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TOPICAL MEDICAMENTS IN THE TREATMENT OF INFECTED DENTAL ROOT CANAL

PRIMENA LOKALNIH PREPARATA U LEČENJU INFICIRANIH KANALA KORENA ZUBA

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Ključne reči

infekcija kanala korena zuba, endodontski tretman, intrakanalni medikamenti

Abstract

Bacteria and their by-products play an essential role in the development of dental pulp necrosis and periapical diseases. Therefore, the removal of pathogenic flora from the root canal system is the ultimate goal in endodontic treatment. Accepted steps of endodontic treatment in eradication of dental root canal infection include instrumental debridement by shaping and cleaning, irrigation by disinfectant solutions, such as sodium hypochlorite (NaOCl) and chlorhexidine (CHX) and in use of the antimicrobial agents. The choice of intracanal medicament depends on the proper diagnosis and of the treated state, as well as on the identification of causative bacteria and the mechanisms of their growth and survival. The most commonly used agents are Ca (OH)₂ and antibiotic pastes. Each of the agents has advantages and disadvantages. Therefore, the further clinical studies are needed in order to select the most effective agent and/or their corresponding combinations.

INTRODUCTION

Infection of the root canal teeth is caused by bacterial invasion from oral cavity, while in rare cases its origin may be periodontic. The most common carriers are *Streptococci*, *Staphylococci* and *Enterobacteriaceae*, including *Enterococcus faecalis*, produces gases followed by pain and swelling.

Untreated, the infection leads to the loss of teeth and jaw damage. Occasionally, the focal infection can spread systematically and cause an infective endocarditis. In some cases, systemic antibiotics are mandatory.

Treatment of the root canal infection is chemomechanical, i.e. instrumental-shaping and cleaning, followed by the use of irrigants and antimicrobials, including calcium hydroxide and antibiotic pastes as intracanal dressing. Antibiotic pastes contain one or more broad spectrum agents, sometimes combined with glucocorticoids, as anti-inflammatory and pain reliever medicaments.

Under the normal physiological conditions, pulp is protected from the injury and from harmful elements of oral cavity by the outer hard structures of dental tissue and the intact periodontium. Pulp may be damaged in several ways: by dental caries (bacteria and their products), traumatic injuries and iatrogenic factors (dentine hydration, toxic effect of filling materials) and damaged by restorations.

Bacteria, their antigens and byproducts of fibrous tissue may penetrate into pulp along open dental canaliculi, even in the early stages of these processes (1). As in all fibrous tissues, pulpa reacts by inflammation. The cause of inflammatory reaction is neutralization and elimination of harmful agents. When in the further development of inflammatory process sufficient number of bacteria reach pulp, local inflammation is irreversible (2). Reactive response may be destructive in nature and ends with severe pain and total tissue destruction (necrosis). Necrotic tissue is convenient medium, serving as primary food for the growth of microorganisms and their multiplication. Course and degree of the response to infection from the root canal depends on the amount of microbes (number of microorganisms and their pathogenic potential), the state of host body's self-protective potential and the passed time (3).

Microorganisms colonizing dental root canal may be freely floating as single (planktonic shape) or mutually bound. When the bacterial cells are densely packed and piled in extracellular polymer matrix from the host or bacterial tissue, the term biofilm is used ⁽³⁾. Biofilms, mostly composed from several types of bacteria, are multilayer and exists as aggregates on dental root canals, or as aggregates in necrotic tissue. Microorganisms, organized in biofilms, are one thousand times more resistant to antimicrobial agents ⁽⁴⁾.

Bacteria colonizing necrotic root canal come in contact with periodontal ligamentum across apical and lateral holes inducing damage and enhancing inflammatory changes ⁽⁵⁾.

Apical periodontitis represents an important defense mechanism, which goal is limitation of bacterial number transported from root canal and to prevent their passage in the neighbouring bone, as well as in the distant parts.

