOCl followed by EDTA using confocal laser scanning microscopic analysis.

Etidronic acid (HEDP) alone demonstrated a weak antimicrobial effect on *C. albicans*, which is most frequently isolated from persistent endodontic infections [37]; however, when mixed with NaOCl, better antimicrobial efficacy was achieved than with NaOCl and EDTA alone, without compromising its antimicrobial properties [33].

Several investigations comparing irrigants reveal that HEDP is the most appropriate chelator to mix with sodium hypochlorite in irrigation protocols, compared with EDTA and Paracetic acid, using scanning electron microscopy to evaluate outcomes. This finding implies that HEDP could be considered the irrigant of choice in combination with NaOCl for root canal disinfection [38-40]. Nevertheless, its impact on dentin properties, such as microhardness and roughness, is negligible [41]. These findings corroborated those of Ballal et al. [42] and Ulusoy et al. [43], who claimed that HEBP had a stronger power to remove smear layers than EDTA. Furthermore, in comparison to EDTA/ NaOCl, Álvarez-Sagües et al. [36] and Morago-Guardia [44] observed that HEDP in combination with NaOCl had a potent antibacterial effect on bacteria residing in dentine tubules, reducing biovolume and eliminating a significant portion of the smear layer [45].

In this study, bioceramic sealer was used since Dual Rinse HEDP does not negatively impact its bond strength [46], these observations were confirmed by Paulson et al., who revealed that the push out bond strength of Biodentine was significantly increased when the root canal was irrigated with 2.5% NaOCl combined with 9% Dual Rinse HEDP; this is because the action of the remaining EDTA on the inner root canal surface that can chelate the ions of calcium which were generated during hydration from the tricalcium silicate cement, disrupting it [47]. Calcium silicate-based sealers have recently enhanced the quality of root canal obturation. Research on this material demonstrates bioactivity, biocompatibility, and exceptional sealing performance when exposed to humidity *in vivo* [48]. Furthermore, numerous giant cell responses to calcium hydroxide-containing sealers have been observed in the periapical region in recent investigations [49]. This action results in a greater reduction in microbial infection in the periapical area, thereby promoting healing. Systemic factors such as age, hormones, and chronic illnesses may affect the host's immune responses and, consequently, the outcomes and healing process of root canal therapy in the restoration of teeth that have undergone endodontic treatment.

Along with following proper clinical procedures, it's critical to acknowledge these factors to achieve a more successful RCT [50]. Certain limitations of this study included a small sample size, a relatively short follow-up period, and the use of radiographic techniques to assess periapical healing. Further well-controlled randomized clinical trials are warranted, with larger sample sizes, longer follow-up periods, the use of different NaOCl concentrations, and cone-beam computed tomographic imaging to evaluate the efficacy of Dual Rinse HEDP in combination with NaOCl for the healing of apical periodontitis.

Conclusion

The use of Dual Rinse HEDP mixed with NaOCl could be an alternative to NaOCl followed by EDTA as a root canal irrigant, promoting satisfactory periapical healing.

Authors' Contributions

NKM	https://orcid.org/0000-0001-5692-8420	Conceptualization, Methodology, Investigation, Writing - Original Draft, Writing - Review and Editing, and Project Administration.
NVB	https://orcid.org/0000-0002-2208-9443	Software, Formal Analysis, Data Curation, and Supervision.
All authors declare that they contributed to the critical review of intellectual content and approval of the final version to be published.		

Financial Support

None.

Conflict of Interest

The authors declare no conflicts of interest.

Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

References

[1] Tibúrcio-Machado CS, Michelon C, Zanatta FB, Gomes MS, Marin JA, Bier CA. The global prevalence of apical periodontitis: A systematic review and meta-analysis. Int Endod J 2021; 54(5):712-735. https://doi.org/10.1111/iej.13467
[2] Siqueira JF, Rôças IN. Present status and future directions: Microbiology of endodontic infections. Inter Endod J 2022; 55(Suppl 3):512-530. https://doi.org/10.1111/iej.13677
[3] Küçük M, Aksoy U, Şehirli AÖ. Possible protective effects of bmal1 gene and melatonin on the prognosis of apical periodontitis. Med Hypotheses 2022; 162:110806. https://doi.org/10.1016/j.mehy.2022.110806
[4] Siqueira JF, Lima KC, Magalhães FA, Lopes HP, de Uzeda M. Mechanical reduction of the bacterial population in the root canal by three instrumentation techniques. J Endod 1999; 25(5):332-335. https://doi.org/10.1016/S0099-2399(06)81166-0
[5] Gluskin AH, Peters CI, Peters OA. Minimally invasive endodontics: Challenging prevailing paradigms. Br Dent J 2014; 216(6):347-353. https://doi.org/10.1038/sj.bdj.2014.201
[6] Mampilly J, Shetty K, Shetty H. Endodontic irrigating solutions, disinfection devices and techniques: A review. IOSR J Dent Med Sci 2020; 8(1):986-997. https://doi.org/10.21474/IJAR01/10392
[7] Pérez AR, Ricucci D, Vieira GCS, Provenzano JC, Alves FRF, Marceliano-Alves MF, et al. Cleaning, shaping, and disinfecting abilities of 2 instrument systems as evaluated by a correlative micro-computed tomographic and Histobacteriologic approach. J Endod 2020; 46(6):846-857. https://doi.org/10.1016/j.joen.2020.03.017
[8] Chubb DW. A review of the prognostic value of irrigation on root canal treatment success. Aust Endod J 2019; 45(1):5-11. https://doi.org/10.1111/aej.12348
[9] Zehnder M. Root canal irrigants. J Endod 2006; 32(5):389-398. https://doi.org/10.1016/j.joen.2005.09.014
[10] Mohammadi Z, Shalavi S, Kinoshita JI, Giardino L, Gutmann JL, Rad SB, et al. A review on root canal irrigation solutions in endodontics. J Dent Mater Tech 2021; 10(3):121-132. https://doi.org/10.22038/jdmt.2021.56003.1431
[11] Teja KV, Janani K, Srivastava KC, Shrivastava D, Jose J, Marya A, et al. Comparison of herbal agents with sodium hypochlorite as root canal irrigant: A systematic review of in vitro studies. Evid Based Compl Alter Med 2021; 2021:8967219. https://doi.org/10.1155/2021/8967219
[12] Jain S, Patni PM, Jain P, Raghuwanshi S, Pandey SH, Tripathi S, et al. Comparison of dentinal tubular penetration of intracanal heated and preheated sodium hypochlorite through different agitation techniques. J Endod 2023; 49(6):686-691. https://doi.org/10.1016/j.joen.2023.04.007
[13] Orlowski NB, Schimdt TF, da Silveira Teixeira C, Garcia LD, Savaris JM, Tay FR, et al. Smear layer removal using passive ultrasonic irrigation and different concentrations of sodium hypochlorite. J Endod 2020; 46(11):1738-1744. https://doi.org/10.1016/j.joen.2020.07.020
[14] Ballal NV, Ray AB, Narkedamalli R, Urala AS, Patel V, Harris M, et al. Effect of continuous vs sequential chelation on the mechanical properties of root dentin: An ex vivo study. J Dent 2024; 148:105214. https://doi.org/10.1016/j.jdent.2024.105214
[15] Murugesan K, Vishwanath S, Kadandale S, Thanikachalam Y, Parthasarathy R, Ilango S. Comparative evaluation of smear layer removal in apical third using four different irrigants with ultrasonic agitation: An in vitro Scanning Electron Microscopy [SEM] analysis. Cureus 2022; 14(3):e23142. https://doi.org/10.7759/cureus.23142
[16] Ballal NV, Kundabala M, Bhat S, Rao N, Rao BS. A comparative in vitro evaluation of cytotoxic effects of EDTA and maleic acid: Root canal irrigants. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009; 108(4):633-638. https://doi.org/10.1016/j.tripleo.2009.05.039
[17] Ballal NV, Sona M, Tay FR. Effects of smear layer removal agents on the physical properties and microstructure of mineral trioxide aggregate cement. J Dent 2017; 66:32-36. https://doi.org/10.1016/j.jdent.2017.08.018
[18] Clarkson RM, Podlich HM, Moule AJ. Influence of ethylenediaminetetraacetic acid on the active chlorine content of sodium hypochlorite solutions when mixed in various proportions. J Endod 2011; 37(4):538-543. https://doi.org/10.1016/j.joen.2011.01.018
[19] Zollinger A, Mohn D, Zeltner M, Zehnder M. Short-term storage stability of NaOCl solutions when combined with Dual Rinse HEDP. Int Endod J 2018; 51(6):691-696. https://doi.org/10.1111/iej.12875
[20] La Rosa GR, Plotina G, Nagendrababu V, Pedulla E. Effectiveness of continuous chelation irrigation protocol in endodontics: A scoping review of laboratory studies. Odontol 2024; 112(1):1-18. https://doi.org/10.1007/s10266-023-00835-8
[21] Ballal NV, Gandhi P, Shenoy P, Belle VS, Bhat V, Rechenberg DK, et al. Safety assessment of an etidronate in a sodium hypochlorite solution: Randomized double-blind trial. Int Endod J 2019; 52(9):1274-1282. https://doi.org/10.1111/iej.13129
[22] Ballal NV, Das S, Rao BS, Zehnder M, Mohn D. Chemical, cytotoxic and genotoxic analysis of Dual Rinse HEDP in sodium hypochlorite solution. Int Endod J 2019; 52(8):1228-1234. https://doi.org/10.1111/iej.13110

