

Review Article

Intra-canal medicaments: Recent concepts and comprehensive review

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ABSTRACT:

Pain may occur as a result of various causes such as microbial factors, change in the periapical tissue pressure, chemical mediators, change in the cyclic mediators, and various physiologic factors. The presence of micro-organisms as a result of failure to properly disinfect the canal is the most common cause of pain. Thus, endodontic therapy is primarily focused on maximum elimination of these bacteria. Antibacterial intra-canal dressing has been advocated to eliminate remaining bacteria after chemo-mechanical preparation. It is doubtful whether an intracanal medicament is routinely needed in root canal treatment of teeth containing vital pulp tissue. When the root canal is extensively infected and when interappointment time periods are long, there is merit in using an antibacterial intracanal medicament as part of controlled asepsis. Hence; in the present review, we aim to highlight the recent advances in the use of antibiotics as intra-canal medicaments.

Key words: Antibiotics, Intra-canal medicaments

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Introduction

Success in endodontic treatment was originally based on the triad of debridement, thorough disinfection, and obturation of root canal system, with each and every aspect equally important. At present, successful root canal treatment is based on much broader principles despite this core behind any successful treatment. This includes diagnosis and treatment planning; knowledge of anatomy and morphology; the traditional concepts of debridement, thorough disinfection, and obturation; and the coronal restoration.¹

Root canal instrumentation is usually accomplished by the use of endodontic instruments and irrigating solutions under aseptic conditions. Endodontic instruments have undergone a revolutionary change during the last decade of past century when they were manufactured mainly out of stainless steel. However, nowadays, NITI instruments have proven to be a valuable adjunct. NITI instruments have undergone a revolution with regards to different designs to produce cutting efficiency and resistance to fracture. In spite of all these advances, the chemo-mechanical preparation

and complete disinfection of root canal is the key to success of endodontic therapy.²⁻⁴

Intracanal medicaments have been thought an essential step in killing the bacteria in root canals; however, in modern endodontics, shaping and cleaning may be assuming greater importance than intracanal medicaments as a means of disinfecting root canals. Intracanal medicament is generally recommended when treatment cannot be completed in one appointment; there are chances that surviving intracanal bacteria often proliferate between appointments. Walton stated that "Intra-canal medicaments have traditionally gone hand-in-glove with endodontics. They are generally considered to be an integral part of treatment and important to the success of root canal therapy." However, intracanal medicaments in modern endodontics have a somewhat different rationale.⁵

Therefore it is important on our part to select a proper case and proper intracanal medicament for each and every patient individually and it is very prudent to understand that irrigation and local antibacterial dressings in the root canal are part of a concerted effort to control endodontic infections. Alone they

cannot guarantee success if there are problems in quality of some other parts of the treatment.⁶

ANTIBIOTICS AS INTRACANAL MEDICAMENTS

Commercial preparations in this group contain either one or a combination of antibiotics, and sometimes incorporate other compounds such as corticosteroids. Antibiotics can be used as an adjunct to endodontic treatment in a number of ways – locally (i.e., intracanal), systemically and prophylactically. Bacteria may be present within areas of the root canal system that are inaccessible to irrigants and to the mechanical cleaning processes within the canal. Hence, an antibiotic contained within an intracanal medicament must be able to diffuse into these areas to reduce the number of viable bacteria. If such a reduction is achieved, an improved periapical healing response would be expected.⁷

Nystatin replaces sodium caprylate as an antifungal agent and is available in the form of PBSN (polyantibiotic paste which suspended a silicone vehicle). Due to potential for sensitivity in topical use in allergic patient PBSN has largely fallen in usage. Neomycin is bactericidal against Gram-negative bacilli but it is ineffective against *Bacteroides* and related species, as well as against fungi. Polymyxin B sulphate is ineffective against Gram-positive bacteria, and it was demonstrated that a routine one-week application of Septomixine Forte was not effective in inhibiting residual intracanal bacterial growth between appointments. In addition, although the anti-inflammatory (corticosteroid) agent, dexamethasone (at a concentration of 0.05%), is clinically effective, triamcinolone is considered to have less systemic side effects.⁸

