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A Review of Chemical Approaches Inherent to Endodontic Disinfection Protocols: Part 2

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ABSTRACT

Objectives

Part two of this chemical endodontic disinfection protocol review discusses adjunctive practices such as irrigant activation techniques and intracanal medicaments with a look into the future of endodontics.

Materials and methods

Scientific platforms such as Pubmed and Google Scholar were (re)searched using the keywords: endodontics, endodontic disinfection, root canal disinfection, endodontic chemical debridement, endodontic irrigation, endodontic solutions, endodontic irrigant activation, and intracanal medicaments. Relevant articles were identified, screened, reviewed, and discussed.

Results

As discussed in part one of this review, sodium hypochlorite in combination with EDTA is still the gold standard for endodontic irrigation. However, anatomical variations and conventional instrumentation limit the effectiveness of these solutions. To overcome these limitations, activation techniques such as ultrasonic irrigation, photo-activated disinfection, and photon-induced photoacoustic streaming have been used. Intracanal medicaments are used to support endodontic disinfection as temporary dressings between appointments, but their usefulness is controversial.

Conclusions

Irrigant activation has shown the potential to improve disinfection. Intracanal medicaments have been losing favour in recent years, and their benefit should be evaluated in each case. Nanoparticles have been suggested to improve the delivery of irrigant solutions. Nanoparticles are relatively new in endodontics, and further research is needed on their optimisation, limitations, and toxicity.

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INTRODUCTION

Caries is a common disease and, when left untreated, causes pulpal pathologies requiring endodontic treatment. Endodontic treatment is a fairly common and routine dental procedure whereby 10% of all teeth will require such treatment.[1] A review by Tibúrcio-Machado *et al.* found that half the adult population worldwide would have at least one tooth displaying signs and symptoms of disease requiring endodontic treatment.[2] For predictable and successful outcomes, the clinician must comprehensively understand endodontic principles.

The main goal of endodontic treatment is debridement and disinfection of the root canal system. In 1992, Chong and Pitt Ford emphasised the importance of controlled asepsis in infected root canals and the primary role of canal debridement and adequate canal preparation in successful outcomes.[3] Ordinola-Zapata *et al.,* also support this concept that what is removed from the root canal is of greater significance with regard to success than what is used to seal the root canal system.[4] Therefore, it is vital for the clinician to have not only an understanding of tooth morphology and pathosis of pulp infection but also an understanding of the materials and techniques available to debride and disinfect the root canal.

Endodontic treatment is a complex multi-step procedure that aims to disinfect the root canal system to allow for the resolution of inflammation, infection and apical periodontitis. Complete disinfection is achieved with a combination of mechanical debridement, chemical irrigation and application of intracanal medicaments.[5] Mechanical debridement is carried out with manual and motorised filing instruments. This removes infected tissue while opening and shaping the root canals to allow for the delivery of antimicrobial and sealing materials. Studies have shown that mechanical instrumentation alone is insufficient to remove microbes from infected root canals, and while microbial loads decrease during instrumentation, positive cultures are still found afterwards.[6] Combining mechanical instrumentation with chemical irrigation has effectively decreased subsequent microbial loads.[6, 7] This two-part review will focus on chemical disinfection protocols, including irrigation solutions, activation methods, and intracanal medicaments. Part one discussed the different irrigant solutions while part two will discuss irrigant activation techniques and intracanal medicaments.

Microorganisms and their endotoxins are responsible for the initiation of root canal infections and persistent endodontic-induced apical periodontitis.[8, 9] A core microbiome of just twenty to thirty species of microorganisms is responsible

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for root canal infections.[10] The root canal system is a closed system limiting bacterial interactions, nutrient availability and produces low oxygen potentials restricting the number of bacterial species in endodontic infections. These conditions allow for mostly facultative and anaerobic microorganisms to dominate the microflora in infected root canals.[11] To further complicate disinfection, the variegated anatomy of the root canal system adds further complexity to endodontic treatment. Complex and intricate anatomical variations such as isthmuses and ramifications often make mechanical irrigation impossible in these spaces. Chemical irrigating solutions are able to flow into these spaces, augmenting mechanical debridement for more thorough disinfection.[7]

However, an irrigant is only beneficial when it comes into direct contact with all parts of the root canal, particularly the most apical parts.[12] Variations in root canal anatomy, such as isthmuses, ramifications, accessory canals and wide oval canals, can hinder fluid flow dynamics into the apical part of the canal, decreasing irrigant efficacy. Straight-forward delivery systems may not be effective enough, so to improve the effectiveness of irrigants, enhancements are made to their delivery and activation protocols. These enhancements include negative apical pressure irrigation, irrigant activation with ultrasonic or sonic instruments, and laser-assisted irrigant activation.[13]

Positive-pressure irrigation systems

Positive pressure irrigation (Figure 2a and 2c) is the most commonly used irrigation technique.[14] This technique uses a syringe and a narrow-gauge side vented needle where the needle is inserted as far as possible into the root canal system. The irrigant is injected as close as possible to the root apex. The irrigant then flows back up towards the pulp chamber and is evacuated with suction. In 1983, Chow demonstrated that the irrigant solution does not penetrate further than the tip of the needle in a closed canal system.[15] As a result, debris and microbes can be left behind in the apical air pocket beyond the needle tip – the dead zone (Figure 2a). Some believe that this air pocket can be popped with an endodontic instrument. This theory is controversial as it defies the laws of physics and mechanical files will only pass through the air pocket. An alternative suggestion to overcome this air pocket is to use a gutta percha cone to manually agitate the irrigation solution, forcing the solution closer to the apex safely (Figure 2b)[16]. It can be difficult to control the pressure applied during positive pressure irrigation, and since the root canal system is a closed system, if too much pressure is exerted, there is a risk of accidental extrusion where the irrigant is pushed under pressure into the periapical tissues and can cause adverse effects such as inflammation, swelling, intense pain and at worse tissue necrosis.[17]

