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Comparative review of endodontic irrigants: Balancing antimicrobial efficacy, tissue dissolution, and biocompatibility

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Abstract
Introduction: The success of endodontic treatment depends on the effective use of irrigants that eradicate biofilms and improve disinfection, which significantly reduces endodontic failures.
Objective: To conduct a comprehensive review of the current scientific literature on the most commonly used irrigating solutions in endodontics, which are sodium hypochlorite (NaOCl), chlorhexidine, saline solution (NaCl), and EDTA, comparing their antimicrobial activity, disinfection capacity, and cytotoxicity.
Methodology: A search was conducted in PubMed, Scopus, and Google Scholar using the keywords: "endodontic irrigants," "sodium hypochlorite," "chlorhexidine," "normal saline," "EDTA," "antimicrobial activity," "smear layer removal," and "cytotoxicity".
Results: The irrigants evaluated showed clear differences in efficacy and clinical function. Sodium hypochlorite obtained the best results in bacterial elimination and tissue dissolution. Chlorhexidine demonstrated good penetration and prolonged residual effect. Saline solution showed low antimicrobial action but excellent biological tolerance. Ethylenediaminetetraacetic acid improved dentin cleaning and enhanced the action of other irrigants, demonstrating its value as a complementary agent in endodontic therapy.
Conclusion: Endodontic irrigants perform complementary functions. Sodium hypochlorite is the most effective but also the most cytotoxic. Chlorhexidine offers residual effect and good penetration. Saline solution is biocompatible, although less effective antimicrobially, and ethylenediaminetetraacetic acid improves dentin cleaning. Their appropriate combination balances efficacy and clinical safety.

Keywords: Endodontic Irrigants," "sodium hypochlorite," "chlorhexidine," "EDTA," "antimicrobial activity", "biocompatibility" and "cytotoxicity"

1. Introduction
The success of endodontic treatment depends on the effective use of irrigants that eradicate biofilms and improve disinfection, which significantly reduces endodontic failures [1].
Endodontic irrigation is a fundamental pillar of treatment, as it allows the removal of organic debris and bacterial biofilms that cannot be removed by instrumentation alone. This practice improves the clinical prognosis and reduces the incidence of therapeutic failures [2].
The most commonly used irrigants are sodium hypochlorite (NaOCl), chlorhexidine (CHX), saline solution, and ethylenediaminetetraacetic acid (EDTA). Each has different properties that influence its antimicrobial efficacy, cleaning ability, and biological safety, factors that determine clinical success [1].
Sodium hypochlorite is an effective irrigant with antimicrobial and tissue-dissolving action, whose effect is enhanced by ultrasonic or thermal activation, improving cleaning in complex anatomical areas [3].
Sodium hypochlorite is the main irrigant due to its antimicrobial action and tissue-dissolving capacity, enhanced by activation to reach difficult areas [4].

A comparison of the most commonly used irrigant solutions is necessary to identify which one offers an optimal balance between antimicrobial efficacy and biological safety. This review seeks to provide current scientific evidence to guide clinicians in choosing the most appropriate irrigant, thereby improving treatment outcomes and reducing costs due to unnecessary retreatment. This study provides a comprehensive review of the current scientific literature on the most used irrigating solutions in endodontics, which are NaOCI, CHX, saline solution, and EDTA, comparing their antimicrobial activity, disinfecting capacity, and cytotoxicity.

2. Methodology

Articles on the subject published through the PubMed, Scopus and Google Scholar databases were analyzed, with emphasis on the last 5 years. The quality of the articles was evaluated using guidelines, i.e., identification, review, choice and inclusion. The quality of the reviews was assessed using the measurement tool for evaluating systematic reviews. The search was performed using Boolean logical operators AND, OR and NOT; with the keywords: “endodontic irrigants,” “sodium hypochlorite,” “chlorhexidine,” “normal saline,” “EDTA,” “antimicrobial activity,” “smear layer removal,” and “cytotoxicity”. The keywords were used individually, as well as each of them related to each other.

3. Results

3.1 Sodium Hypochlorite (NaOCI)

A study evaluated the antimicrobial efficacy of 2.5% NaOCl and photodynamic therapy in eliminating Enterococcus faecalis in infected root canals. Both methods significantly reduced the bacterial load, but NaOCl showed superior antimicrobial activity, eliminating the bacteria more effectively compared to laser treatment [5].

The antimicrobial efficacy of different concentrations of 2.5% and 5.25% NaOCl was compared against Enterococcus faecalis, concluding that both concentrations showed significant antimicrobial activity [6].

The application of heated intraductal and extraductal NaOCl showed improved antimicrobial efficacy against Enterococcus faecalis, suggesting that heating the irrigant may enhance its antimicrobial activity [7].