Epidemiological studies, performed on the samples formed from various populations, show that the apical periodontitis was frequently present in adult patients. In the series of published papers the prevalence of apical periodontitis ranged from 22% to 80% of the tested subjects. In the west countries, root canal filling is frequently practiced, and the cut off studies show that in the various types of population between 25% and 75% individuals have at least one tooth with filled root canal ⁽³⁾.

Microorganisms from the samples of root canal tooth prevalently are the same as those found in dental plaque, periodontal pockets and carious lesions. The majority of isolated strains from the initial cultures are obligate-strict anaerobes. Many genders and strains that are lately identified from the canal belong to the strict and facultative oral bacteria (3). They were Gram-positive cocci (Streptococcus, Enterococcus, Peptostreptococcus), Gram-positive bacilli (Actinomyces, Lactobacillus), Gram-negative cocci (Neisseria) Gram-negative bacilli (Prevotella, Fusobacterium) and fungi.

In order to provide successful root canal treatment, the precise cause of infection is essential. Bacterial culture has been for the long time considered as the standard method used in the research. However, the recent technological developments enabled the introduction of new methods: microscopic, immunological and molecular⁽⁶⁾.

Molecular methods (PCR-polymerase chain reaction) are much easier to perform, faster and much more sensitive compared to the standard methods ⁽⁶⁾. They also enable identification of the greater number of bacterial strains present in infected root canal, including those which identification previously has not been possible ⁽⁷⁾. The basic limitation of PCR is inability to differentiate dead from live bacteria, since the method is based on the gene segments identification.

Pathological processes in pulp and periapical tissue take place in the parts of teeth which are invisible by visual inspection. Instead, in order to make diagnosis, the clinician has to rely on the indirect information. Patient's awareness of pain, especially of its character, serves as an important clue of the endodontic state disease. Besides the anamnesis, diagnosis is made on the basis of the vitality test, by percussion, palpation and radiography ⁽³⁾.

Radiographic image shows the periapical tissue reaction as localized lightening around the root apex, since due the inflammatory process, the adjacent bone is resorbed. This state may, but not necessarily has to be followed by pain, teeth sensitivity to touch and by various degree of swelling.

Treatment of necrotic pulp in the essence is teeth root canal treatment aimed at the fight of intracanal infection. The treatment is essential in the prevention of the passage of bacteria and their byproducts from root canal to the other

organs. If the treatment is successful, clinical symptoms of apical periodontitis (sensitivity, pain, swelling, fistula) disappear ⁽³⁾. Successful treatment is confirmed by radiographic image which show the disappearance of apical periodontitis and complete tissue reorganization.

If there was no active treatment, infective processes connected with canal system may cause not only complications with local manifestations, but also the lesions in the other organs, including infective endocarditis.

TREATMENT

The main goal of endodontic treatment is complete removal of bacteria, their byproducts and pulp remnants from the infected root canal before its filling. The procedure of root canal cleaning and shaping is the most efficient way in removing bacteria, but due to the dental tube complex anatomy of root canal, it can't eliminate them completely. Because of the complexity of root canal system some of the bacteria take refuge in ramifications, isthmuses, apical deltas and dentinal tubules even after chemomechanical preparation that needs to be eliminated by using intracanal medicaments (8). In the elimination of microorganisms from root canal system, various mechanical instrumental techniques, irrigation and medication are used.

Accepted treatment procedures to eliminate the infection include mechanical shaping or smoothing, irrigation with disinfectant agents such us sodium hypochlorite or chlorhexidine, application of an inter-appointment dressing containing an antimicrobial agent and sealing of the root canal ⁽⁹⁾.

Table shows the active substances and their form of application in the treatment of infected dental root canal.

