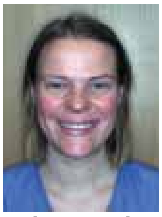

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Endodontic 'Solutions' Part 1: A Literature Review on the Use of Endodontic Lubricants, Irrigants and Medicaments

Abstract: Endodontic lubricants, irrigants and medicaments help prepare and disinfect root canal systems (RCS) but primary and secondary cases involve different microbes and therefore it is unlikely that one protocol will be effective for both case types. Each individual 'solution' or sequence of 'solutions' could play a significant role in each case type, but there are no detailed published guidelines in existence. To help inform clinical practice it was decided to undertake a literature review followed by a UK and Republic of Ireland wide audit on current endodontic 'solution' usage within dental schools. The literature review was undertaken under the following headings: pre-op oral rinse; file lubricants; root canal irrigants and intracanal medicaments and provides an evidence base for protocol development for both primary and retreatment cases. The audit project and the protocols developed from the findings of both the literature review and audit will be presented in Part 2.

Clinical Relevance: As our clinical practice should reflect evidence-based dentistry, it is important to be aware of the current literature on endodontic lubricant, irrigant and medicament use.

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The aim of endodontic treatment is to disinfect the root canal system and prevent re-infection. In a study by Peters *et al*[1] examining root canal instrumentation, they found that half of the canal wall surface remained untouched by endodontic instruments. Therefore, in order to achieve the treatment aims, cleaning and shaping are essential. There are many endodontic 'solutions' available which can be categorized as lubricants, irrigants and intracanal medicaments. Their purpose is to prepare and disinfect the root canal system (RCS) adequately to enable the host response to favour healing of the periapical tissues.

Apical periodontitis is an inflammatory disorder of periradicular tissues caused by persistent microbial infection within the root canal system.[2] The infection can be described as primary where the tooth has not yet been root-treated, or secondary where a previous endodontic treatment has failed.

The microbes involved in root canal infections are cocci, rods, filaments, spirochaetes, fungi and viruses.[3,4] These microbes are organized into protective adhesive biofilms[5] which, in addition to the anatomical complexity of the root canal system, make root canal disinfection challenging if not impossible.[6] Primary infections are polymicrobial, mainly involving gram negative anaerobic bacteria containing 10–30 species per canal plus fungi.[3] Secondary cases, however, tend to involve fewer microbial species (1–5 per canal), such as *Enterococcus faecalis* and *Candida albicans*. *Enterococcus faecalis* is the most common isolate in 22–77% of retreatment cases[7–9] and they can survive in harsh environments, including highly alkaline pH, such as when calcium hydroxide is used as an intracanal medicament.[10]

As the British Endodontic Society (BES), the European Society of Endodontology (ESE) and the American Endodontic Society (AES) currently have no detailed guidelines on the use of endodontic 'solutions', it was

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decided to undertake a literature review to help inform clinical practice.

Literature review

Pre-op oral rinse

Chlorhexidine digluconate is a bisguanide antiseptic which is available as a mouthwash. It has broad antimicrobial action[11] and substantivity of more than 12 hours.[12] There is no evidence to support its use as a pre-op oral rinse in endodontic cases, but it may be advisable if isolation with rubber dam is incomplete.

File lubricants

Lubrication of endodontic files improves the cleaning action and thereby antibacterial effect and also reduces the risk of instrument fracture. Chlorhexidine digluconate as a 4% solution has been suggested as a lubricant and its properties, already mentioned, are favourable. *In vitro* studies have shown its effectiveness against *Candida albicans* and *Enterococcus faecalis* which can be associated with retreatment cases.[13,14] It is, however, unable to dissolve organic or inorganic tissue. EDTA paste is more commonly used as a canal lubricant as it can help reopen sclerosed canals and remove the smear layer[15] created by instrumentation, although it has limited antimicrobial action.[16]

Root canal irrigants

The aims of irrigation include debridement, smear layer removal, disinfection, lubrication, dissolution and final preparation for obturation. As no single irrigant fulfils all of these desired properties, more than one solution is required each with an adequate concentration, formulation, volume and time to act.[17] It is essential that the irrigants reach the apical portion of the root canal system in order to have an effect throughout.[18] The more recent increased taper preparations allow more irrigant delivery to this area.[19] A master apical ISO file size of 30 allows a 27gauge needle to irrigate to within 3 mm of the working length(WL).[20] The desired technique is therefore slow passive irrigation with a 27 or 31 gauge side-venting needle placed freely in the apical third of the root canal to within 1–3 mm of the WL. In a paper by Sedgley *et al*[18] the mechanical efficiency of an irrigant in removing bacteria was significantly greater when delivered 1 mm from the working length. There are numerous irrigant solutions on the market. These will be mentioned with their properties under the headings: antimicrobial solutions; and solutions used to remove the smear layer.