The primary interest of Schroeder and Triadan in the development of Ledermix paste was based on the use of corticosteroids to control pain and inflammation while the antimicrobial properties at the time were catered for by formalin based paste called Asphalin (introduced in 1921). The sole reason for adding the antibiotic component to Ledermix paste was to compensate for what was perceived to be a possible corticoid-induced reduction in the host immune response. Schroeder and Triadan initially incorporated chloramphenicol in their first trials but when Lederle Pharmaceuticals became the manufacturer, the antibiotic was changed to demeclocyclineHCl. Today, Ledermix paste remains a combination of the same tetracycline antibiotic, demeclocyclineHCl (at a concentration of 3.2%), and a corticosteroid, triamcinolone acetonide (concentration 1%), in a polyethylene glycol base. The two therapeutic components of Ledermix paste (i.e., triamcinolone and demeclocycline) are capable of diffusing through dentinal tubules and cementum to reach the periodontal and periapical tissues.⁹

Tetracyclines exhibit a level of substantivity due to their ability to form complexes with bivalent and

trivalent cations. It is for this same reason that they are deposited in teeth and bones during calcification. Ledermix is now the preferred medicament to use immediately after replantation as it reduces both inflammatory and replacement resorption. In another study, Ledermix paste, Septomixine Forte, and Calasept (a calcium hydroxide in saline paste) (Nordiska Dental, Angleholm, Sweden) were spiraled into root canals and left for seven days. Bacteriological samples were taken before and after the two-visit endodontic treatment.¹⁰

Ciprofloxacin is a synthetic fluoroquinolone with rapid bactericidal action. It inhibits the bacterial enzyme DNA gyrase, which nicks the double stranded DNA, introduces negative supercoil and then reseals the nicked end. The bactericidal action probably results from digestion of DNA by exonucleases whose production is signaled by the damaged DNA. It exhibits very potent activity against gram negative bacteria but very limited activity against gram positive bacteria. Most of the anaerobic bacteria are resistant to ciprofloxacin. Hence it is often combined with metronidazole in treating mixed infections.¹¹

LEDERMIX

Ledermix is a solution to the pain and inflammation patients experience in cases of pulpitis. Ledermix combines the antibiotic action of demeclocycline with the anti-inflammatory action of triamcinolone and is particularly useful as an emergency measure in endodontic therapy, where it can be used in root canals between appointments. Ledermix is available in combination kits comprising the dental paste and dental cement, with hardeners for fast or slow setting. The dental paste contains one third more steroid than the cement, and is preferred in the treatment of exposed pulp.¹²⁻¹⁵

Ledermix is used both as pulp capping agent and as an intracanal medicament. Ledermix paste is a combination of 3.2% demeclocyclineHCl and a steroid 1% triamcinoloneacetamide in polyethylene glycol base. Steroids mainly reduce the inflammation and pain, while the antibiotics limit the infection by the microbes. A modification of the paste system is available in cement form consisting of 0.7% triamcinolone, 3% demeclocycline and calcium salts, used for pulp capping, pulpotomy procedure and also as a liner for hypersensitive dentin.¹⁴⁻¹⁶

In a previous study, authors stated that the steroid and tetracycline lower the inflammatory response along with inhibition of clastic cell mediated resorption and also promoting periodontal healing in replanted teeth. One advantage of ledermix, paste is, it is water soluble, well rinsed out easily and does not cause systemic side effect in intradental use. In another study, author studied the discoloration caused by ledermix paste when used as an intracanal medicament and found this is mainly because of the presence of tetracycline in the formulation. It was

suggested that if the paste is placed in the canal below the CEJ, it reduced the staining effects.¹⁵⁻¹⁷

TRIPLE ANTIBIOTIC

Antibiotic therapy has become an inseparable part of diverse medical and medical-related treatments, and acts as the one of the main fronts against microorganisms. Various antibiotics with divergent formulas are used, for prevention and prophylaxis, to cure active and acute infections and diseases. There are different routes in classifying antibiotics; for example, these drugs can be divided into several subclasses; cillins, mycins and azoles etc, are some of examples of such divisions. In other schools of thought, they are categorized according to the types of bacteria they are effective against; like antibiotics that affect gram positive and gram-negative microorganisms or the ones which target obligate and facultative aerobes and anaerobes. Also, different sets of drugs, like penicillin and its derivatives, consist of diverse formula which represents their characteristics, features, and properties; e.g., amoxicillin differs from ampicillin and penicillin V, both in the range of bacteria it affects and in the way the drug is prescribed. Also, clindamycin, in spite of belonging to the same class of antibiotics, is different from erythromycin as far as microorganisms are concerned. Cillins generally strike gram-positive bacteria whilst an antibiotic like metronidazole is useful for combating gram-negative ones.¹⁸⁻²⁰

