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Endodontic Irrigation- Unveiling the Hidden Pathways

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Abstract

Root canal infections are usually polymicrobial involving complex interactions among bacteria. The main aim of endodontic treatment is to eliminate infected material from the root canal system, allowing a pre-existing periapical lesion to heal or preventing further infection of the periradicular tissues. Since instrumentation alone cannot reach every part of the canal walls, irrigation becomes an essential step in endodontic therapy. However, the intricate anatomy of the root canal system makes thorough cleaning difficult. Although syringe-and-needle irrigation combined with chemical agents is still the most commonly used method, it does not always ensure complete disinfection or optimal canal cleanliness. For this reason, both alternative irrigating solutions and various activation systems have been introduced to enhance the chemical and physical action of irrigants.

Keywords: Root Canal Irrigation; Apical Periodontitis; Biofilms; Endodontic Disinfection

Introduction

Clinical trials are prospective biomedical or behavioral research studies conducted on human participants to evaluate the safety, efficacy, and dosage of interventions, including drugs, devices, and treatment protocols, and they form the basis of evidence-based clinical practice[1,2]. In endodontics, chemo-mechanical preparation remains the cornerstone of treatment and is aimed at removing inflamed or necrotic pulp tissue while shaping the root canal system to facilitate disinfection, biofilm disruption, and subsequent obturation [3–5].

Mechanical instrumentation alone has been shown to significantly reduce intracanal bacterial load. Byström and Sundqvist demonstrated that instrumentation with saline irrigation can reduce bacterial counts from 10^4–10^6 to 10^2–10^3, while further reductions are achieved with improved techniques[12,13]. However, complete eradication of microorganisms is rarely achieved, necessitating the use of chemical irrigants.

Outcome Measures and Microbial Basis of Disease

Our outcome measures during an endodontic treatment can be classified under:

Primary outcome-

1. Prevention / healing of the apical periodontitis
2. Quality of life (includes pain and tooth survival)

Surrogate outcome:

1. Microbial reduction (microbial killing, endotoxin reduction)
2. pulp tissue removal
3. Accumulated hard tissue removal
4. Debris/microbial extrusion

Microbiota are integral to cause infection to periradicular disease. The presence of bacteria leads to pulp necrosis and the development of apical periodontitis, a relationship that was clearly demonstrated in the landmark study by Kakehashi et al. in 1965 [6]. Root canal irrigation has been recommended as an essential component of endodontic therapy due to its significant impact on reducing intracanal bacterial load, as evidenced by clinical studies conducted by Byström and Sundqvist in 1981 and 1983[12,13]. However, counterintuitively, the effect of different irrigants, irrespective of their antibacterial properties, and even variations in sodium hypochlorite (NaOCl) concentration, do not appear to produce substantial differences in periapical healing outcomes. This has been documented in several studies, including those by Sjögren et al. (1997), Ricucci and Siqueira (2010), and subsequent systematic analyses by Ng et al. (2008, 2011) [7–10]. This seemingly paradoxical observation suggests the presence of an underlying biological phenomenon that warrants further exploration.

The evolution of evidence in endodontics can be understood within the broader context of the medical and dental evidence-based era (1980–present), which followed an earlier phase driven by the focal infection theory (1911–1940). Contemporary evidence-based approaches emphasize the quality of evidence and the formulation of clinical practice guidelines, although debate persists regarding whether guideline-driven protocols or clinician expertise-based approaches are more effective in improving outcomes. Endodontics operates within a complex healthcare framework influenced by clinical, economic, and technological factors.

The nature of root canal treatment and the determinants of its success are multifactorial and remain challenging to fully delineate. Factors influencing periapical healing are typically categorized as pre-operative, intra-operative, and post-operative, each encompassing multiple interacting variables. This complexity contributes to findings that often appear contradictory or counterintuitive, particularly in the context of the ongoing technical versus biological debate in endodontics. Nevertheless, when examined through a multidisciplinary perspective, these apparent inconsistencies can be reconciled into a coherent understanding of the mechanisms underlying treatment success.

Root canal retreatment is generally considered in relation to primary treatment, as most determinants of outcome are shared. However, retreatment cases exhibit a comparatively reduced probability of healing, largely due to compromised access to apical canal ramifications and altered host–microbial interactions [11].