Sterile water

Sterile water can be used to flush root canals between two solutions that are known to react unfavourably. Alternatively, fast aspiration and paper points can be used to dry up the reservoir of the first solution before introducing the second, or copious amounts of the second irrigant can ensure the desired properties are eventually available.

Antimicrobial solutions

Sodium hypochlorite

Sodium hypochlorite (NaOCl) is a caustic solution with a pH of 12–13 which, if diluted and stored out of the light at room temperature, is stable for only one week.[21] It is efficient in dissolving organic components of dentine, but its ability to remove inorganic components is limited. It has a broad antimicrobial spectrum against bacteria, bacteriophages, spores, yeasts and viruses. At high concentrations, however, it can damage soft tissues and dentine.[22] Conflicting evidence exists as to the most effective non-toxic concentration of NaOCl for endodontic usage. Several clinical studies have shown that, even after irrigation at 5% concentration during instrumentation, nearly one third to one half of the root canals remained contaminated.[23,24] Berber *et al*[25] found that only higher concentrations of NaOCl were able to disinfect *E faecalis* infected canals independent of the canal preparation technique used. The proteolytic effect of NaOCl is dependent on the amount of free available chlorine. The chlorine is exhausted by reacting with inorganic reducing substances, so frequent irrigation with a lower concentration can equate with higher concentrations.[24] It is apparent from the current available evidence that there is no rationale for using NaOCl at concentrations over 1%[26] as this offers the best balance of tissue dissolution capacity, antimicrobial activity and biocompatibility. Copious irrigation with l% concentration can achieve the desirable clinical effects.[27]

The question then is what volume per canal? Yamada *et al*[28] found that 20 ml per canal, 10 ml 17% EDTA and 10 ml 5.25% NaOCl, produced the cleanest canal. In an *in vitro* study analysing the quantity of dentine debris remaining following irrigation with different volumes of 2% NaOCl and flushing methods, the authors found that there was no significant difference between 6 ml or 12 ml at a rate of 2 ml/30 s or 50 ml continuous flow.[29] This is twice the concentration advocated above so it may be reasonable to assume that, from these two papers, 10–20 ml per canal would suffice. However, there is insufficient evidence to date to support this.

It has also been shown in a number of *in vitro* studies that warming NaOCl improves its efficiency.[30,31] A 1% solution at 45 °C has the equivalent effect as 5.25% at 20 °C, according to Sirtes *et al*.[31] However, there are no clinical studies to support these findings and, in addition, it is unknown what effect this heat has on adjacent tissues.

Another method of increasing the temperature of NaOCl is with acoustic microstreaming caused by ultrasonic activation. This removes more organic and inorganic debris plus bacteria.[32] According to Al-Jadaa *et al*,[33] pulp dissolution occurs in the main plus accessory canals and temperatures of 55 °C were measured. Zeltner *et al*,[34] however, found no temperature increase if a continuous flow was used.

Chlorhexidine (CHX)

Chlorhexidine digluconate is a bisguanide antiseptic with broad antimicrobial action and substantivity of more than 12 hours.[11,12] The microbial flora associated with primary endodontic infections is largely gram negative anaerobes, unlike that of secondary cases where gram positive organisms such as *E faecalis* and yeast predominate. CHX is more effective against gram positive bacteria[12] and therefore may have a role as an endodontic irrigant in retreatment cases. *In vitro* studies have shown it to be effective against *Candida albicans* and *E faecalis*.[13,14] CHX solution at 1% and 2% concentrations was shown to be as fast as 5.2% NaOCl in killing *E faecalis*.[14] According to Zamany *et al*[35] the 2% concentration is best for endodontic use. In some clinical studies, CHX was shown to be as effective as NaOCl in root canal disinfection,[36] although it lacks the ability to dissolve organic tissue and therefore is less effective in removing necrotic pulps.[37] Improved disinfection was obtained when combined with NaOCl.[35] CHX cannot be advocated as a main irrigant in endodontic cases but it may be useful as a final rinse following NaOCl, especially in retreatment cases.[27] It should, however, be noted that combined use of chlorhexidine and NaOCl can cause discoloration,[38] so the use of sterile water or paper points is indicated following NaOCl and before CHX.

