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The antimicrobial effects of root canal irrigation and medication

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The role of microorganisms in the development and maintenance of pulpal and periapical inflammation have been well documented. The success of root canal treatment largely depends on the elimination of microbial contamination from the root canal system. Although mechanical instrumentation of root canals can reduce bacterial population, effective elimination of bacteria cannot be achieved without the use of antimicrobial root canal irrigation and medication. This review will discuss the antimicrobial effects of the known root canal irrigants and medicaments and explore future developments in the field. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103:560-9)**

The contribution of microorganisms to the development of pulpal and periapical disease has been well documented.[1-3] The bacteria associated with primary endodontic infections are mixed but are predominantly gram-negative anaerobic rods, whereas the bacteria associated with secondary infection comprise only one or a few bacterial species—the most important of which is *Enterococcus faecalis*.[4,5] In addition, yeastlike microorganisms have also been found to be associated with secondary endodontic infections, particularly *Candida albicans*.[6,7]

Successful treatments of both primary and secondary endodontic infections involve effective eradication of the causative microorganisms during root canal treatment procedures. The chances of a favorable outcome with root canal treatment are significantly higher if infection is eradicated effectively before the root canal system is obturated. However, if microorganisms persist at the time of obturation, or if they penetrate into the canal after obturation, there is a high risk of treatment failure.[8]

The pattern of colonization of the root canal microbiota often shows the characteristic of a climax community, which may require special considerations regarding its elimination and the prevention of clinical problems. In addition, the observed propagation of the microorganisms throughout the entire root canal system in teeth associated with periradicular lesions demonstrates that therapeutic measures are necessary to eliminate the microorganisms completely.[9] Bystrom and Sundqvist[10] evaluated the antibacterial effectiveness of mechanical instrumentation and irrigation. They found considerable reduction in bacterial counts after instrumentation and irrigation with saline, yet all the teeth had a positive culture after the first appointment. When they used sodium hypochlorite (NaOCl) separately or combined with ethylene diamine tetraacetic acid (EDTA), the elimination of bacteria was significantly improved.[11,12] The importance of using an antimicrobial irrigant to reduce the bacteria load during root canal treatment, regardless of the irrigant or instrumentation technique, has been recently reported.[13] The bacteria located in areas such as isthmuses, ramifications, deltas, irregularities, and dentinal tubules will not be eliminated by mechanical means alone. The use of chemical disinfectants such as root canal irrigants and

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antimicrobial medications between appointments for elimination of these bacteria and for disinfection of the root canal system is therefore important.

ROOT CANAL IRRIGATION

One of the important requirements of an ideal irrigant is its ability to eliminate microorganisms from the root canal system. This antimicrobial effect can be a direct chemical effect or indirectly by facilitating the mechanical disinfection through lubrication, tissue dissolving, and flushing of contaminated debris accumulated during root canal preparation. In addition, the root canal irrigants should be biocompatible with oral tissues. A large number of substances have been used as root canal irrigants, including acids (citric and phosphoric), chelating agent (EDTA), proteolytic enzymes, alkaline solutions (sodium hypochlorite, sodium hydroxide, urea, and potassium hydroxide), oxidative agents (hydrogen peroxide and Gly-Oxide), local anesthetic solutions, and normal saline.[14]