Active substance	Formulation
Sodium hypochlorite (0,5% -5,25%)	Solution
Chlorhexidine 2,5%	Solution
Chlorhexidine 2,5%	Gel
Calcium hydroxide	Paste
Demeclocycline HCl (tetracycline) +	
Triamcinolone acetonide (corticosteroid)	Paste
(LedermixTM pasta) *	
Neomycin + Polymin B sulphate	
(Septomixine forte) *	Paste
Metronidazol + Cirofloksacin + Minocycline	
(3 – MixMP) *	Paste

Table 1. Preparations for the local use in the treatment of infected teeth root canal
*Not so far approved for the use in our country

The aims of irrigation and requested properties of irrigants

The aims of irrigation are:

- decrease of intracanal microorganisms number and neutralization of endotoxins
 - dissolution of vital and necrotic pulp tissue
 - lubrication of canal barrier and instruments
 - removal of dental remnants

Requested irrigant's properties

- wide antimicrobial spectrum
- biocompatibility
- the ability of tissue disruption

No one of the existing solutions for the irrigation possesses all mentioned properties. It has to be pointed out that the efficacy of the irrigation agents, regarding their desinfectant power is limited, due to the inter-reaction of the solution with dentin, dentin detritus and organic components present in canals with necrotic pulp, as well as with serum proteins and mass of bacteria. This means that the endodontic desinfectants are not clinically efficient as in *in vitro* studies. The most frequently used irrigant agents are NaOCl and CHX.

Sodium hypochlorite (NaOCl)

NaOCl solution is the most frequently used irrigant in endodontics ⁽¹⁰⁾. This compound dissociates in water in sodium and hypochlorite ions. Between pH 4 and pH 7, chlorine from NaOCl exists predominantly as HClO (hypochlorous acid), whereas above pH 9, OCl- predominates ⁽¹¹⁾. Although the antimicrobial effectiveness of hypochlorous acid is greater than that of hypochlorite, in the clinically used NaOCl solutions, the entire available chlorine is in the form of OCl-, as the pH of the solution is normally about 12 ⁽¹⁰⁾.

In endodontic treatment, NaOCl is used in concentrations ranging from 0.5% to 5.25% ⁽¹¹⁾. Unbufferred solutions with pH ranged from 11 to 12, in 0.5% up to 5.25%, or Dakin's buffered solution with pH of 9 is also available. The antimicrobial effects of these solutions are equal.

NaOCl solution dissolves pulp remnants of vital and necrotic tissues, organic dentin components and organic remnants of smear layer. The ability of NaOCl to disrupt tissues is significantly higher from the other irrigants. Neutralization or inactivation of lipopolysaccharides is recorded during the use of NaOCl solution ⁽¹²⁾. However, NaOCl is not able to remove the smear layer.

Sodium hypochlorite is characterized by having strong antibacterial activity with comparably short contact times (11). Even the resistant Candida albicans was killed in vitro investigation (14) and one clinical study (15) confirmed the susceptibility of C. albicans to NaOCl. In addition, several Gram-negative anaerobic bacteria, typically found in primary root canal infection, displayed a high susceptibility to NaOCl in concentrations ranging from 0,5% to 5% (14). In contrast to this, based on the results of both laboratory studies and one clinical report evaluating microbiological samples of previously root-filled teeth with apical periodontitis (15), E. faecalis was much more resistant to NaOCl than the aforementioned microbes. However, despite the reduced effectiveness of NaOCl against E.faecalis, NaOCL has the unique ability to disrupt or to remove biofilms (16). In a comparative study on the effect of different irrigants against E. faecalis biofilms, both 5,25% and 1% NaOCl killed more than 99.7% of bacteria after contact times of 1 or 5 minutes, while 2% chlorhexidine and MTDA killed only 60.5% and 16% of the biofilm bacteria respectively (17). Therefore current evidence indicate that NaOCl is distinctly more effective in rendering biofilm bacteria nonviable and physically removing the biofilm compared with other commonly used irrigants. Most in vivo studies showed no significant difference in antibacterial activity between 0,5%, 1%, 2,5% and 5% solutions against both *E.faecalis* and a mixed anaerobic flora ⁽¹⁸⁾. The tissue-dissolution capability and the antimicrobial efficacy, as well as the toxicity of NaOCl depend on the concentration of the solution. The higher the concentration of the solution the greater is cytotoxicity ⁽¹⁹⁾. Thus, 5.25% solution shows higher toxicity than 0.5% or 1% solutions