Tetracycline, including tetracycline-HCl, minocycline, demeclocycline and doxycycline are a group of broad-spectrum antibiotics effective against a wide range of microorganisms. Metronidazole is a nitroimidazole compound which exhibits a broad spectrum of activities against protozoa and anaerobic bacteria. Since it is famous for its effective antimicrobial activities against anaerobic cocci as well as gram-negative and gram-positive bacilli, it has been used widely in the periodontology in both systemic and local forms. Ciprofloxacin is a second-generation fluoroquinolone antibiotic. Its range of effect includes most strains of bacterial pathogens responsible for gastrointestinal, respiratory, urinary tract, and abdominal infections, including *Escherichia coli*, *Legionella pneumophila*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Moraxella catarrhalis*, *Pseudomonas aeruginosa*, methicillin-sensitive but not methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Enterococcus faecalis*, and *Streptococcus pyogenes*. Ciprofloxacin and other fluoroquinolones are being used for this wide broad spectrum of activities, their availability in both oral and intravenous formulations and their excellent tissue penetration.²⁰⁻²³

According to the various species of bacteria in an infected root canal, single empirical antibiotic does not seem to be enough in disinfecting a root canal. A non-specific antibiotic therapy will only result in

suppressing the natural microbial flora, and an opportunity for the persistent, virulent residual bacteria to repopulate the canal space. Therefore, in order to eliminate the canal pathogens thoroughly and break the resistance of the virulent bacteria, using a combination of antibiotics is necessary. The first experience of using antibiotics in endodontics was reported by Grossman which was a paste so called "PBSC" or "polyantibiotic paste". PBSC was a mixture of penicillin, streptomycin, bacitracin and caprylate sodium. Penicillin was effective on gram-positive organisms, streptomycin for gram-negative organisms, bacitracin for penicillin-resistant strains and caprylate sodium to target yeasts.²⁴⁻²⁶

Recently 'triple antibiotic paste' (TAP) was introduced especially for the regeneration and revascularization protocol and the treatment of open apex teeth with necrotic pulp. This material has also shown other applications in endodontics. Initially, TAP was largely developed by Hoshino and colleagues, who investigated the effectiveness of the paste on the removal of microorganisms from the root canals. Researchers have also used TAP in vitro to disinfect *Escherichia coli*-infected dentin. Later, particular attention was given to the antibiotic paste and its effect against microorganisms present in carious dentin and infected pulp. The outcome showed excellent results in the eradication of the bacteria from the radicular system.²²⁻²⁴

TAP is a combination of ciprofloxacin, metronidazole and minocycline. Metronidazole, as a nitroimidazole compound, is particularly toxic to anaerobes and is considered an antimicrobial agent against protozoa and anaerobic bacteria. Minocycline is bacteriostatic and shows activity against gram-positive and gram-negative bacteria. It also causes an increase in the amount of interleukin-10, which is an inflammatory cytokine. Moreover, ciprofloxacin — as a synthetic fluoroquinolone — possesses fast bactericidal action and exhibits high antimicrobial activity against gram-negative bacteria, whilst limited activity against gram-positive ones. Many anaerobic bacteria are resistant to ciprofloxacin. Hence, it is often used with metronidazole in treating mixed infections to compensate for its limited scope. Therefore, TAP can affect gram-negative, gram-positive, and anaerobic bacteria, and this combination can be effective against odontogenic microorganisms.²⁴⁻²⁶

CONCLUSION

When a tooth does not respond to root canal treatment, bacteriological sampling may be needed to determine the bacteria present in the root canal system. This will aid the choice of intracanal medicament and monitoring of the progress of treatment. Every case should be judged on the advantages and disadvantages of using an intracanal medicament. After all, what is removed from the root canal is of greater significance with regard to the

success of root canal treatment than what is placed in the root canal system.

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