Negative-pressure irrigation systems

Negative pressure irrigation systems (Figure 2d) minimise the risk of accidental irrigant extrusion.[18, 19] This method uses a needle or master delivery tip (MTD), a macro cannula and a micro cannula. The needle is placed in the pulp chamber to deliver the irrigant, and the macro cannula and micro cannula are placed in the root canal to safely pull the irrigant into the canal, towards the apex and then draw it back up the cannula, preventing any risk of extrusion.[20] An added advantage of negative pressure systems is that it stabilises irrigant flow rate to keep a constant "flow" of irrigant in the canal to flush out debris. Examples of these systems are Endo Vac and RinsEndo. Konstantinidi *et al.* reviewed the effectiveness of negative pressure irrigation against conventional syringe irrigation. The study analysed the following outcomes: antimicrobial effects and removal of pulp tissue remnants, hard tissue debris or both pulp and hard tissue. There was no significant difference between the two methods in disinfecting and debriding the main root canal. Negative pressure irrigation demonstrated an

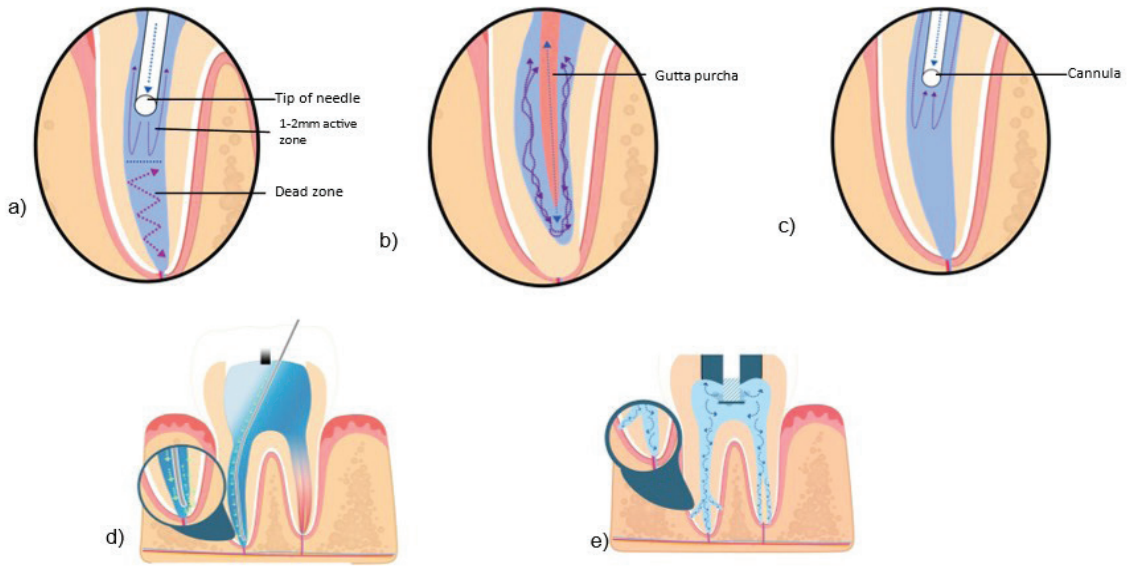

Figure 1: a) Positive pressure irrigation systems. The irrigant does not penetrate further than 1-2mm beyond the tip of the needle (154). **b)** Diagrammatic representation of a gutta percha cone manually pumping the irrigant deeper into the canal (154). **c)** Diagrammatic representation of irrigant beyond the cannula and being "pulled" back up into the cannula to prevent extrusion (154). **d)** Negative pressure system (EndoVAc) with MTD to introduce the irrigant into the root canal and the microcannula demonstrating the "pulling" of the irrigant out of the canal and into the cannula allowing the cannula tip to safely penetrate deeper into the root canal. **e)** The GentleWave system delivering the irrigant in a sealed environment, and activation of the irrigant enhances fluid dynamics.

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advantage when analysing isthmuses and uninstrumented oval extensions. These "unreachable" areas were debrided significantly better with negative pressure irrigation than syringe irrigation.[18]

Ultrasonic and Sonic irrigant activation

Ultrasound is a vibration of the same nature as sound but at a frequency higher than the highest frequency perceptible to the human ear (approximately 20,000 Hz).[12] These vibrations are mechanical energy that produces powerful shearing forces. Ultrasonic and sonic irrigation involves applying this energy to a liquid to generate cavitation and acoustic streaming effects. Bacterial biofilms, common in root canal infections, are more resistant to antimicrobial chemicals, and their disruption comes with its own set of challenges. Koo *et al.* theorised that applying ultrasonic-induced shear forces in combination with antimicrobial chemicals would be more effective in biofilm obliteration.[21] It is thought that as ultrasound-induced acoustic streaming causes deagglomeration of bacteria disrupting the biofilm, it gives rise to planktonic bacteria, which are more susceptible to the antibacterial effects of the irrigant used.[22] Ultrasonic-induced cavitation may also temporarily weaken the cell membrane, making bacteria more permeable to NaOCl and other irrigants.[22] In endodontics, this energy is applied with ultrasonic endodontic files and is the most common method to enhance root canal irrigation.[14]