One of the first comprehensive evaluations of treatment outcomes was provided by Ng et al. (2011a, 2011b), who conducted a prospective observational study assessing the influence of irrigant concentration on periapical healing. Their findings demonstrated that increasing the concentration of sodium hypochlorite from 2.5% to 5% resulted in negligible differences in healing outcomes [9,10].

Evidence-Based Endodontics and Clinical Context

Endodontic treatment outcomes are influenced by a complex interplay of pre-operative, intra-operative, and post-operative factors, including microbial status, procedural quality, and host response [11]. This complexity often leads to findings that appear contradictory, particularly when comparing laboratory-based evidence with clinical outcomes. Retreatment cases, for instance, exhibit lower healing rates due to anatomical challenges and altered host–microbial interactions [11].

Guideline-Based Interpretation

According to the European Society of Endodontology (ESE) S3-level clinical practice guidelines, in patients with asymptomatic apical periodontitis in permanent teeth, irrigation with sodium hypochlorite (NaOCl) in concentrations ranging from 1% to 5.25%, followed by EDTA, is recommended, and NaOCl within the same concentration range may also be considered [17]. Furthermore, in cases where adequate clinical procedures have been performed, a single-visit approach without the use of interappointment calcium hydroxide dressing is recommended [17].

A critical interpretation of these guidelines indicates that NaOCl concentration does not significantly influence clinical outcomes. This is supported by the study of Byström and Sundqvist (1985), which demonstrated that variations in NaOCl concentration do not substantially alter treatment outcomes [13]. Similarly, in a study conducted by Verma et al. (2009), healing based on PAI scores at 12 months was evaluated with 43 samples per group. Although greater healing was observed in the 5% NaOCl group compared to the 1% NaOCl group in cases with preoperative PAI scores of 3 or 4, there was no statistically significant difference in healing between the two concentrations after 12 months [14].

The choice of irrigation solution, whether NaOCl or chlorhexidine (CHX), also appears to have minimal impact on clinical outcomes. No specific recommendations are provided regarding irrigant volume or duration, and single-visit endodontic treatment without interappointment calcium hydroxide dressing is preferred [17,18]. Additionally, irrigant activation approaches are not routinely recommended based on current evidence [25].

Further supporting evidence is provided by clinical studies evaluating pain, microbial reduction, and healing outcomes. In the study conducted by Almeida et al., pain was assessed at 24 hours, 48 hours, 72 hours, and 7 days, with no significant differences observed in microbial reduction, healing, or pain scores [15]. Similarly, Siqueira et al. reported no significant difference in microbial reduction between 2.5% NaOCl and 0.12% chlorhexidine[4,14]. Katle et al. (2023) also demonstrated that 1% NaOCl and 2% CHX showed no significant difference in radiographic healing [17].

Moreover, Rossi-Fedele and Rödig (2023) concluded that single-visit endodontic treatment results in better healing outcomes compared to multiple-visit approaches[17]. These findings are consistent with earlier studies by Weiger et al. (2000), Peters and Wesselink (2002), and Parades et al. (2012), which collectively demonstrated comparable or improved outcomes with single-visit treatment protocols [19,20,18].

From a clinical perspective, the guideline-based conclusions indirectly reinforce that traditional irrigation strategies, regardless of variations in concentration or type, may not significantly alter biofilm-related outcomes. The lack of strong dependence on irrigant concentration or type suggests that factors beyond conventional antimicrobial activity—particularly biofilm structure, microbial interactions, and host response—play a more critical role in determining treatment success.

The observation that neither NaOCl concentration nor the choice between NaOCl and chlorhexidine significantly affects healing outcomes highlights the inherent resistance of biofilms to conventional chemomechanical approaches. This further supports the need for advanced antibiofilm strategies that go beyond simple microbial reduction. Additionally, the recommendation against routine use of adjunctive activation techniques.[25] suggests that current methods of enhancing irrigant efficacy may not sufficiently overcome biofilm-related challenges in clinical settings.

Collectively, these findings emphasize that while conventional irrigation protocols remain essential, their limitations in addressing complex biofilm dynamics necessitate the exploration of more targeted and innovative antibiofilm strategies to improve endodontic treatment outcomes.