Sodium hypochlorite is at present the most popular irrigant.[15] It is a broad spectrum antimicrobial agent that has proven to be effective against bacteria, bacteriophages, spores, yeasts, and viruses.[11] It had been shown that 5.2% NaOCl completely destroyed *C albicans, E faecalis,* and *Bacillus* species.[16] The antimicrobial efficacy of NaOCl is due to its ability to oxidize and hydrolyze cell proteins and to some extent, osmotically draw fluids out of cells due to its hypertonicity.[17] Sodium hypochlorite has a pH of approximately 11 to 12, and when hypochlorite contacts tissue proteins, nitrogen, formaldehyde, and acetaldehyde are formed within a short time and peptide links are broken, resulting in dissolution of the proteins. During the process, hydrogen in the amino groups is replaced by chlorine, thereby forming chloramine, which plays an important role in antimicrobial effectiveness. As a consequence, NaOCl is highly toxic to vital tissues at undiluted high concentrations. At very low concentrations, NaOCl induces an inflammatory reaction when it comes into contact with vital tissues.[18] At higher concentration, for example, 1:10 (vol/vol) dilution, the tissue irritation may be substantial,[17] and displacing highly concentrated NaOCl into periapical tissues can cause severe tissue damage.[19] Heggers et al.[20] studied the toxic effects of NaOCl on wound healing and concluded that NaOCl at a concentration of 0.025% is safe and therapeutically efficacious as a fluid dressing because it preserves bactericidal properties without any detrimental effect on wound healing. However, this low concentration does not seem to have an adequate antimicrobial action for endodontic treatment and will be discussed later. At present, there is some dispute regarding the most effective concentration of NaOCl, but theoretically the concentration should be kept to the lowest level that is effective. Higher concentrations have been reported to be more effective by using agar diffusion tests.[21-23] However, direct extrapolation to the clinical situation of agar diffusion test should be treated with caution. When used in contaminated canals of extracted teeth, Siqueira et al.[24] found no difference in the antibacterial effect of 1%, 2.5%, and 5.2% NaOCl. They suggested that copious irrigation with NaOCl may maintain a chlorine reserve that is sufficient to eliminate bacterial cells and compensate for the effect of concentration. Under clinical conditions, the use of NaOCl has proven less effective. Several clinical studies[12,25] have shown that even at high concentration of 5%, nearly one third to one half of the root canals remain contaminated after instrumentation and irrigation with NaOCl. Berber et al.[26] studied the efficacy of various concentrations of NaOCl and instrumentation techniques in reducing *E faecalis* within root canals and dentinal tubules. They found no differences among concentrations in cleaning the root canals, but only at the higher concentrations was NaOCl able to disinfect the dentinal tubules independent of the canal preparation technique used. Others also demonstrated that lower concentrations are as effective or ineffective in eliminating bacteria.[25,27] Since the proteolytic effect of NaOCl is dependent on the amount of free available chlorine that is used up during the process by reacting with inorganic reducing substances, frequent irrigation with a lower concentration may achieve as much of a proteolytic effect as the use of a higher concentration.[24] In the light of these clinical studies, it can be concluded that the combination of an efficient microbial effect at low concentration—and a proportional increase in toxicity with higher concentration but with no demonstrable clinical effectiveness—demonstrates that NaOCl at concentrations higher than 0.5% to 1% offers little therapeutic value.[28]

The biocompatibility problems associated with the use of concentrated NaOCl have led to the use of substances with known antimicrobial properties and less toxicity, such as chlorhexidine. Chlorhexidine is an effective antiplaque agent and is routinely used in periodontal therapy and caries prevention. Its effectiveness against *Streptococcus mutans* and *Lactobacillus* is the basis for its use in caries prevention. Chlorhexidine gluconate is a cationic molecule that acts by adsorbing onto the cell wall of the microorganism, disrupting the integrity of the cytoplasmic membrane and causing leakage of the intracellular components. Chlorhexidine possesses adequate antimicrobial properties for an endodontic irrigant with 0.2% chlorhexidine, as shown by significant reduction in colony-forming units.[29,30] Sen et al.[31] found chlorhexidine to be effective against

C albicans. It has also been shown to be effective in eliminating bacteria penetrate up to 500 μm within dentinal tubules.[32] Chlorhexidine is bacteriostatic at low concentrations of 0.2%, bactericidal at high concentrations of 2%, and adsorbs to dental tissue and mucous membrane, resulting in its prolonged gradual release at therapeutic levels.[33] There is no doubt chlorhexidine has antimicrobial properties, but it is by no means clear if it is better than NaOCl as an endodontic irrigant. In an in vitro evaluation of the antimicrobial activity of chlorhexidine and sodium hypochlorite, it has been found that the timing required for 1.0% and 2.0% chlorhexidine liquid to eliminate all microorganisms was the same as that required for 5.25% NaOCl.[34] Similarly, Gomes et al.[35] found chlorhexidine in the liquid form at all concentrations tested (0.2%, 1%, and 2%) was as effective as 5.2% NaOCl in killing *E faecalis,* and Yesilsoy et al.[22] found 2.0% chlorhexidine to be as effective as 5.2% NaOCl in a Petri dish test using *S mutans*, *Peptostreptococcus micros*, *Prevotellaintermedia,* and *Porphyromonas gingivalis*. On the other hand, 4% NaOCl was found to be statistically better than 0.2% and 2% chlorhexidine against 4 black-pigmented gram-negative anaerobes and 4 facultative anaerobes.[23] Differences in the bacterial strains tested, growth media, methods, and conditions of these experiments could account for the conflicting results. Similar conflicting results have also been reported in experiments using extracted teeth, where a number of investigators found chlorhexidine to be more effective than NaOCl,[36-38] whereas others found either no difference in the efficacy of similar concentrations of chlorhexidine and NaOCl in elimination of bacteria from infected dentinal tubules in vitro[39] or found NaOCl to be superior to chlorhexidine in disinfecting the dentinal tubules.[40]