The results of comparative studies did not show the differences in disruption efficacy among the NaOCl solutions of various concentrations. The 1% solution of NaOCl is sufficient for the dissolution of pulp tissue. The tissue dissolution capacity depends more on the amount of the solution than on its concentration. The NaOCl solution has to be several times replaced during the treatment. It is advised in clinical practice to use the concentration of solutions ranging from 0.5% to 1% (10). Solutes of these concentrations possess the best balance among the capacity of tissue dissolution, antimicrobial efficacy and biocompatibility. Instead of using higher solution concentrations, the activity of NaOCl can be improved by the increase of temperature of lower concentrations (10). Several studies have reported that the warmer NaOCl solution dissolved organic tissue much better than non-warmed one. It has been proven that 1% NaOCl solution at the temperature of 450C dissolves pulp tissue more efficiently than 5.25% solution at the temperature of 200C (20).

The volume of irrigant is also clinically relevant. However, an increasing in the volume of the irrigant used is correlated with the reduction of intra-radicular microorganisms, and improves canal cleanliness. Yamada at al.⁽¹³⁾ recommended at least 10-20 ml of irrigant for each canal, followed by a final high volume flush of more than 5 ml after the shaping procedure has been completed.

Although allergic reactions to NaOCl are rare, there are several studies concerning the potential risk for the development of such reactions. NaOCl is caustic if accidentally extruded into periapical tissues or adjacent anatomical structures such as the maxillary sinus. In the case of accidental injection of NaOCl into periapical tissues, emphysema may develop within 10-20 min. Furthermore, oedema and paraesthesia may result due to the tissue dissolving capability of NaOCl. An even more serious development is ecchymosis, which is associated with severe pain and profuse interstitial bleeding (21).

Chlorhexidine (CHX)

The solution of CHX is an accepted agent for the tooth canal irrigation and is used in 2% concentration. It has wide antimicrobial spectrum of activity and is efficient against Gram positive and Gram negative bacteria, as well as against fungi. It is also used as a gel.

The mechanism of its action is based on the interaction between CHX cation negative phosphate groups on the bacterial cell wall. The permeability of cell wall is increased, enabling thus penetration of CHX with its consequent toxic effects. In the lower concentrations, CHX shows bacteriostatic effect, while its higher concentrations are bactericidal, causing cytoplasm precipitation or coagulation ⁽²²⁾.

Due to its cationic properties, CHX may be bound to dentin and to enamel $^{(23)}$ and be by the time gradually

released. Due to this phenomenon, which has not been observed with the other irrigants, CHX has prolonged antimicrobial action 10 min after its flush. That is why the irrigant antimicrobial effect of CHX is unique, surpassing its flushing duration ⁽⁴⁾.

Recent studies confirmed biocompatibility of 2% CHX solution (24).

CHX gel was proposed as an alternative for 5.25% NaOCl, used as a root canal disinfectant solution. Gell consists of the base (1% natrosol), which represents nonionic, highly efficient, inert and hydrosoluble agent with 2% gluconate (pH 7,0) used as endodontic irrigans in an *in vitro study*. The results have shown that 2% CHX as a gel led to the cleaner surface of the teeth root canal, with the similar antimicrobial effects as NaOCl or CHX solutions. Dametto et al. (25) in an *in vitro* study have evaluated antimicrobial efficacy of CHX 2% gel applied to the teeth infected with *E. faecalis* and compared it with the other endodontic irrigants (CHX 2% and 5.25% NaOCl solutions). The results have shown that 2% CHX gel and CHX solution demonstrated higher antimicrobial activity in relation to 5.25% NaOCl solution.