In Vitro–In Vivo Disconnect

A significant discrepancy exists between laboratory findings and clinical outcomes in endodontics. This disconnect arises from methodological limitations, including the use of simplified biofilm models, selective microbial sampling, and the inability of culture-based methods to detect viable but non-cultivable bacteria [21,22]. Molecular techniques such as PCR, while more sensitive, cannot differentiate between live and dead microorganisms, further complicating interpretation.

Confounders

The concentration of sodium hypochlorite does not matter according to Byström and Sundqvist in 1985 [13]. NaOCl reduces the endotoxin levels significantly greater than chlorhexidine [5]. Endotoxin levels after calcium hydroxide placement in root canals irrigated with continuous or sequential chelation as described by Sanjeev et al. in 2025 has a marked significance. Clinical data comparing the NaOCl concentrations and NaOCl vs CHX have a confounder. Interappointment calcium hydroxide dressing in multiple visits is a major confounder. Most clinical studies are underpowered as the sample sizes are not sufficient.

Biofilms reduce antimicrobial diffusion. Matrix reduces antimicrobial effect. Matrix can be recolonized and persister bacteria inside the biofilm may be present. Biofilm matrix is a diffusion barrier to antimicrobials. The matrix is inflammatory. It does not pose any problem to the microbes. Nososymbiocity is also called community pathogenicity. The microbial community is more than the sum of its parts. Pathogenic effects of the biofilm are the combination of microbes, matrix components, toxins, and spatiotemporal organization which evaluates biofilm thickness, biovolume, and diffusion. Matrix is a critical component of the biofilm. Antibiotics are ineffective against biofilms.

Our irrigant is basically judged by antimicrobial activity and biofilm. Viswanath et al. conducted a study which showed 10 species in the biofilm got altered in 15 mins of irrigation in response to chlorhexidine [21,22]. Increased EPS fraction in chlorhexidine treated biofilm is noticed. Extracellular polymeric substances (EPS) are microbial aggregates containing a protein fraction, polysaccharide fraction, and other components. Antibiofilm activity of NaOCl is dependent on concentration and time. Antimicrobial and antibiofilm activity are not synonymous. Minimum syringe irrigation time required with 6% NaOCl is 15–20 min to dissolve biofilm matrix components. Chlorhexidine has no antibiofilm effects on making or killing the bacteria further difficult or structural repositioning. Antibiotic pastes have poor or no antibiofilm effects. In adverse conditions, antibiotic pastes have toxic effect on stem cells.

Current clinical evidence shows that increase in concentration of sodium hypochlorite causes disruption of the biofilm and causes its dissolution. This was proved by Petridis et al. in 2019 and Wang et al. in 2020 [23,24]. Biofilm is concentrated in the anatomic eccentricities like isthmus, fins, and lateral canals. In patients with apical periodontitis in permanent teeth, the current evidence shows not to use adjunct therapy in addition to traditionally delivered irrigant. Caputd et al. advised that activation of irrigants is optimum for its activity [25].

Sodium hypochlorite, considered the gold standard in endodontic therapy, has been supported in this review, where increasing the concentration of NaOCl from 2% to 5% increased the rate of biofilm disruption. However, the issue of cytotoxicity remains [5].

Antibiofilm Strategies

Another study attempts to decrease the concentration of NaOCl to decrease cytotoxicity and includes high-purity nisin, which is generally nontoxic to the oral cells, but this nisin does not improve the efficacy of NaOCl or in combination with EDTA. However, a contradicting study shows a synergistic effect between nisin and EDTA against biofilms formed by Salmonella after 24 h post-treatment [26]. Owing to the effectiveness of high-purity nisin (>95% purity) against oral microorganisms, particularly those that cause root canal infections, another study investigated the antibiofilm effects of high-purity nisin with chlorhexidine, a cationic bisbiguanide that damages the bacterial cell wall. Nisin was not found to be a better antibiofilm agent than CHX [27].