The application of chlorhexidine combined with Natrosol gel (Aqualon, Wilmington, DE) has been suggested as an intra canal medication.[41] Natrosol gel is a nonionic, inert, water soluble agent that can be completely removed from the canal with a flush of distilled water. Ferraz et al.[30] compared the antimicrobial and cleansing abilities of chlorhexidine solution alone and when combined with Natrosol gel. They found no significant difference between the gel and the solution in suppressing bacteria growth; however, the gel was found to produce a cleaner dentine surface, suggesting a better cleaning ability.

Chlorhexidine is an effective antimicrobial with low toxicity, but its main drawback is lack of tissue-dissolving ability. Attempts have been made to improve its properties by combining it with NaOCl. Kuruvilla and Kamath[37] compared the separate and combined effects of 2.5% NaOCl and 0.2% chlorhexidine in vivo. Teeth treated with chlorhexidine and NaOCl combined showed the greatest reduction in the number of microorganisms. This may be due to the formation of "chlorhexidine chloride," which has an increased ionizing capacity. Although this combination had good antimicrobial and tissue-dissolving abilities, it lacked the ability to remove the smear layer and then failed to achieve disinfection of the dentinal tubules.

Elimination of bacteria from infected dentinal tubules is crucial in the disinfection process of the root canal system. Penetration of bacteria into the dentinal tubules has been reported to range from 10 to 300 μm.[9,42] Despite the controversy regarding the effect of the smear layer on the bacterial colonization of the dentinal tubules[43,44] and because the smear layer itself can be contaminated and has the potential to protect bacteria within the dentinal tubules, it is sensible to remove the smear layer and allow disinfection of the entire root canal system.[45] Although NaOCl is efficient in dissolving organic components of the smear layer, its ability to remove inorganic components is limited. The combined use of NaOCl and a material that has an ability to remove the smear layer, such as EDTA, has therefore been advocated. Ethylene diamine tetraacetic acid has been used widely as root canal irrigant. It was found to be effective in lubricating instruments and in aiding mechanical preparation. It possesses antibacterial effects that may be considered suitable for clinical usage;[23] however, its antibacterial capabilities have recently been questioned.[40,46] A major advantage of EDTA over NaOCl is the action on the smear layer. Ethylene diamine tetraacetic acid was found to be effective in removing the smear layer[47,48]; however, it has been shown that EDTA is effective in removing the inorganic element but not the organic components.[49] Yoshida et al.[50] studied the effect of EDTA on removing the smear layer clinically. They found no bacteria in canals irrigated with EDTA compared with saline irrigation after 1 week. They concluded that because saline only removed the superficial bacterial, the remaining bacteria then repopulate the root canal. They further concluded that EDTA was successful in removing the smear layer and the bacteria.

The advantage of EDTA in removing the inorganic element of the smear layer and that of NaOCl in removing the organic components has led to the adoption of a combination of the 2 irrigants to achieve patent dentinal tubules and a clean surface even in the apical portion of the root canal.[51,52] Superior results have been reported when NaOCl is used as the last irrigant;[51] however, this combination has been shown to alter the mineral content of the root dentine.[52]