Sodium hypochlorite has clinical advantages over other solutions such as QMix, showing greater removal of the dentinal smear layer and a significant reduction in bacterial load, which supports its position as the irrigant of choice in endodontics [8].

A 2.5% sodium hypochlorite (NaOCl) solution acts as an effective disinfecting agent in direct pulp capping by removing necrotic and infected pulp tissue during lavage. This action reduces inflammation and significantly improves pulp survival in teeth with carious exposures [9].

Its capacity to dissolve organic tissue, a key mechanism of its disinfecting action, can be enhanced through activation techniques. A study evaluating 5.25% NaOCl demonstrated that its activation significantly improved pulp tissue dissolution [10]. Furthermore, in direct comparisons with other irrigating solutions, NaOCl has shown superior efficacy in tissue dissolution [11].

NaOCl is a widely used irrigant in endodontics due to its benefits, but it has high cytotoxicity and can cause severe tissue damage if it leaks outside the root canal. This damage can be permanent and have significant medical and legal consequences, so it is essential that clinicians are aware of the factors that predispose them to these accidents in order to prevent them [12].

It is the most widely used irrigant in endodontics, its high cytotoxicity can cause damage to periapical tissues if it leaks, requiring precautions during use [13].

NaOCl is a highly effective irrigant due to its potent antimicrobial action, cleaning and tissue dissolution capacity, and its enhanced effect with activation or increased concentration. However, its high cytotoxicity poses risks if it extravasates, requiring controlled and precise use to maximize benefits and avoid complications.

3.2 Chlorhexidine

2% chlorhexidine (CHX) has antimicrobial capacity in endodontics, and its effectiveness depends on its penetration into the dentinal tubules. Passive ultrasonic irrigation was the technique that allowed the greatest penetration of CHX, which promotes better disinfection of the root canal system [14].

2% chlorhexidine instills residual antimicrobial activity in instrumented root canals. Teeth treated with chlorhexidine showed a significant reduction in bacterial load, highlighting its substantivity and ability to maintain antimicrobial activity over a prolonged period [15].

CHX prevents microbial activity in the root canal system for up to 48 hours after application, suggesting its effectiveness in root canal disinfection [16].

Chlorhexidine has a strong residual effect (substantivity), capable of maintaining prolonged antimicrobial activity within the dentinal tubules, making it a complementary irrigant of high clinical value [17].

CHX is an antimicrobial agent widely used in endodontics as an irrigant and intracanal treatment due to its effective activity against bacteria and biofilms, as well as its residual capacity (substantivity) which prolongs its effect. Although it does not dissolve tissue, its low cytotoxicity and chemical stability make it an ideal alternative to sodium hypochlorite in special cases, offering effective disinfection of the root canal system [18].

2% chlorhexidine is significantly more effective than saline solution as a final irrigant during the first appointment, achieving a greater reduction in bacterial load [19].

The antimicrobial efficacy of chlorhexidine gluconate as an irrigant in root canal therapy was evaluated, confirming its ability to eliminate bacteria, although without the ability to dissolve organic tissue as sodium hypochlorite does [20].

CHX exhibits high cytotoxicity, especially after 48 hours, while EDTA is less toxic. Combining both irrigants with the DJK-5 peptide significantly reduces their toxicity, with DJK-5 being the compound with the lowest cytotoxicity. Thus, DJK-5 improves the biocompatibility of endodontic irrigants [21]. (Praveen, 2025) [21]

The cytotoxic effects of different root canal irrigants, including chlorhexidine, were evaluated. Although less cytotoxic than sodium hypochlorite, its effects depend on concentration and exposure time, requiring controlled use [22].

CHX is an effective irrigant due to its prolonged antimicrobial activity, good penetration into dentinal tubules, and residual effect. Although it does not dissolve tissue like sodium hypochlorite, its substantivity and low reactivity make it useful as a complementary or alternative irrigant. Its cytotoxicity is lower, but depends on the concentration and exposure time, so it requires careful use.

3.3 Saline Solution

NaOCl, known for its potent antimicrobial action, did not

show significant superiority over saline solution in terms of treatment success, suggesting that saline solution may be a valid alternative in terms of clinical outcome, even though its antimicrobial activity is lower or different [3]. In the *in vivo* study on primary teeth, NaOCl, saline solution, and laser-assisted disinfection were compared. Saline solution was significantly less effective in reducing aerobic and anaerobic bacteria compared to NaOCl and laser [23].

Irrigation with saline solution can significantly reduce the bacterial load in infected canals, although its efficacy is clearly inferior to that of irrigants with antibacterial action such as NaOCl, CHX, EDTA, or MTAD [24].

A study evaluated the antimicrobial efficacy of a solution of nanosilver, sodium hypochlorite, and saline in the irrigation of root canals of primary teeth contaminated with Enterococcus faecalis. The results showed that sodium hypochlorite had the highest disinfecting capacity, eliminating significantly more bacteria than the other solutions. Although the nanosilver solution exhibited antimicrobial activity, it was less effective than sodium hypochlorite, while the saline solution was the least efficient [25].