Cavitation is the formation of gas bubbles within a liquid. During each ultrasound cycle of refraction and compression, these bubbles expand during refraction and collapse during compression repeatedly, thus growing with each subsequent cycle (Figure 3a). During these cycles, gas cannot be transported through the bubble-liquid interface, limiting amounts of gas within the bubble. Eventually, without new gas entering the bubble, the expanding bubble violently implodes (Figure 3a). On implosion, high-amplitude shock waves and high-velocity micro jets are released, exerting high shear forces on the surrounding biofilm, disrupting it and lifting it off the surface.[23]

Acoustic streaming is fluid flow caused by momentum transfer from the acoustic wave to the propagation liquid (Figure 3b).[24] When acoustic streaming occurs on a small scale, it is referred to as microstreaming. Microstreaming is fluid flow around the expanding and collapsing gas bubbles. The drag forces generated by these microstreams can detach the biofilm within its vicinity and carry it away from the surface.[23, 25]

In the root canal environment, such forces can disrupt bacterial biofilms, rupture bacterial cell walls, and remove debris and the smear layer from the root surface. An additional benefit is shockwave generation, which can also increase the breakdown of agents such as H2O2, enhancing the disinfection and debridement actions of the irrigation solutions.[26] Ultrasound activation improves access cavity preparation, cleaning, shaping and sealing of canals, eliminates obstructions, intracanal medicament removal and endodontic surgery.[27]

There are many different endodontic ultrasound devices available on the market. To simplify matters, there are two ultrasound irrigation methods: active and passive. Active ultrasound irrigation involves the simultaneous use of an irrigant with an active cutting tip, and passive ultrasound irrigation (PUI) is irrigation without simultaneous instrumentation using a non-cutting tip.[28] PUI is considered to be safer than active ultrasound irrigation as there is less risk of creating aberrant dentine defects.[29] PUI uses ultrasonic power with a non-cutting smooth oscillating wire or file, typically with a polymer tip, to transmit energy to the irrigant. Studies have shown that PUI is significantly more effective than standard needle irrigation. [27, 30, 31]

There are two theories regarding the best time to use ultrasound irrigation. The first is that PUI must be used as part of the initial protocol as this improves the flow action of the irrigant, enabling the irrigant to flow towards the apical part of the canal using fine files. However, the more popular opinion is that ultrasound should be used after mechanical canal preparation. Effective ultrasound irrigation depends on the vibratory potential of the instrument, and wider canals allow for unrestricted vibratory movement. Therefore, ultrasound irrigation is more suited to prepared canals. There is also a risk of defect formation when instruments touch a narrow canal wall during cavitation and, so a wider canal with narrower files is recommended to limit this risk.[12] Other important physical parameters to consider during irrigation are the depth of needle insertion, the volume of irrigant delivered and the contact time of the irrigant.[18] Căpută *et al.* tested the effectiveness of ultrasound irrigation on the healing of apical periodontitis, removal of pulp, hard tissue debris and smear layer.[32] Their study found that ultrasound irrigation was superior to conventional methods in removing these substances. However, ultrasound irrigation provided no significant advantage in healing apical periodontitis.[32] Mozo *et al.* reviewed methods to increase the activation of irrigating solutions and found that NaOCl combined with ultrasound or a wave vibration system had the most excellent antibacterial effect.[12] Another study by de Gregorio *et al.*, determined that ultrasonic and sonic NaOCl activation was more effective than using NaOCl alone as it allows for improved irrigant penetration.[33] Elnaghy *et al.*, also found that supplementing irrigation activation with ultrasonic and sonic protocols improved irrigation efficiency.[34]

There are a variety of irrigant activator systems available on the market today. A few of these systems are GentleWave System (GWS; Sonendo, Inc, Laguna Hills, CA), EDDY (VDW), MM1500 Sonic Air (Micro-Mega) and EndoActivator System (Dentsply Tulsa Dental Specialties, Tulsa, OK). Although each system varies in its armamentarium, the mechanisms by which they work are similar. Gentlewave (Figure 2e) uses a specialised handpiece to deliver NaOCl into the root canal under pressure and is activated by acoustic waves, while suction removes the outflowing fluid through the handpiece simultaneously.[35] A silicon ring surrounding the extremity of the handpiece creates a tight seal with the artificially created flat tooth surface. This establishes a vented and closed-loop fluid flow within the root canal[36] and is meant to improve irrigation dynamics in minimally mechanically prepared canals.[35]

Sonic-powered irrigation involves using a noncutting plastic tip mounted on an airscaler or specialised air-driven handpiece operating at a lower frequency than ultrasonic to produce sonic agitation of the irrigant. Kaloustian *et al*, compared the effectiveness of EDDY and MM1500 Sonic Air in reducing root filling remnants and found no statistical difference between the two systems with both systems improving the removal of residual filling material from distal

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canals of mandibular molars.[37] Conflictingly, a review by Boutsioukis and Arias-Moliz determined that sonic agitation occurs at too low a frequency and too large an oscillation amplitude to create effective acoustic streaming or transient cavitation. This review found that systems which used a higher frequency with a subsequent decrease in oscillation amplitude were more effective, and the authors questioned the rationale of using sonic agitation.[38]