CHX gel is less toxic to the periapical tissue. Gel viscosity maintains the contact of active agent with the root canal barrier and dentine tubules.

In a study in rats, root canals with induced periapical periodontitis were temporarily filled with CHX 2% gel. Histological studies after seven days have shown that the use of the gel had the favourable effect on periapical regeneration, with no signs of inflammation ⁽²⁶⁾. These results correlated with the findings in periapical regeneration in dogs, after the use of 2% CHX solution for root canal irrigation ⁽²⁷⁾. CHX has shown to be compatible, since it did not induce significant inflammatory response ⁽²⁴⁾.

According to the *in vitro* studies, CHX inhibits *E. fae-calis* after the short period of contact and at the low concentrations. In the *in vitro* studies CHX was more effective than NaOCl. In several other studies also *in vitro*, CHX was very effective against fungi ⁽²⁷⁾. Two microorganisms, *E. faecalis* and *C. albicans* are responsible for endodontic disease and in most of the cases are linked with apical periodontitis. Due to the efficacy of CHX against Gram positive bacteria, *E. faecalis* and *C. Albicans*, CHX is recommended in the root canal recurrent treatment.

Although the sensitivity to CHX is rare, it has been shown that CHX may be the potential cause of anaphylactic reactions, even anaphylactic shock ⁽²⁸⁾. Hypersensitivity reaction was described as the contact dermatitis and photosensitivity. The application of CHX on oral mucosa or intact skin may cause allergic reactions.

Intracanal agents

Valton wrote: "Intracanal medicaments traditionally go hand in hand with endodontium. They are considered to be integral part of the treatment and are important for the success of the root canal treatment".

Intracanal agents are used in endodontic treatment in order to:

- Eliminate or destroy the residual viable bacteria in the root canal system, which have not been destroyed chemomechanically

- Decrease periradicular inflammation, reducing thus pain
 - Help in elimination of apical exudates if present
- Prevent recurrent root canal infection, since they act as chemical and physical barrier, if in the meantime transitory restoration fails.

Intracanal medication is mostly needed in the cases of bacterial resistance to the routine treatment, and when endodontic treatment cannot be performed because of the pain or permanent exudation.

Calcium hydroxide (Ca)OH),

Calcium hydroxide was used for the first time by Herman 1830. for pulp dressing, while today is used in stomatology, particularly in endodontology as intracanal medicament.

It is considered that Ca(OH)₂ can fulfil many properties of an ideal canal medicament, due to its antibacterial effectiveness, as well as to its ability to provoke tissue formation and provide canal closure.

Calcium hydroxide is slightly soluble in water, with the high pH (12.5 to 12.8) and is insoluble in alcohol. Its low water solubility is a useful feature, because it enables the direct, long term contact with vital tissue before it becomes dissolved in the tissue fluid. Calcium hydroxide also denatures and detoxifies bacterial byproducts, such as lipopolysaccharides. Calcium hydroxide must be placed in tight contact with the root canal walls because its effectiveness depends on the degree of contact with the walls as well as its antibacterial activity *per se*. Due to the inherent dentine buffer properties, diffusion of OH- ions is slow ⁽²⁹⁾. The presence of calcium ions at the sight of its action is useful, because of its role in cell stimulation, migration and mineralization ⁽³⁰⁾.

Calcium hydroxide acts on bacteria by chemical and physical mechanisms. Chemically, it damages microbial cytoplasmatic membranes by direct action of OH- groups, inhibits the enzyme activity, disrupts metabolism of cells and prevents DNA replication. Physically, Ca(OH)₂ acts as a barrier fulfilling intracanal space and preventing the passage of bacteria into the root canal system. It also kills residual microorganisms by withholding the substrates for their growth and replication.