Although the chemical properties of the irrigant are important determining factors of its antimicrobial capabilities, other factors such as irrigation techniques may affect the final outcome of the antimicrobial effects of root canal irrigation. The use of ultrasonic energy together with root canal irrigation have been shown to be effective in removing debris and smear layer.[53-55] The direct effect of ultrasonic over syringe irrigation to remove bacteria from root canal walls has been studied by many investigators. Huque et al.[56] found ultrasonic irrigation with a high concentration of NaOCl superior to syringe irrigation, using the same concentration, for eliminating bacteria within the root dentine. However Siqueira et al.[57] found no difference in the antimicrobial effect of NaOCl with or without ultrasonic irrigation, and Briseno et al.[58] found 1% NaOCl syringe irrigation to be superior to 2% NaOCl ultrasonic irrigation for eliminating bacteria from infected root canals in vitro. The antibacterial effect of ultrasonic instrumentation in the treatment of infected root canals has also been evaluated clinically. Sjogren and Sundqvist[59] found that ultrasonic irrigation with 0.5% NaOCl eliminated the bacteria from the canals more efficiently than hand instrumentation alone. Other factors such as the depth of penetration of the irrigating needle have also been found to influence the mechanical removal of bacteria from the root canal, even when the irrigant has no antimicrobial effect. The mechanical efficacy of the irrigant in reducing intracanal bacteria was found to be significantly greater when the irrigant was delivered 1 mm compared with 5 mm from the working length.[60]

FUTURE DEVELOPMENT IN ROOT CANAL IRRIGATION

None of the previously mentioned root canal irrigation regimens is without limitations, and the search for an ideal root canal irrigant continues with the development of new materials and methods. One of these developments is the electrochemically activated (ECA) solutions that are produced from tap water and low-concentration salt solutions.[61,62] The physical and chemical nature of ECA solutions is not yet fully understood; however, it is claimed that 2 types of ECA solutions are produced, the anolyte and catholyte solutions. Anolyte has a high-oxidation potential and possesses antimicrobial properties. Catholyte is an alkaline solution with a high-reduction potential and is reputed to have a strong cleaning or detergent effect. After production, both these solutions remain in the active state for approximately 48 hours before the solution returns to the stable state, becoming inactive once more. Strong evidence for the antimicrobial nature of anolyte was reported,[63-65] where anolyte solution was found to be highly effective against *Mycobacterium tuberculosis, Escherichia coli, E faecalis,* and *Pseudomonas aeruginosa,* in addition to viruses, fungi, and protozoa.

The antimicrobial effectiveness of ECA solutions as endodontic irrigants has also been investigated. Marais and Williams[66] did not find ECA solution to be superior to NaOCl in eliminating bacteria in root canals in vivo. Solovyeva and Dummer[67]studied the cleaning effectiveness of root canal irrigation with ECA solution and found that it was similar to NaOCl in debris removal but was more effective that NaOCl in smear layer removal. Earlier studies found ECA solution to be effective in removing the smear layer.[68,69] In view of its safety compared with NaOCl, ECA solutions may have potential as a root canal irrigant and warrant further investigation.

Another material with a potential use as an antimicrobial root canal irrigant is Bio Pure MTAD (Dentsply, Tulsa, OK). It is a mixture of a tetracycline isomer, an acetic acid, and a detergent (Tween 80). MTAD was introduced by Torabinejad et al.[70] as a material to remove the smear layer. Subsequent in vitro experiments showed that this material effectively removed the smear layer.[71] When the antimicrobial effects of MTAD were compared with those of NaOCl and EDTA by using standard in vitro microbiological techniques, MTAD was significantly more effective;[46] however, these effects have recently been challenged by different investigators. Ruff et al.[72] reported superior antifungal effect of 6% NaOCl and 2% chlorhexidine compared with MTAD, and Clegg et al.[73] questioned the ability of MTAD to remove or disrupt bacterial biofilms in root canals. On the other hand, cytotoxicity studies of MTAD in comparison to the commonly used root canal irrigants and medicaments showed that MTAD is less cytotoxic than eugenol, 3% hydrogen peroxide, calcium hydroxide paste, 5.25% NaOCl, Peridex, and EDTA, and more cytotoxic than 2.63%, 1.31%, and 0.66% NaOCl.[74] More research will be needed before this material can be used routinely as a root canal irrigant.