Iodine

Iodine preparations can also help eliminate *E faecalis* and *C albicans*,[39] which are often associated with persistent endodontic infections. Iodine potassium iodine (IKI) is known for its ability to diffuse through dentinal tubules and kill bacteria *in vivo*.[40] However, the duration of its antimicrobial effect is short. It has been shown that 5 min irrigation with 5% IKI reduces the number of *E faecalis* recovered from root canals in cases of chronic apical periodontitis associated with both primary and secondary infection.[41] Iodine is also antiviral[42] and viruses have recently been implicated in the pathogenesis of periradicular periodontitis.[4] It is important only to consider the use of iodine in patients with no reported allergy to iodine or seafood.

Ozone

The use of strong oxidizing agents, such as ozone, are being investigated as potential antimicrobial root canal solutions. Although manufacturers (KaVo Dental, Bismarckring, Germany) claim that effective treatment can be completed in a single visit using gaseous exposure to ozone, the available research evidence is still controversial. Nagayoshi *et al*[43] observed that ozonated water had nearly the same antimicrobial activity as 2.5% NaOCl during irrigation, especially when combined with the use of ultrasonics. Huth *et al*[44] also reported potential benefits of using ozone in root canal treatment when used in high concentrations. Hems *et al*,[45] however, on evaluating the ability of ozone to kill an *E faecalis* strain, found that its antibacterial efficacy was not comparable to that of NaOCl. Estrela *et al*[46] found ozone to have no antimicrobial activity against *E faecalis*. These findings and others have cast doubts on the efficacy of ozone as an antimicrobial agent in endodontic infections.

Photo-activated disinfection (PAD)

Photo-activated disinfection involves the placement of a dye into the RCS, which is then activated by lasers causing disruption of bacterial cell walls and subsequent bacterial death. At present, there is insufficient evidence to support this method.[47]

Solutions used to remove the smear layer

Ethylenediaminetetraacetic acid (EDTA)

EDTA (a chelator) 15–17%, with pH 7, is widely used as a root canal irrigant in both primary and secondary cases. It effectively removes the smear layer[15] but has limited antibacterial properties.[16] The smear layer is debris that covers the root canal walls formed by root canal instrumentation. It can protect the biofilm and reduce sealer adaptation to canal walls so its removal should improve treatment outcome. It is important to note that strong chelators can cause dentine erosion over time.[48] Kuah *et al*[49] found that a relatively short (1 min) application with ultrasonics was effective in the apical region. When EDTA is used in combination with NaOCl, both the inorganic and the organic elements are removed, achieving patent dentinal tubules and clean surfaces even in the apical portion.[50] Superior results have been reported when NaOCl is used as the last irrigant.[50] EDTA, however, interacts with NaOCl and this can reduce the amount of chlorine available in solution, thereby compromising the tissue dissolving ability and antimicrobial effect of NaOCl.[51] In an alternating irrigating regimen, copious amounts of NaOCl should be administered to wash out remnants of the EDTA, to ensure effective use of NaOCl as a final rinse, especially in multiple visit treatments.[27]

Citric acid

Citric acid 10–50% is another demineralizing solution which can remove the smear layer following canal instrumentation. Zehnder *et al*[52] demonstrated that the less toxic 10% strength was effective. Citric acid like EDTA also interacts with NaOCl, but at a faster rate, reducing the availability of chlorine and therefore the effect on bacteria and organic tissue.[52] Most studies have not found a significant difference between the chelation properties of citric acid and EDTA.[53,54]

Bio Pure™ MTAD™

A relatively new irrigant Bio Pure™ MTAD™ Cleanser (Dentsply International, York, PA, USA) was briefly introduced to the market as a potential replacement for EDTA. This product has three components: doxycycline, an antibiotic from the tetracycline family; citric acid, a chelating agent; and a detergent. The recommended protocol for use is irrigation with 1.3% NaOCl for 20 min followed by MTAD for 5 min. Torabinejab *et al*[55] found that it successfully removed the smear layer. Beltz *et al*[56] found high dentine binding of doxycycline. According to Davis *et al*[57] MTAD is more effective than 5.25% NaOCl against *E faecalis* and Zhang *et al*[58] found MTAD to be less cytotoxic than 5.25% NaOCl, EDTA and $Ca(OH)_2$. MTAD, however, is not currently available owing to concerns regarding a risk of intrinsic staining of dentine caused by the oxidation of MTAD following the use of NaOCl, and other effects on dentine.[59] As with any product containing antibiotics, there is also a risk of bacterial resistance.