A comparative study by Azim *et al*. tested four different irrigation protocols: Standard needle irrigation, EndoActivator (specially designed sonic handpiece used with non-cutting polymer tips to agitate root canal irrigants), XP Endo finishing file (FKG Dentaire SA, La Chaux-de-Fonds, Switzerland) is a highly flexible mechanical endodontic file that is used to mechanically activate the irrigant solution in the root canal and Photo-induced photoacoustic streaming (PIPS). This study found that while all the tested protocols were able to significantly reduce the bacterial biofilm, the XP Endo finishing file was the most effective in eliminating bacteria from the canal. PIPS, however, was the most effective at the apical third of the canal. The poorest-performing protocol was standard needle irrigation.[13] Donnermeyer *et al.*, compared the efficacy of sonic activation using EDDY, PUI and mechanical activation with XP Endo finishing file in removing CaOH from artificial grooves in straight canals. Their results were slightly different than Azim *et al.*, in that the EDDY and PUI systems were significantly more effective in the removal of calcium hydroxide than the XPendo Finisher regarding the apical region, while the poorest performing system in this study was also standard needle irrigation.[39]

In conclusion, irrigant activation in some form appears to be more effective at root canal disinfection and medicament removal than standard needle irrigation.

Laser-assisted endodontic disinfection

The popularity of lasers in medical treatments is increasing. The field of dentistry is no exception, and lasers have been used to enhance endodontic disinfection. Lasers activate photosensitisers that associate with bacteria[40] or activate irrigant solutions by the transfer of pulsed laser energy.[35] Photo-activated disinfection (PAD) is laser-induced photochemical disinfection whereby non-toxic photosensitisers are applied to the affected tissues and then activated by light at precise wavelengths (Figure 3c and d) 26). Photosensitisers are molecules that can use light absorption energy to activate chemical reactions in cells.[41] Photosensitisers are specially chosen to have a specific affinity to bacterial membranes without affecting the viability of host cells.[42] When a photosensitiser molecule absorbs light, it is excited to a higher level. The molecule will then lose energy, which is transferred to the environment, and this energy transfer may lead to cytotoxic oxidative reactions, which occur in the vicinity of a microbe or the intracellular space.[41, 43] PAD is bactericidal and has been effective against both gram-positive and negative bacteria, viruses and, to a lesser degree, fungi.[44, 45]

PAD is a promising aid to endodontic disinfection protocols. Studies have shown that traditional root canal debridement may not remove all microbes, and PAD can improve endodontic disinfection.[7, 26, 44] Furthermore, chemical irrigants can be toxic and are known to cause structural changes to dentine, which can decrease the tooth's structural and flexural strength.[44] PAD has less affinity for cells of the body and is a potentially viable alternative to these conventional protocols with fewer adverse effects.[7, 44, 45] Common photosensitisers used in endodontics are methylene blue or toluidine blue with a wavelength of 665nm.[46, 47] Tolonium chloride has also been used with 635nm wavelengths.[48]

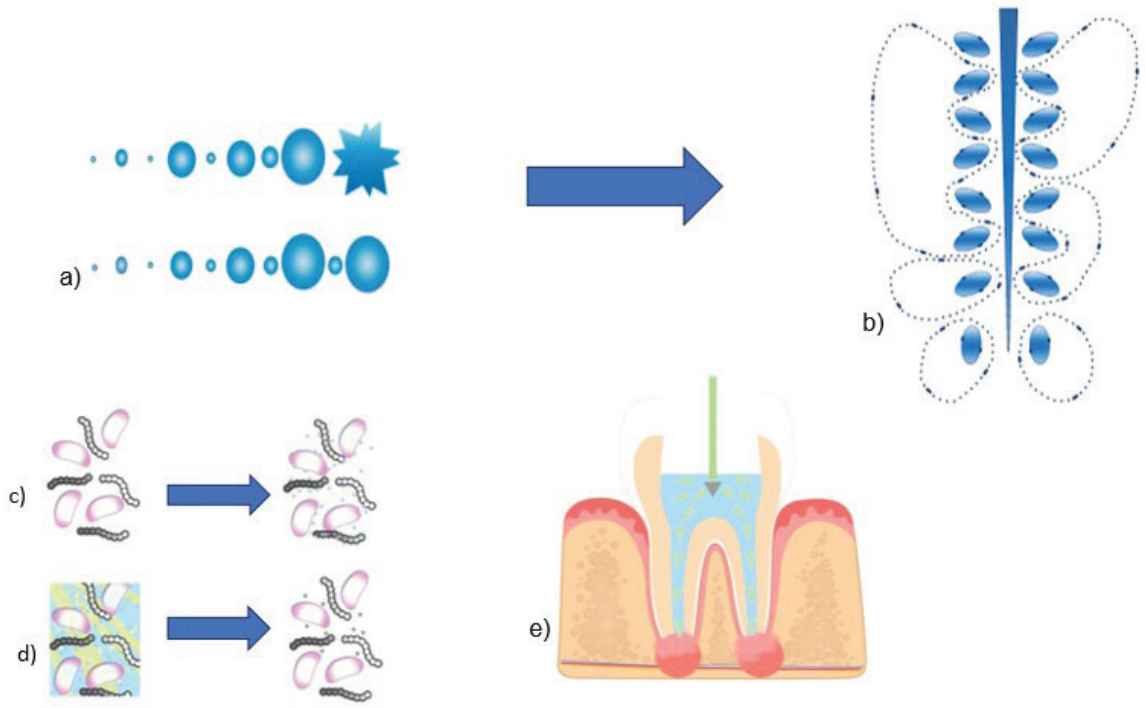

Figure 2: a) Schematic representation of inertial cavitation and non-inertial cavitation during ultrasound activation (163). **b)** Schematic representation of acoustic streaming when ultrasound is applied to fluid (166). c and d) diagrammatic representation of PAD at work. **c)** Bacteria are selectively tagged by PAD solution (photosensitisers). **d)** Exposure to red light activates the solution eliminating the bacteria (187). **e)** Photon-induced photoacoustic streaming. Low-power Er:Yag lasers generate photoacoustic shockwaves (195).