[23] Ballal NV, Ivica A, Meneses P, Narkedamalli RK, Attin T, Zehnder M. Influence of 1-hydroxyethylidene-1,1-diphosphonic acid on the soft tissue dissolving and gelatinolytic effect of ultrasonically activated sodium hypochlorite in simulated endodontic environments. Materials 2021; 14(10):2531. https://doi.org/10.3390/ma14102531
[24] Ballal NV, Roy A, Zehnder M. Effect of sodium hypochlorite concentration in continuous chelation on dislodgement resistance of an epoxy resin and hydraulic calcium silicate sealer. Polymers 2021; 13(20):3482. https://doi.org/10.3390/polym13203482
[25] Ulusoy Öİ, Ballal NV, Narkedamalli R, Ulusoy N, Shetty KP, Luke AM. Dislodgement resistance and structural changes of tricalcium silicate-based cements after exposure to different chelating agents. PLoS One 2024; 19(1):e0296647. https://doi.org/10.1371/journal.pone.0296647
[26] Asawaworarit W, Pinyosopon T, Kijsamanmith K. Comparison of apical sealing ability of bioceramic sealer and epoxy resin-based sealer using the fluid filtration technique and scanning electron microscopy. J Dent Sci 2020; 15(2):186-192. https://doi.org/10.1016/j.jds.2019.09.010
[27] Khandelwal A, Janani K, Teja K, Jose J, Battineni G, Riccitiello F, et al. Periapical healing following root canal treatment using different endodontic sealers: A systematic review. Biomed Res Int 2022; 2022:3569281. https://doi.org/10.1155/2022/3569281
[28] Santos-Junior AO, Tanomaru-Filho M, Pinto JC, Tavares KI, Torres FF, Guerreiro-Tanomaru JM. Effect of obturation technique using a new bioceramic sealer on the presence of voids in flattened root canals. Braz Oral Res 2021; 35:e028. https://doi.org/10.1590/1807-3107bor-2021.vol35.0028
[29] Faul F, Erdfelder E, Lang A, Buncher A. G* Power: A flexible statistical power analysis program for the social, behavioural, and biomedical sciences. Behavior Res Methods 2007; 39:175-191. https://doi.org/10.3758/bf03193146
[30] Ruddle CJ. Cleaning and shaping of the root canal system, 8th ed. In: Cohen S. St Louis, MO: Mosby; 2002.
[31] Strindberg LZ. The dependence of the results of pulp therapy on certain factors-an analytical study based on radiographic and clinical follow-up examination. Acta Odontol Scand 1956; 14:1-175.
[32] Elbahary S, Haj-Yahya S, Khawalid M, Tsesis I, Rosen E, Habashi W, et al. Effects of different irrigation protocols on dentin surfaces as revealed through quantitative 3D surface texture analysis. Sci Rep 2020; 10(1):22073. https://doi.org/10.1038/s41598-020-79003-9
[33] Castagnola R, Martini C, Colangeli M, Pellicciotta I, Marigo L, Grande N, et al. In Vitro Evaluation of Smear Layer and Debris Removal and Antimicrobial Activity of Different Irrigating Solutions. Eur Endod J 2024; 9[1]: 81-88. https://doi.org/10.14744/eej.2023.19042
[34] Zhong Y, Chasen J, Yamanaka R, Garcia R, Kaye EK, Kaufman JS, et al. Extension and density of root fillings and postoperative apical radiolucencies in the veterans affairs dental longitudinal study. J Endod 2008; 34(7):798-803. https://doi.org/10.1016/j.joen.2008.03.022
[35] Lottanti S, Gautschi H, Sener B, Zehnder M. Effects of ethylenediaminetetraacetic, etidronic and peracetic acid irrigation on human root dentine and the smear layer. Inter Endod J 2009; 42(4):335-343. https://doi.org/10.1111/j.1365-2591.2008.01514.x
[36] Álvarez-Sagües A, Herce N, Amador U, Llinares-Pinel F, Nistal-Villan E, Presa J, et al. Efficacy of EDTA and HEDP chelators in the removal of mature biofilm of enterococcus faecalis by PUI and XPF file activation. Dent J 2021; 9(4):41. https://doi.org/10.3390/dj9040041.
[37] Arias-Moliz MT, Camilleri J. The effect of the final irrigant on the antimicrobial activity of root canal sealers. J Dent 2016; 52:30-36. https://doi.org/10.1016/j.jdent.2016.06.008
[38] Giardino L, Del Fabbro M, Morra M, Pereira T, Bombarda de Andrade F, Savadori P, et al. Dual Rinse® HEDP increases the surface tension of NaOCl but may increase its dentin disinfection efficacy. Odontol 2019; 107(4):521-529. https://doi.org/10.1007/s10266-019-00436-4
[39] Karale R, Odedra KM, Srirekha A, Champa C, Shetty A, Pushpalatha S, et al. Effect of dentin on the antimicrobial efficacy of 3% sodium hypochlorite, 2% chlorhexidine, 17% ethylenediaminetetraacetic acid, and 18% etidronic acid on Candida albicans: An in vitro study. J Conserv Dent 2016; 19(5):455-460. https://doi.org/10.4103/0972-0707.190023
[40] Zeng B, Li MD, Zhu ZP, Zhao JM, Zhang H. Application of 1-hydroxyethylidene-1, 1-diphosphonic acid in boiler water for industrial boilers. Water Sci Technol 2013; 67(7):1544-1550. https://doi.org/10.2166/wst.2013.021
[41] Bedier MM, Gawdat SI. Evaluation of the efficacy of dual rinse and glycolic acid as root canal irrigation on superficial chemical structure and microhardness of radicular dentine. Egy Dent J 2024;70(1):653-661. https://doi.org/10.21608/edj.2023.232077.2693
[42] Ballal NV, Kandian S, Mala K, Bhat KS, Acharya S. Comparison of the efficacy of maleic acid and ethylenediaminetetraacetic acid in smear layer removal from instrumented human root canal: a scanning electron microscopic study. J Endod 2009; 35: 1573-1576. https://doi.org/10.1016/j.joen.2009.07.021
[43] Ulusoy OL, Zeyrek S, Çelik B. Evaluation of smear layer removal and marginal adaptation of root canal sealer after final irrigation using ethylenediaminetetraacetic, peracetic, and etidronic acids with different concentrations. Microsc Res Tech 2017; 80: 687-692. https://doi.org/10.1002/jemt.22851
[44] Morago-Guardia AY. Efecto de los detritus de dentina y barrillo dentinario en la actividad antimicrobiana de soluciones en hipoclorito sódico. Granada: Universidad de Granada, 2019 [In Spanish].