The efficacy of CHX was also tested in combination with a short D-enantiomeric, protease-resistant peptide having broad-spectrum antibiofilm activity, and showed enhanced destruction of multispecies biofilms at much shorter times (1–3 min) [28]. Another peptide, GH12, although it showed lesser reduction in microbial biomass but was not found to be erosive even at a higher concentration of 16 mg/mL as opposed to the high erosive effects of 5% NaOCl [29].

A triple antibiotic paste (TAP), along with metronidazole, emerged as the strongest antibiofilm agents when compared to other chemicals such as ciprofloxacin, doxycycline, clindamycin, amoxicillin, and clavulanate [30,31]. In another report, replacing a component of this TAP, minocycline with nitrofurantoin, further decreased the bacterial count in the biofilms[31].

An antioxidant N-acetylcysteine was capable of complete disruption of mature multispecies endodontic biofilms consisting of Actinomyces naeslundii, Lactobacillus salivarius, Streptococcus mutans, and Enterococcus faecalis, most probably affecting the extracellular metabolites secreted by the biofilm-forming microorganisms [32]. Issues of cytotoxicity have been addressed by many research groups by combining natural and synthetic products. Epigallocatechin-3-gallate and fosfomycin have been known to exhibit synergistic effects by disintegration of the extracellular matrix and disorganization of biofilms while remaining non-cytotoxic [33].

Biofilm complexity and resistance to common antibiotics allow biofilm to mature and age, further complicating eradication. Therefore, calcium silicate repair cements and sealers were assessed for antibiofilm activity, where higher antibacterial activity was exhibited by Biodentine and BioRoot RCS, with Biodentine capable of sustaining its antibacterial activity even after a protracted aging period [34]. However, challenges associated with calcium silicate-based sealers include high genotoxicity, acute inflammation, tooth discoloration, and controversies regarding fracture resistance, apical patency, and withdrawal, demanding engineering with various other constituents to overcome these challenges [34].

Nanotechnology-Based Approaches

Conventional root canal disinfectants are unsuccessful in treating persistent endodontic infections because they are not biologically safe. The creation of nanomaterials has shown promise as a means of eliminating biofilm-building microorganisms. This review includes one such study where a simple and adaptable method was used to create GMNPs in order to examine their potential for eliminating PEI-related bacterial/fungal biofilms via the production of ROS, movement of GMNPs by the magnetic field, and nutritional starvation[38]. The dense biofilm matrix is destroyed when it interacts with the bacterial or fungal biofilms. Additionally, the in vitro experiment demonstrates the high cytocompatibility and blood compatibility of the synthesized GMNPs [38]. For possible clinical use, GMNPs provide a novel approach to treating PEI-causing microorganisms.

Another study investigating silver nanoparticles with calcium hydroxide showed that upon comparison to $Ca(OH)_2$ alone, AgNPs + $Ca(OH)_2$ combinations confirmed improved biofilm eradication, regardless of nanoparticle size[35,36]. This is consistent with prior findings and is mostly due to the synergism depicted by the two. $Ca(OH)_2$ mainly manifests its bactericidal effects through the steady and measured release of calcium and hydroxyl ions, while AgNPs release and accumulate Ag ions within the cell[35,36]. The antimicrobial characteristics of $Ca(OH)_2$ have also been investigated in another study included in this review, where nanoparticles of $Ca(OH)_2$ have been employed to overcome the shortcomings of toxicity and bioavailability associated with it [37].

Whereas intracanal TAP could be beneficial in some aspects, such as effective disinfection and minimizing potential systemic complications compared to antibiotic treatment (e.g., antibiotic-resistant strains, cytotoxic activity, and allergy), TAP has the issue of discoloration of teeth[30,31]. In an attempt to develop biocompatible intracanal disinfectants, triple antibiotic-eluting polymer nanofibers were developed to effectively eliminate multispecies biofilms in a dentin tissue slice model, like triple antibiotic paste, while addressing the issue of tooth discoloration[30,31]. With the advancements in technology, these strategies are more ready for clinical translation in endodontics, despite currently being in the in vitro phase. This is because they can be easily integrated into the already existing protocols, such as the current irrigant systems, sealers, or medicaments, without refurbishing the clinical workflows. This, combined with scalable production and growing market presence, makes them one of the most promising emerging technologies for combating multispecies biofilms in root canal therapy.