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However, anatomical complexities can hinder the effectiveness of PAD as its effects are limited to areas where light can penetrate. Isthmuses, ramifications, and curves prevent effective light distribution. Some studies have shown that the effectiveness of PAD is limited and not comparable to NaOCl.[47] To improve its effectiveness, there needs to be deeper light penetration and distribution into the apical portions of the root canal. Sabino and co-workers have experimented on methods to improve light penetration by using diffuser fibres attached to the laser and found that this improved light penetration and significantly improved the effectiveness of PAD.[44] These diffusers or optic fibres ensure uniform light distribution not only through the canal but also in a 360° direction, allowing for improved irradiation near the root apex and along the length of the root which improves disinfection outcomes.[49, 50] Radial tips have also been suggested to improve light distribution.[44] As with any irrigation method, it is important to remember that the instrument's tip needs to be as close as possible to the root apex to be effective in the apical third of the canal, otherwise known as the tip-to-target distance.

Other important considerations with PAD are the power level, duration of exposure, light absorption in the tissues, light wavelength, and photosensitiser absorbance.[43, 51-54] At this stage, PAD demonstrates potential and is a promising adjunct to endodontic disinfection protocols, bearing in mind the anatomical limitations and it cannot be used as a solitary disinfection protocol.

Photon-induced photoacoustic streaming (PIPS) involves using a erbium/yttrium-aluminium garnet (Er:YAG) laser light in a liquid solution to produce photoacoustic shockwaves (Figure 3e). These shockwaves create three-dimensional fluid flow through the isthmuses, anastomoses and lateral canals, allowing for a deeper cleaning of the entire root canal system.[55] The laser system is equipped with a fiberoptic delivery tip and subablative parameters, enhancing bubble dynamics and improving irrigant flow within the root canal.[35] Current evidence on the effectiveness of PIPS in root canal irrigation is contradictory.

Guneser *et al.* compared various techniques for removing precipitate formed after irrigation with NaOCl and CHX. They compared conventional syringe irrigation, CanalBrush, EndoActivator system, PIPS, and manual instrumentation techniques during which 5 mL of distilled water was used for 1 minute. All experimental groups contained residual precipitate and the authors concluded that none of these techniques were able to completely remove the orange-brown precipitate from the root canal surface.[56] Arslan *et al.* compared the efficiency of the PIPS technique with conventional, sonic and ultrasonic irrigation on the removal of apically placed dentinal debris from an artificial groove created in a root canal. The authors found that PIPS was significantly more effective than both sonic and ultrasonic irrigation in removing this debris.[57]

In a randomised clinical trial by Mandras and co-workers, the ability of PIPS technique to reduce root canal bacterial count in vivo was evaluated and compared to conventional irrigation. While there was a reduction in bacterial load with both techniques, PIPS demonstrated greater antibacterial efficacy. However, this difference between the two groups was not statistically significant. Within the limits of this study, the authors concluded that the PIPS technique could be considered a viable protocol for endodontic disinfection, especially in the case of simplified operational protocols and reduced instrumentation times.[55] Li *et al.* compared CaOH removal between PIPS, EndoActivator and needle irrigation. Their study showed that PIPS was more effective at removing CaOH from the central canal and isthmus in maxillary premolars than either of the two techniques.[58] Al Shahrani *et al.* compared the effectiveness of the PIPS technique combined with NaOCl, the PIPS technique with saline and NaOCl alone. They observed that the PIPS technique combined with NaOCl showed the most efficient bacterial biofilm eradication. They concluded that laser-activated irrigation utilising PIPS may enhance the disinfection of the root canal system.[59]

Studies have shown that even when placing the PIPS optic tip only in the pulp chamber, it can drive the irrigation solution to the end of the canal without harming the apical tissues and still be effective at removing debris through the length of the canal up to the apex.[60-62] In comparison with other techniques, where it has been observed that instrumentation and irrigation needle tips need to be as close to the root apex as possible to be effective along the length of the root canal, PIPS may offer a unique advantage. An added advantage of laser-assisted disinfection is the biostimulatory effects which can enhance healing and reduce inflammation.[63, 64] Despite the contradictory literature on the effectiveness of PIPS technique, it appears that there may be value in this technique as an adjunct for endodontic disinfection. Further research in this field is required.

INTRACANAL MEDICAMENTS

Endodontic treatment can be completed during single or multiple visits. Both techniques carry benefits; single-visit treatment decrease the number of appointments and allows for good patient acceptance and practice management considerations.[65] Multiple visits offer the advantage of time between root canal preparation and obturation allowing for drainage of apical periodontal infections, resolution of inflammation with its associated symptoms and shorter appointments minimising operator and patient fatigue. A common thread in considering single or multiple visit treatment is the risk of post-operative flare-ups. Dhyani *et al.* define flare-ups as "severe uncontrollable amount of inter-appointment and postoperative pain that is not relieved by medication, requiring an unscheduled visit to the dental surgery for active treatment".[66] There is no clear evidence in support of one technique over the other, as there seem to be as many studies in support of single-visit endodontic treatment as there are in support of multiple-visits.[65, 67-74] Factors that contribute to the decision-making tree of single vs multiple appointments range from operator skill, longer working times, trauma to the periapical tissues which can cause a more severe acute inflammatory response and postoperative pain to psychosocial factors such as high levels of distress before appointments and a patient's desire to control the anticipated unpleasantness associated with treatment.[69, 74-76] Each clinical case must be evaluated on its own merit to determine the most predictable and effective protocol for complete endodontic disinfection. A consensus is that the more severe the pre-operative symptoms are, the less likely a single visit is indicated.