Electrochemically-activated water

Electrochemically-activated water (ECA), such as Sterilox® is known to reduce microbial contamination, endotoxins and the biofilm in dental unit water lines.[60] When applied to endodontics, however, Marais and Williams[61] found ECA to be a less effective antimicrobial agent than 3.5% NaOCl. Owing to the reduced toxicity and tissue damage associated with these solutions, future research is indicated.

Root canal medicaments

Although cleaning and shaping of the root canal greatly reduces the number of bacteria,[62] it has been shown that it is impossible to obtain complete disinfection in all cases.[62,63] Concerns therefore exist as to the fate and subsequent activity of the remaining micro-organisms in the root canal system. Byström and Sundqvist[62] showed that, if a canal is left without a disinfectant dressing between visits, bacteria multiply, close to the original counts, within days. It is generally believed that the number of remaining bacteria can be controlled between appointments by placing an antimicrobial intracanal dressing.[63] In multiple visit root canal treatment the use of intracanal medicaments has been considered important, not only to control residual bacterial infection, but also for other possible properties, including anti-inflammatory properties, prevention of re-infection and prevention of inflammatory root resorption. The ideal technique for medicament placement in a dry canal is slow, passive injection with a syringe tip measured to within 1 mm of the WL.

Calcium hydroxide

The main benefit of calcium hydroxide as an intracanal medicament lies in the bactericidal effect conferred by its high pH during a one week application. The antimicrobial effects of calcium hydroxide have been extensively evaluated. In some clinical studies the use of calcium hydroxide has been shown as an effective root canal disinfectant,[63,64] whilst results from other studies were not as good.[65,66] A limited antimicrobial effectiveness of calcium hydroxide has been confirmed in a recent systemic review and meta-analysis undertaken by Sathorn *et al*.[67] Several studies have reported that calcium hydroxide is not effective in eliminating *E faecalis*, which is often associated with persistent endodontic infections.[68,69] Such bacteria can invade the dentinal tubules and survive by buffering the high pH produced by calcium hydroxide.[70] In addition, dentine has also been found to have a buffering effect on high pH,[71] further compromising the antimicrobial effect of calcium hydroxide. There is some evidence to suggest injection of a thinner 10% mix[72] partially improves its efficacy as this increases contact with bacterial cell walls. Calcium hydroxide products can use one of three vehicles: aqueous, viscous or oil-based. Aqueous solutions release ions more quickly, however, calcium hydroxide has low solubility and therefore limited ability to diffuse into parts of the root canal system that are not in direct contact.[73] Nerwich *et al*[74] found that it took 3–4 weeks for pH levels to peak in outer dentine but longer-term dressings (180 days) can lead to significantly reduced dentine fracture resistance.[75] The low solubility poses a potential problem when attempting its removal, however, there is evidence that 2% NaOCl with passive ultrasonic irrigation was more effective than NaOCl alone.[32] Chelating solutions, such as EDTA, would also aid removal owing to their affinity for calcium ions.

Iodine

Unlike calcium hydroxide, iodine potassium iodine (IKI) is known for its ability to diffuse through dentinal tubules and kill bacteria *in vivo*.[40] However, the duration of its antimicrobial efficiency is short. Molander *et al*[76] suggested that dressing canals for 3–7 days with 5% IKI following instrumentation may reduce the frequency of *E faecalis* recovery from root canals. Baker *et al*[77] found 2% IKI or 10% povidone iodine significantly better than calcium hydroxide against *E faecalis*. It is essential, however, to check for patient allergies before use.

Iodine and calcium hydroxide

In retreatment cases, the combined use of calcium hydroxide and iodine potassium iodine (IKI) has been suggested. However, Molander *et al*[76] demonstrated that dressing canals for 3–7 days with 5% IKI following instrumentation, then placing calcium hydroxide for 2 months, showed no improvement in antimicrobial action, although the use of IKI seemed to reduce the frequency of *E faecalis* recovery from root canals. Various products on the market, such as Metapex™ (Meta Biomed Co Ltd, Chungbuk, Korea), combine calcium hydroxide with iodoform and silicone oil. There is some evidence that these are more effective against *E faecalis* than calcium hydroxide mixed with IKI or calcium hydroxide alone.[78] There is some concern, however, that washing out these oily products would prove difficult, although the use of chelators and a microscope should help. Again it is essential to check for patient allergies before use.