Tran et al. emphasized that small-scale robotics are delivering innovative therapeutic and diagnostic approaches with high precision and efficacy [39]. These methodologies are swiftly transitioning from proof-of-concept investigations to translational biomedical applications utilizing ex vivo, animal, and clinical models. This text examines the essential and translational dimensions of microrobots' targeting of infection sites to undermine the structural and functional characteristics of biofilms and their mechanisms of antimicrobial resistance[39]. Consequently, contemporary methods of mechanochemical disruption and localized drug delivery are substantiated by in vivo models and preclinical evaluations, simultaneously emphasizing diagnostic potential.

A 2025 study examined the efficacy of light-responsive therapy, highlighting deeper tissue penetration as a randomized controlled trial modality [40]. They noted that the advent of light-induced phototherapy and the development of nanoplatforms, characterized by significant penetration depth and minimal drug resistance, is expected to overcome this obstacle [40].

Translational Gap

In vitro models employed in endodontic research frequently fail to replicate the structural and biological complexity of the human root canal system. Many of these models are based on flat surfaces, artificial canal systems, or simplified substrates that do not adequately represent key anatomical features such as lateral canals, apical deltas, and dentinal tubules. Furthermore, laboratory studies commonly utilize single-species biofilms or artificially constructed multispecies communities, which do not accurately reflect the diversity, metabolic interactions, and resilience of polymicrobial biofilms observed in persistent clinical infections. An additional limitation is the absence of host immune responses in these experimental models, which play a critical role in disease progression and healing.

Methodological inconsistencies further contribute to the discrepancy between laboratory findings and clinical outcomes. Experimental protocols often involve the use of higher antimicrobial concentrations, prolonged exposure times, and idealized activation techniques—such as specific light energy parameters or optimized nanoparticle dispersion—that are not always clinically feasible or safe. Importantly, there is a notable lack of well-designed randomized controlled trials evaluating the safety, efficacy, and patient-centered outcomes of emerging biofilm eradication strategies, including parameters such as periapical healing, postoperative pain, and retreatment rates.

The limitations of in vitro studies are compounded by their inability to fully account for anatomical variability, including root canal curvature and complex internal morphology, as well as the dynamic nature of multispecies biofilms. Additionally, heterogeneity in experimental design—such as differences in irrigant concentration, laser parameters, and duration of exposure—limits the comparability of results across studies. Standardization of these variables, along with the implementation of large-scale randomized clinical trials, is essential to establish the clinical validity of emerging disinfection techniques.

Currently, sodium hypochlorite and chlorhexidine remain the most widely used antimicrobial irrigants in endodontic practice; however, both exhibit inherent limitations. Sodium hypochlorite, while highly effective in organic tissue dissolution and antimicrobial activity, is associated with significant cytotoxicity and poses a risk of periapical tissue damage if extruded beyond the apical foramen. Chlorhexidine, in contrast, lacks tissue-dissolving capability and may form undesirable precipitates when used in combination with other irrigants. Moreover, both agents demonstrate limited penetration into dentinal tubules and biofilm structures, as well as relatively weak substantivity, which may contribute to persistent infection and treatment failure.

Alternative strategies, including the use of natural products, have been explored due to their favorable biocompatibility and antimicrobial properties. However, their clinical applicability is limited by factors such as poor penetration, short shelf life, low solubility, and variability in composition. These challenges underscore the need for innovative approaches, particularly nanoparticle-based drug delivery systems, which offer potential advantages in targeted antimicrobial delivery and enhanced biofilm disruption.

Finally, certain methodological limitations of the present review must be acknowledged. Language bias may have influenced the selection of studies, as non-English publications were excluded. Additionally, the omission of unpublished data may have affected the comprehensiveness of the analysis. The significant heterogeneity among included studies further precluded the performance of a quantitative meta-analysis.

Conclusion

Endodontic success is influenced by a complex interplay of microbial, anatomical, and procedural factors rather than by irrigant type or concentration alone. While sodium hypochlorite remains the gold standard irrigant, emerging antibiofilm strategies and nanotechnology-based approaches offer promising avenues for improving treatment outcomes. However, robust clinical evidence is required before these innovations can be routinely integrated into practice.

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