With technological advancements such as magnification, heat-treated nickel-titanium instruments and new irrigation protocols, single visit treatment outcomes have improved. [4]

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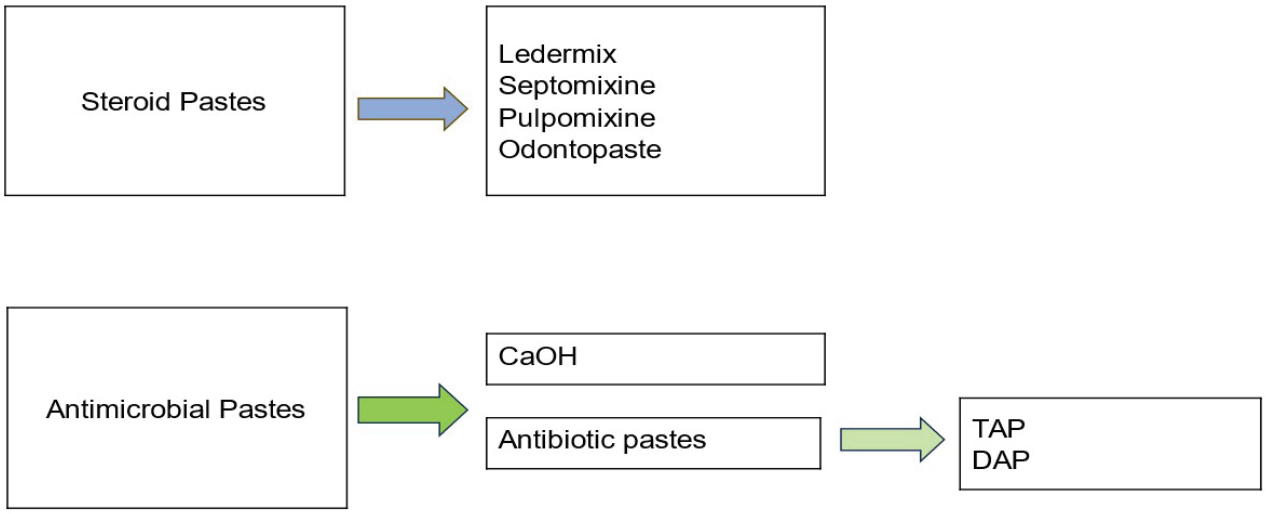

Figure 3: Classification of intracanal medicaments.

However, not all clinical scenarios can be treated with a single visit. In cases with persistent infection, difficulty to target micro-organisms in canals with complex anatomy, presence of large apical cysts or in patients with reduced immune competence, multiple visits, using intracanal medicaments between appointments, improves prognosis. Intracanal medicaments allow time for improved disinfection as the medicaments have time to diffuse and eradicate remaining microbes after canal preparation and provide time to confirm symptom improvement before final sealing of canals.[3, 77]

In cases where multiple visits are indicated, intracanal medicaments with high residual inhibitory effects can achieve successful outcomes and prevent reinfection.[78] However, the effects of intracanal medicaments are unpredictable in areas of debris and cannot be a substitute for thorough debridement of the canal.[79] Instead, intracanal medicaments should augment complete disinfection protocols.

According to Chong and Pitt Ford, intracanal medicaments should:[3]

1. Eliminate any remaining microbial populations after mechanical instrumentation.
2. Reduce inflammation of periapical tissues and pulp remnants.
3. Render canal contents inert and neutralise tissue debris.
4. Act as a barrier against leakage from the temporary filling.
5. Aid in drying persistently wet canals.

Intracanal medicaments can be classified according to their mechanism of action into steroid based pastes and antimicrobial pastes (see Figure 3).

Steroid pastes

Steroids are known to reduce inflammation and pain, and steroid preparations are used as an adjunct in endodontic disinfection. Gurney stated that local delivery of corticosteroids into the root canal and periapical tissues may provide symptomatic relief from post-treatment pain (80). Smith *et al.* observed that corticosteroids effectively decreased inflammation secondary to instrumentation.[81] However, corticosteroids are known to suppress the body's immune response, which may result in a bacteraemia.[82] Therefore, it is recommended to add an antibiotic to the corticosteroid preparation to protect against this potential bacteraemia and its associated symptoms.[83] Use of a corticosteroid/antibiotic paste has shown a rapid reduction in pain levels, with Schneider stating that once these pastes are applied, the majority of patients feel pain relief within an hour of leaving the dental office, and there was no occurrence of postoperative pain and swelling.[82] Common corticosteroid/antibiotic pastes available today are Ledermix paste, Septomixine Forte, Pulpomixine and Odondopaste.