Chlorhexidine +/- calcium hydroxide

Results from studies on the combined use of calcium hydroxide and chlorhexidine are controversial. Manzur *et al*[79] compared the antibacterial properties of 2% chlorhexidine, calcium hydroxide, or both and found no difference in primary cases. Oncag *et al*[80] reported that CHX alone, or in combination with $Ca(OH)_2$, was more effective than $Ca(OH)_2$ alone on *E faecalis* in primary cases, whereas Zerella *et al*[81] found no difference in the antibacterial effect between the three preparations in retreatment cases. More research is required.

Triamcinolone and demeclocycline

An alternative intracanal medicament *Ledermix* paste (Lederle Pharmaceutical, Wolfrathausen, Germany) is water-soluble and contains 1% triamcinolone steroid and 3% demeclocycline HCl antibiotic. *Ledermix* has been shown to reduce the incidence of postoperative pain in endodontics effectively.[82] However, the superiority of *Ledermix* over calcium hydroxide in reducing the incidence of post-operative pain associated with acute apical periodontitis is controversial.[83] The control of post-perative pain and inflammation attributable to the use of *Ledermix* appear to be more likely to be related to the anti-inflammatory effects of corticosteroid rather than its antibacterial effects. The antibiotic component does not appear to be ideal and the use of other antibiotics may help to improve the antimicrobial effect. However, the frequent use of any antibiotic-containing product can produce bacterial resistance. *Ledermix* offers no advantage over $Ca(OH)_2$, except possibly in external and internal inflammatory resorption cases, where the tetracycline component may offer an anticlastic effect.

Future developments

More recently, studies are being undertaken on lowering the pH of NaOCl in order to improve its properties.[84] This can be accomplished by the addition of chemicals such as etidronic acid (1-hydroxyethylidene-1, 1-bisphosphonate HEBP), which is a common ingredient of soap. Lottanti *et al*[48] have shown per acetic acid (PAA) to be an effective final irrigant owing to its antimicrobial and smear layer removal properties, but further research is required. There is also a new product (Hyben® Plaque Biofilm Removers, EPIEN Medical Inc, Saint Paul, MN, USA) being suggested for removal of the intracanal biofilm. It is a concentrated mixture of sulphates which absorb water from plaque biofilm causing biofilm detachment and coagulation. Products such as this may emerge as safer alternatives to existing irrigants.

Waltimo *et al*[85] has demonstrated that mixing calcium hydroxide powder with hydrochloric acid as an intracanal medicament speeds up canal disinfection, although it is not known what long-term effect this dressing may have on dentine.

Discussion and Conclusion

It is clear from the evidence that more than one 'solution' is required to prepare and disinfect the RCS and that these 'solutions' need to reach the apical portion to maximize their effect. There are only a small number of 'solutions' that are supported by sufficient evidence, these include NaOCl, EDTA or CA, CHX or iodine preparations and $Ca(OH)_2$.

Copious amounts of 1% NaOCl fulfil many of the desired properties whilst limiting potential toxicity. Concurrent use of ultrasonic activation further improves the debridement of the RCS whilst increasing the temperature which improves the efficiency of NaOCl. The use of chelating agent 15–17% EDTA or 10% CA for 1 min with ultrasonics removes the smear layer. This important step unblocks infected dentinal tubules thus allowing antimicrobial 'solutions' to penetrate deeper and disinfect more thoroughly. Use of both NaOCl and EDTA (or CA) is indicated in primary and secondary cases, but secondary cases can also require an additional antimicrobial agent to help eliminate specific microbes involved. The choice is between 2% CHX or an iodine preparation. CHX is readily available and relatively cheap with low toxicity, but the evidence on its antimicrobial properties is still unclear. Iodine has the advantage of being effective against many micro-organisms, including viruses. This may be important in non-responding cases, although some patients may be allergic.

According to research, multiple-visit cases should have antimicrobial intracanal medicaments placed between visits to help control residual infection. $Ca(OH)_2$ is the medicament of choice for both primary and secondary cases, although it is not as effective an antimicrobial agent as was once thought and it does not help in the elimination of *E faecalis*. If a more persistent infection is involved, $Ca(OH)_2$ plus iodine can be considered. These medicaments are best removed at subsequent visits with a chelating solution, such as EDTA, ultrasonic activation and visualization under a microscope.

As new products and supporting evidence emerge, the current recommendations will need to evolve. Part 2 of this paper will present an audit on the current use of endodontic lubricants, irrigants and medicaments in the UK and ROI dental schools. The findings of this literature review and the audit will then form the basis for endodontic 'solution' protocols for primary and secondary cases in Belfast Dental School.

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