Photoactivated disinfection is new technology that may be a less toxic alternative to chemical disinfectants and uses a combination of photosensitizing dye and a light of specific wavelength. This combination had been shown to kill a high population of bacteria in planktonic suspension, collagen, and carious dentine.[75,76] The use of photoactivated disinfection on commonly found bacteria in root canals has been reported to be effective.[77] Ozonated water has also been investigated as a root canal irrigant. Ozone is known to act as a strong antimicrobial agent[78] and has been shown to effectively disinfect bovine dentinal tubules in vivo.[79]

These developments in the field of root canal disinfection provide encouraging results for future development of novel irrigation materials and techniques that can be used instead of or as adjunct to the conventional materials currently in use.

ROOT CANAL MEDICATION

Following instrumentation and irrigation, the use of interappointment medication has been widely advocated to help eliminate remaining bacteria within the root canal system, reduce periapical inflammation and pain, and induce healing. Some medicaments are also claimed to help eliminate or reduce apical exudates, control inflammatory root resorption, and prevent contamination between appointments. It has been shown that the number of residual bacteria following instrumentation is usually low, but should the canal be left empty between appointments, the remaining bacteria can multiply to nearly the original levels.[11]

Root canal medicaments can be classified according to their chemical basis into phenolic compounds (e.g., eugenol and camphorated monochlorophenol [CMCP]), aldehydes (e.g., formocresol), halides (e.g., iodine-potassium-iodide), calcium hydroxide, antibiotics, and various combinations. The majority of these preparations are not used in contemporary endodontic practice due to the reported toxicities; however, calcium hydroxide and antibiotic-containing preparations remain the most commonly used root canal medicaments.

Calcium hydroxide

Calcium hydroxide was introduced to dentistry by Hermann at the beginning of the 20th century, and since then it has been widely used in endodontics.[80] It is a strong alkaline substance with a pH of approximately 12.5 and has various biologic properties that promoted its use in several clinical situations. Its dental use relates chiefly to its antibacterial properties and the ability to induce repair and to stimulate hard-tissue formation.[81] The main benefit of calcium hydroxide as an intracanal medicament lies in the bactericidal effect conferred by its high pH, and endodontic microorganisms are unable to survive in the highly alkaline environment provided by calcium hydroxide.[82]

The antimicrobial property of calcium hydroxide is related to the release of hydroxyl ions in an aqueous environment. Hydroxyl ions are highly oxidizing free radicals that destroy bacteria by damage to the cytoplasmic membrane, protein denaturation, and damage to the bacterial DNA. Several studies have demonstrated that calcium hydroxide exerts lethal effects on bacterial cells[83,84]; however, these effects were observed only when the substance was in direct contact with bacteria in solution, a situation that might not always be achievable clinically. Calcium hydroxide exerts antibacterial effects only if maintaining a very high pH. If calcium hydroxide diffuses widely, the hydroxyl ion concentration decreases and its antibacterial actions will be reduced. For calcium hydroxide to be an effective root canal dressing, the hydroxyl ions must be able to diffuse through dentine to kill bacteria in dentinal tubules. Studies have shown that hydroxyl ions derived from calcium hydroxide do diffuse through root dentine, but the change produced in dentine pH is both time and distance dependent,[85,86] making the placement technique and the dressing period important factors to be considered in evaluating the antibacterial effects of calcium hydroxide. The vehicle in which calcium hydroxide is mixed to form the paste affects not only the physical and chemical properties of the compound but also its antimicrobial effects and its clinical application.[87] In general, 3 types of vehicles are used: aqueous, viscous, or oily. Aqueous vehicles are water-soluble substances. They promote a high degree of solubility and rapid turnover of the paste, necessitating multiple redressing to achieve the desired effects. Viscous vehicles, on the other hand, promote slow solubility and hence longer dressing intervals. The high molecular weight of these vehicles minimizes the dispersion of calcium hydroxide into the tissues and maintains the paste in the desired area for as long as 2 to 4 months.[88] Examples of viscous vehicles are glycerin, polyethylene glycol, and propylene glycol. Oily vehicles are nonwater soluble and offer the lowest solubility and diffusion of the paste, and may remain within the root canal system for longer than the pastes containing aqueous or viscous vehicles. However, it has been shown recently[89] that pastes prepared with glycerin and polyethylene glycol needed more time to eliminate the microorganisms than the other pastes, confirming the work of Safavi and Nakayama,[90] who reported that high concentrations of glycerin and propylene glycol used as vehicles might decrease the effectiveness of calcium hydroxide, slowing the release of hydroxyl ions.