Ledermix paste contains 1% triamcinolone and 3,2% demeclocycline in a polyethylene glycol paste.[84] Its active ingredients exert potent anti-inflammatory and antimicrobial effects. Triamcinolone is a steroid decreasing pulpal and periapical inflammation and aids in pain relief. Demeclocycline, a tetracycline derivative, has broad-spectrum antibacterial effects against gram-positive and gram-negative bacteria. It has been observed that patients whose teeth were dressed with Ledermix experienced less pain than those who had CaOH dressings or no dressings at all.[85] Ledermix paste can prevent external inflammatory root resorption, has no damaging effects on the periodontal membrane and is effective in treating progressive root resorption in traumatically injured teeth.[86, 87]

Septomixine and Pulpomixine pastes contain the antibiotic neomycin and framycetin, respectively, and dexamethasone as its steroid component. These agents are not as potent against common endodontic pathogens, and dexamethasone is less effective than other steroid agents used in alternative endodontic pastes.[88] Odontopaste is a zinc oxide-based paste with 5% clindamycin hydrochloride and 1% triamcinolone acetonide. Clindamycin is effective against many endodontic pathogens, is bacteriostatic, and prevents bacterial repopulation within the root canal.[89] The steroid triamcinolone acetonide is more potent than dexamethasone and temporarily reduces inflammation and postoperative pain.[90]

Antimicrobial pastes

The risks with systemic use of antibiotics are well known, with drug-resistant infections on the increase. Another limitation of systemic antibiotics within the context of root canal infections, is the anatomically complex and closed root canal system where limited amounts of antibiotic reach the infected pulp tissue.[91] Hence, an intracanal antibiotic paste provides a

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local delivery system, lowering the risk of antibiotic-resistant infections and increasing antibiotic effectiveness.

Calcium hydroxide

Calcium hydroxide (CaOH) is a broad-spectrum antimicrobial commonly used as a disinfectant dressing for vital inflamed pulp between visits. CaOH has an alkaline pH, is biocompatible with bactericidal effects, and has good tissue dissolution capability.[4, 92] CaOH works by decreasing the nutrient supply to any lingering microbes and so prevents root canal reinfection, neutralises endotoxin and also neutralises the lactic acid produced by osteoclasts and prevents dentine demineralisation while stimulating hard tissue repair and regeneration.[7, 78, 93, 94] Its mechanism of action is mediated by the release of hydroxyl ions which create free radicals that damage the cytoplasmic membrane, causes protein denaturation and damages bacterial DNA. In addition, bacteria are unable to survive in a high pH environment.[7]

CaOH has been shown to decrease microbial loads after mechanical instrumentation. In a study by Shuping *et al.*, where mechanical debridement was followed with 1% NaOCl irrigation and CaOH as an intracanal dressing, 61% of cases were bacteria-free after instrumentation and irrigation. After applying CaOH, 92% of cases did not have a positive culture. The results revealed that the apical size of the preparation and the use of the intracanal medication contributed to the reduction in the microbial load.[95] Sjögren *et al.* evaluated the effects of CaOH as a short-term intracanal dressing and found that CaOH was effective at eliminating bacteria that may be left behind after instrumentation and that predictable results can be achieved by dressing the canal for seven days.[96] CaOH is not without its limitations. CaOH has shown limited effectiveness against *E. faecalis*, which is the predominant pathogen in secondary infections and therefore, CaOH is more effective in primary endodontic infections than in secondary infections and alternative medicaments are recommended.[26]

There have been some additions to CaOH to improve its antibacterial and anti-inflammatory effects. In previous years, it was advised to combine CaOH with steroid pastes such as Ledermix. As the two pastes provide different effects, the combination was thought to provide improved antibacterial and anti-inflammatory properties.[97, 98] However, recent studies have shown that CaOH, being alkaline, degrades the steroid component of the second paste, and there was no benefit in combining the two pastes. It was recommended that its use be reviewed.[93] To improve the physical properties and radio-opacity of CaOH, iodoform has been added to CaOH. Iodoform maintains the paste's consistency and pH, making it easier to work with.[99] Iodoform also demonstrates antibacterial effects with restorative properties, and any excess material is resorbable.[100] Known materials in this category are Vitapex and Metapex.[94] The downside of such materials is their ability to prevent an adequate seal, and meticulous care must be taken to remove all excess material from the canal.[101]

Recently, Afkahami and co-workers tested a novel approach of adding silver nanoparticles (AgNPs) to CaOH. AgNPs are small, inert and biocompatible particles.[102] AgNPs create a cavity in the bacterial cell wall, decreasing bacterial adhesion and preventing biofilm formation.[103] These nanoparticles also prevent bacterial invasion into dentine.[104] In addition, AgNPs have demonstrated excellent antimicrobial activity with a low risk of microbial resistance.[35] Akhahami and co-workers showed that the addition of silver nanoparticles to CaOH has a two-fold effect: it enhances the antibacterial effects of CaOH at low concentrations and increases the residual antibacterial effects of CaOH as an intracanal medicament.[78] Studies by Fernandez *et al.* and *Yousefshahi et al*.support the idea that AgNPs increase the antibacterial properties of CaOH and are effective as intracanal medicaments.[105, 106]

Antibiotic pastes

Antibiotic pastes are typically used in teeth with incomplete root formation where regenerative and revascularisation of immature teeth allow apical closure of open apices and thickening of dentine walls.[107, 108] The microbial biofilm's complexity and diversity necessitates using an antibiotic combination rather than a single antibiotic to increase its efficacy. Triple antibiotic paste (TAP) is most commonly a combination of metronidazole, ciprofloxacin and minocycline, usually in 1:1:1 ratio and mixed with sterile water.[78] Studies have shown that these pastes can eliminate the microorganisms infecting the root canal and prevent recolonisation.[109-111] Ordinola-Zapata *et al.*, compared the antimicrobial activity of TAP, 2% CHX gel and CaOH paste on intraorally infected dentine biofilm models and found that TAP was the most effective at killing live microorganisms. However, the minocycline component causes dentine staining, so an alternative antibiotic paste was suggested. An alternative TAP combination of metronidazole, ciprofloxacin and clindamycin can be used,[91] or removal of minocycline from the original TAP without replacement making it a double antibiotic paste [78]