An antimicrobial comparison, tissue dissolution capacity, and cytotoxicity were performed between NaOCl, CHX, EDTA, saline solution, and QMix. NaOCl has the highest antimicrobial activity, while saline solution showed the lowest efficacy in both eliminating microorganisms and dissolving organic tissue [26].

A study results established that sterile saline solution exhibited the lowest cytotoxicity compared to other solutions such as MTAD, EDTA, QMix, NaOCl, and CHX. The cytotoxicity ranking, from highest to lowest, was as follows: MTAD > EDTA > QMix = NaOCl > CHX > sterile saline solution. This suggests that sterile saline is the safest option in terms of cytotoxicity for use in endodontic treatments. However, its antimicrobial efficacy is limited compared to other irrigants [27]. This low cytotoxicity profile has been corroborated across different cellular models; when evaluated on human periodontal ligament cells, saline showed significantly lower toxicity compared to irrigants like sodium hypochlorite and chlorhexidine [28]. Likewise, in human mesenchymal stem cells, saline also demonstrated a low cytotoxicity profile, supporting its clinical safety [29].

Saline solution has low cytotoxicity and high biocompatibility, making it a safe choice as an irrigant. However, its antimicrobial efficacy and cleaning ability are limited compared to active irrigants such as sodium hypochlorite or chlorhexidine. Its main use is as a complementary flushing solution, helping to remove debris and dilute other more aggressive solutions.

3.4 EDTA

EDTA (Ethylenediaminetetraacetic acid) is a chelating agent used in endodontics that binds to metal ions, especially calcium present in dentin, forming soluble chelates. This facilitates the removal of the dentin smear layer during root canal treatment. Although its main function is to modify the dentin structure to improve cleaning, its antimicrobial activity is limited and is not its primary function in endodontic disinfection [30].

A study investigated the bactericidal effect of alkalized EDTA in infected root canals. The results suggest that alkalized EDTA could be an effective cleaning agent for the treatment of difficult root canals, as it suppresses bacterial growth [31].

The antibacterial activity of 17% EDTA against Enterococcus faecalis was evaluated, finding that its effect was weaker compared to other irrigants. They attributed this activity to the alteration of bacterial cell membrane permeability [32].

The antimicrobial activity of EDTA may vary depending on its pH. Alkaline solutions show a more pronounced bacteriostatic effect against Enterococcus faecalis, although they remain less effective than other active irrigants, reaffirming their complementary rather than primary role in disinfection [33].

A study analyzed the effect of irrigating solutions such as 1% sodium hypochlorite (NaOCl) and 17% EDTA—used individually and in combination—on dentin hardness. While it did not directly assess antimicrobial capacity, NaOCl is recognized as a potent disinfectant that eliminates bacteria and dissolves organic tissue, whereas EDTA acts as a chelating agent, cleaning and opening dentinal tubules to facilitate the action of the disinfectant. Their combination significantly enhances the cleaning and disinfection of the root canal system [34].

The efficacy of these protocols is increased by activation techniques. For example, passive ultrasonic activation with 17% EDTA and QMiX improved the removal of the smear layer and sealer penetration into dentinal tubules, particularly in the middle and apical thirds [35]. Similarly, in the removal of debris during rotary preparation, both liquid and paste formulations of EDTA have been observed to be effective, although the paste formulation demonstrated greater efficacy [36].

The synergy between chelating agents and physical activation further optimizes cleaning. The combined use of EDTA with sonic or ultrasonic activation enhances the penetration of NaOCl into simulated lateral canals [37]. This strategy markedly improves smear layer removal and facilitates the penetration of other irrigants, achieving superior cleaning even in anatomically complex areas [38].

The chelating agents used in endodontics (chitosan, acetic acid, and EDTA) have an initial cytotoxic effect on cells, but this cytotoxicity decreases over time and disappears after 24 hours. Therefore, after one day of exposure, these agents do not exhibit significant cellular toxicity [39].

The cytotoxicity of EDTA is time-dependent. After 24 hours, EDTA shows better cell viability compared to 2% chlorhexidine [40].

EDTA has low antimicrobial action but is effective in removing the dentin smear layer and enhancing other irrigants such as sodium hypochlorite. Its effectiveness is improved by ultrasonic activation and it has low cytotoxicity, making it useful as a complementary irrigant in endodontic disinfection.

4. Conclusion

Endodontic irrigants perform complementary functions. Sodium hypochlorite is the most effective but also the most cytotoxic. Chlorhexidine offers residual effect and good penetration. Saline solution is biocompatible, although less effective antimicrobially, and ethylenediaminetetraacetic acid improves dentin cleaning. Their appropriate combination balances efficacy and clinical safety.

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