The antimicrobial effects of calcium hydroxide have also been evaluated by clinical studies where calcium hydroxide has been shown to successfully disinfect root canals following 1 month dressing in 97% of treated cases.[91] In a later study by the same group, the effectiveness was confirmed even when the dressing was retained in the root canal for only 1 week;[92] however, these impressive results with calcium hydroxide have not been reproduced in other studies where Cvek et al.,[93] Orstavik et al.,[94] and Peters et al.[95] have cast doubts over the antimicrobial effectiveness of calcium hydroxide by demonstrating in clinical studies that calcium hydroxide did limit bacterial growth but did not totally eliminate the bacteria from the root canals. Waltimo et al.[96] evaluated the clinical efficacy of chemomechanical preparation of the root canals with sodium hypochlorite and interappointment medication with calcium hydroxide in the control of root canal infection and healing of periapical lesions. They found that calcium hydroxide dressing between the appointments did not show the expected effect in disinfecting the root canal system and in treatment outcome. Similar results had also been shown by Tang et al.[97] in a clinical study on the antimicrobial effect of calcium hydroxide used as interappointment dressing. The disparity in the findings between these studies might be attributable to differences in methods adopted and the type of bacteria studied. Bacteria associated with persistent apical infections such as *E faecalis* are often more challenging to eradicate. Several studies have reported that calcium hydroxide is not effective in eliminating *E faecalis*, which is often associated with persistent endodontic infections.[98-100] Such bacteria can proficiently invade the dentinal tubules and have the ability to survive and buffer the high pH produced by calcium hydroxide.[101] In addition, dentine has also been found to have a buffering effect on high pH,[102] further compromising the antimicrobial effect of calcium hydroxide in disinfection of the dentinal tubules and effective elimination of *E faecalis*.

To improve its ability to disinfect the dentinal tubules, attempts have been made to combine calcium hydroxide with other medications such as iodine potassium iodine (IKI) to produce additive or synergistic effects. Unlike calcium hydroxide, IKI is known for its ability to diffuse through dentinal tubules and kill bacteria in vivo;[103] however, the duration of its antimicrobial efficiency is short. The combination of IKI and calcium hydroxide in vivo has been shown to be significantly better than pure calcium hydroxide in disinfecting the dentinal tubules.[104] In a clinical study, it was reported that treatment of root canals with IKI prior to calcium hydroxide dressing did not significantly reduce the amount of bacteria but that it might reduce the frequency of persisting strains of *E faecalis*.[105] The ability of calcium hydroxide to kill *E faecalis* has been shown to be improved by combining it with IKI or chlorhexidine.[106] Furthermore, the addition of chlorhexidine or IKI did not affect the alkalinity of the calcium hydroxide suspensions, and cytotoxicity tests indicated that the combinations were no more toxic than their individual components. A combination of calcium hydroxide/CMCP glycerin paste has been shown to rapidly eliminate bacteria in root canals.[8,100,107] The combination of calcium hydroxide with corticosteroid-antibiotic preparations has also been advocated as a root canal medicament. The mixing of these medicaments has been shown to alter the speed of diffusion of active ingredients to achieve higher intracanal concentration. In addition, the antibacterial effect was increased and the toxicity to periradicular tissues decreased.[108]

Despite the limitations of calcium hydroxide discussed in the aforementioned paragraphs, a recent evidence-based analysis of the antimicrobial effectiveness of intracanal medicaments showed that calcium hydroxide remains the best single medicament currently available to reduce the endodontic microbial flora.[109] Calcium hydroxide is being used heavily in dentistry, and particularly as a root canal medicament, with safe and with satisfactory clinical outcomes. Further research to develop mechanisms to maximize the antimicrobial efficacy of calcium hydroxide, in particular against *E faecalis,* is needed.