Nanoparticles

Nanotechnology is becoming increasingly popular in the medical field and uses nanoparticles as its delivery system. Nanoparticles are small particles with diameters between the range of 1 and 100 nm with increased chemical activity due to their large surface area.[112] Nanoparticles can be derived from various sources: metals such as silver and gold, polymers such as chitosan poly (lactic-co-glycolic acid), or even metallic oxides such as calcium oxide, zinc oxide, magnesium oxides and titanium oxide.[113, 114] As discussed earlier, CaOH has been impregnated with silver nanoparticles and has shown excellent antimicrobial activity with a low risk of microbial resistance.[35] Nanoparticles, with their higher reactivity and larger surface area, can improve the delivery, reach and effectiveness of irrigant solutions. The potential uses of nanoparticles can be broad, from combining with antibiotics to improve their efficacy while preventing antimicrobial resistance, being loaded with photosensitisers to improve photoactivated disinfection, or even combined with restorative dental materials providing a substantive antimicrobial effect. Nanoparticles are relatively new in endodontics, and further research is needed on their optimisation, limitations, and toxicity.

A dentist's perspective and the future of endodontic disinfection

Endodontic treatment is a routine dental procedure. It is essential for the clinician to understand tooth morphology, pathosis of pulp infection, and the materials and techniques best suited to debride and disinfect the root canal. Despite the lack of a single ideal irrigant, NaOCl combined with ethylenediaminetetraacetic acid as a chelator remains the most popular protocol for disinfection as it is effective and economical. The limitations of conventional irrigation are well

documented, so agitating techniques have been employed to overcome these limitations. Techniques such as ultrasonic activation have been useful in improving disinfection and overcoming limitations around anatomical variations and apical access of irrigants. The introduction of technologies such as laser into the disinfection armamentarium has also shown promising results. To effectively gain maximum output from these technologies, the clinician must understand the mechanisms at work and appreciate the relevant limitations of such technologies. The choice of irrigant and medicaments depends on clinical time, cost, and effectiveness. Effective and predictable combination solutions, such as continuous chelator irrigants have the potential to simplify irrigation while reducing chair time.

The use of intracanal medicaments is still controversial. It is now understood that with the continuous advancements in technologies and if the clinical situation is favourable to single-visit endodontic treatment, then the success rate of single-visit treatments has improved. However, there are still scenarios where multiple visits would be favoured. In cases where the risk of post-operative flare-ups is higher and when shorter appointments better serve operator or patient factors such as in-chair comfort and fatigue, multiple visits are still advised. Furthermore, psychological factors such as the degree of patient anxiety, fear of dentists, and previous traumatic experiences may impact the patient's pain perception and post-operative responses. In these scenarios, it may be beneficial from a psychological perspective to undergo multiple visits to ease the patient into treatment slowly and decrease the likelihood of post-op flare-ups. Therefore, each case should be evaluated on its own merit to determine if a single or multi-visit approach should be used.

Medical treatment is moving away from the generic and generalised approach towards individuality, targeting specific cells or pathogens for a more significant localised effect to minimise unwanted systemic and generalised adverse reactions. Custom antimicrobial functional peptides are a potential source for individualising endodontic disinfection and can be designed to target precise microbial pathogens. Specific endodontic challenges are three-fold: the complexity of the endodontic micro-flora, protease production by pathogens which could degrade these peptides and the high cost of custom peptide manufacturing.[115] Nevertheless, bespoke medical intervention is an exciting new field that can target specific endodontic pathogens, and further research is needed.

The future for endodontics includes dental pulp regeneration with revitalising and revascularising diseased pulp. The principles of regeneration hold for dental tissues: an extracellular matrix to provide scaffold support for cellular interactions, stem cells, and secretome complexes to mediate and influence cellular interactions. The first step in successful tissue regeneration is to eliminate infection to provide a clean and biologically healthy environment to facilitate tissue regeneration. This is where endodontic disinfection protocols are critical. The standard disinfection protocols aim to eliminate microbial infection and diseased tissue, destroying all cellular components within the root canal. Therefore, there is a need to create a biologically supportive disinfection protocol that will not only eliminate infection but retain or even stimulate positive cellular responses. Elnawam *et al.* proposed a novel concept, "minimally invasive regenerative endodontic procedures", by amalgamating the sciences of minimal invasive endodontics with regenerative endodontic procedures (116). This concept will not only regenerate lost tooth structures but conserve those that remain while maintaining the dentinogenic capacity of pulpal stem cells.[116] In the quest to regenerate dental pulp, a new biologically friendly disinfection protocol needs to be developed. This protocol must provide a balance between antimicrobial disinfection and preservation of stem cells to allow for cellular interactions. To this end, some alternative irrigants and medicaments such as ozonated oils, morinda citrifolia juice, Photo-activated disinfection, nitric oxide releasing nanomatrix, nanoparticles or dual effect scaffolds have been suggested.[116, 117] Regenerative endodontics is an exciting and developing field, and further research is needed.

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Data availability statement

No datasets were generated or analysed during the current study.

Competing Interests

The Authors declare no Competing Financial or Non-Financial Interests.

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Online CPD in 6 Easy Steps

The Continuing Professional Development (CPD) section provides for twenty general questions and five ethics questions. The section provides members with a valuable source of CPD points whilst also achieving the objective of CPD, to assure continuing education. The importance of continuing professional development should not be underestimated, it is a career-long obligation for practicing professionals.