[45] Paulson L, Ballal NV, Bhagat A. Effect of root dentin conditioning on the pushout bond strength of biodentine. J Endod 2018; 44(7):1186-1190. https://doi.org/10.1016/j.joen.2018.04.009
[46] Reszka P, Nowicka A, Lipski M, Dura W, Droździk A, Woźniak K. A comparative chemical study of calcium silicate-containing and epoxy resin-based root canal sealers. Biomed Res Int 2016; 2016:9808432. https://doi.org/10.1155/2016/9808432
[47] Al-Haddad A, Che Ab Aziz ZA. Bioceramic-based root canal sealers: A review. Int J Biomater 2016; 2016:9753210. https://doi.org/10.1155/2016/9753210
[48] De-Deus G, Zehnder M, Reis C, Fidel S, Fidel RA, Galan J Jr, et al. Longitudinal co-site optical microscopy study on the chelating ability of etidronate and EDTA using a comparative single-tooth model. J Endod 2008; 34(1):71-75. https://doi.org/10.1016/j.joen.2007.09.020
[49] Ricucci, D., Grande, N.M., Plotino, G. and Tay, F.R. Histologic response of human pulp and periapical tissues to tricalcium silicate–based materials: a series of successfully treated cases. J Endod 2020; 46[2]:307-317.
[50] Iandolo A, Amato A, Martina S, Abdellatif DA, Pantaleo G. Management of severe curvatures in root canal treatment with the new generation of rotating files using a safe and predictable protocol. Open Dent J 2020; 14:421-425. https://doi.org/10.2174/1874210602014010421