Antibiotic preparations

Antibiotic-containing preparations can be used in endodontic therapy as topical agents. However, the potential for bacterial resistance, the risk of drug hypersensitivity, and the potential to mask certain etiologic factors limit their usefulness. There is no clear scientific evidence for the use of topical antibiotics in root canal therapy. Early investigations evaluated 2 antibiotic-containing preparations: Grossman's polyantibiotic paste, which contains penicillin, bacitracin or chloramphenicol, and streptomycin,[110] and the second a mixture of neomycin, polymyxin, and nystatin.[111] Both of these had some limited efficacy as intracanal medicaments. A more recent study has shown that clindamycin gave no advantage as a root canal dressing when compared with conventional root canal dressings such as calcium hydroxide.[112] Further in vitro investigations have produced more favorable results when antibiotic mixtures such as ciprofloxacin, metronidazole, and minocycline have been used as topical root canal agents.[113,114] In an animal study, Windley et al.[115] examined the effects of a triple antibiotic paste of metronidazole, ciprofloxacin, and minocycline and found that it was effective in the disinfection of immature dog's teeth with apical periodontitis.

Topical corticosteroids have been used as anti-inflammatory agents in endodontics for many years,[116] and studies have shown that they are effective in reducing pain in teeth with vital pulps, but ineffective when the pulps were necrotic. Therefore, their use in painful necrotic pulps has not been advocated.[117] The most common commercial paste preparations available for use as root canal medicaments that contain antibiotics and corticosteroids are Septomixine, Pulpomixine (Septodont, St. Murr DesFosses, France), and Ledermix paste (Lederle Pharmaceutical, Wolfrathausen, Germany). Septomixine and Pulpomixine pastes contain neomycin and framycetin, respectively; however, none of these antibacterial agents is effective against the bacteria commonly involved in endodontic infections. The anti-inflammatory component of these preparations is the corticosteroid dexamethasone, which is less potent than other corticosteroids such as triamcinolone.

Ledermix is a water-soluble paste containing 1% triamcinolone and 3% demeclocycline. Triamcinolone is 4 times more potent than cortisone and hence can be used in low concentrations that are unlikely to result in systemic side effects.[118] Originally the manufacturer (Lederle Pharmaceutical) intended the corticosteroid to be the active ingredient; the antibiotic was added not for disinfection but rather to prevent overgrowth of microorganisms following the impairment of the immune defense by the corticosteroid. Studies on the antimicrobial effects of Ledermix produced conflicting results. Barker & Lockett[119] found Ledermix to be ineffective in eliminating *Streptococcus viridians* in root canals of dogs. Abbott et al.[118] investigated the distance and concentration of infiltration of Ledermix in dentinal tubules of teeth dressed with the medicament by using absorption spectrophotometry. They estimated that demeclocycline attained its highest concentration in the dentine adjacent to the root canal within the first day of application, with the initial rate of release about 10 times that of the release rate after 1week. A similar phenomenon was observed in the peripheral dentine. These results suggest that demeclocycline may be effective against bacteria within the first few days after Ledermix placement but the effect would not be of long duration. It has been reported that gram-positive microorganisms are more susceptible to lower concentrations of tetracycline than are gram-negative microorganisms.[120] Because gram-negative species dominate established endodontic infections,[4] the efficacy of Ledermix in treating endodontic infections may thus be questionable. Ledermix has some attractive features as an endodontic medicament and has proven to be useful clinically. Several studies have demonstrated its efficiency in treating acute pulpal and periapical inflammation.[121,122] Ledermix has been shown to effectively reduce the incidence of postoperative pain in endodontics.[123] However, the superiority of Ledermix over calcium hydroxide in reducing the incidence of postoperative pain associated with acute apical periodontitis is controversial. Ehrmann et al.[123] reported superior results with Ledermix over calcium hydroxide in reducing postoperative pain, whereas Fava[124] found no difference between the 2 medicaments in reducing postoperative pain. The control of postoperative pain and inflammation attributable to the use of Ledermix appear to be more likely 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 effects of Ledermix.

CONCLUSION

Elimination of microbial contamination from the root canal system is a prerequisite to the successful outcome of root canal treatment. The evidence shows that mechanical instrumentation, irrigation, and use of interappointment medication were all important in this regard. However, all of the currently available antimicrobial materials for root canal irrigation and medication have limitations, and the search continues for the ideal irrigant and intra-appointment medicament.[39]

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