Biological features of Ca(OH)₂ include biocompatibility (due to its low water solubility and limited diffusion), the ability to induce the treatment of periapical and hard tissue around the teeth with infected canals and to stimulate periapical healing (31).

Limited efficacy during the short-term use of $Ca(OH)_2$ in disinfection of dentine tubules is the consequence of several factors ⁽³²⁾:

- The inhibitory effect of dental proteins, particularly in regard to the ability of OH- ions to reach the apical third and perform their antibacterial effect. Hydroxyl ions diffuse faster through dentine in the cervical third of the root than in apical third, due to the fewer canal numbers and smaller diameter in the apical third.
- Low solubility and slow diffusion of Ca(OH)₂ may impede fast pH increase to the level necessary for the bacterial elimination in dentine tubules.

- Dense bacterial biofilms in dental tubules protect bacteria present deeper in the tubules
- Necrotic tissue in ramifications and irregularities protect bacteria from Ca(OH)₂ action
- The ability of *E. Faecalis* to colonize inside dentine tubules, avoiding thus the action OH-ions.

Shortages of $Ca(OH)_2$ are also the difficulties in removing it from the teeth root canal.

Several studies questioned the use of Ca(OH)₂ in bacterial eradication. Sandquist et al. ⁽³³⁾ have shown that Ca(OH)₂ eliminates E. Faecalis when present in the small number, as in infected teeth without previous root filling, but not in the teeth with previous root filling, where *E. Faecalis* is present in the large number. De Souza et al. ⁽³⁴⁾ used Ca(OH)₂ and recorded the decrease of the most present strains, but with the modest increase of the number of *A. actinomycetemcomitans, E. Corrodens* i *E. Nodatum organisms*. Waltimo et al. ⁽³⁵⁾ have shown in a in vitro study that Candida was more resistant to the action of saturated Ca(OH)₂ than *E. faecalis*. Enterococci and fungi persist in the high alkalinity, and are capable to survive in the canal fullfilled with Ca(OH)₂ ⁽³⁾.

Regarding the limited efficiency on *E. faecalis* and *C. albicans*, calcium hydroxide cannot be considered as the medicament for all cases of root canal infections.

Antibiotic pastes

The root canal infections are polymicrobial, i.e. arise from aerobic and anaerobic bacteria, and it is hard to believe that single antibiotic will be sufficient for the canal sterilization. Common products from this group contain one antibiotic or their combinations, sometimes combined with glucocorticoids.

Antibiotics in endodontics may be used locally, systemically and prophylactically.

Bacteria may be present in canal space which is inaccessible for the irrigation agents and to the instruments for mechanical cleaning. But antibiotics can diffuse to the root canal and eliminate bacteria.

The first use of local antibiotic in endodontic treatment was registered in 1951, when Grossman used polyantibiotic paste known as PBSC ⁽³⁶⁾. PBSC contained penicillin against Gram positive microorganisms, bacitracin for penicillin resistant microorganisms, streptomycin for Gram negative microorganisms and sodium caprylate against fungi. Penicillin is not used today, because of the increased resistance and potential allergic reactions.

Two the most known current antibiotic preparations are Ledermix paste and Septomixine forte. They both contain glucocorticoids as anti-inflammatory agents.

Ledermix paste

Ledrmix paste was approved for the use in Europe in 1962. Its composition has meanwhile been changed, containing now demeclocycline HCl (3.2%) and triamnicolone acetonide (1%).

The two components of Ledermix paste are able to diffuse through dentine tubules and cement and reach periodontal and periapical tissues ⁽³⁷⁾. Abbott et al. ⁽³⁸⁾ have shown that the dental tubules are the main supplier of periradicular tissue by active components, while apical foramen is of less importance.

Ledermix paste has also been shown to be useful in pain decrease after chemomechanic preparation of root canal. Ehrman et al. ⁽³⁹⁾ found that Ledermix paste led to the greatest postoperative pain relief, compared to the other teeth treated by Ca(OH)₂, being also confirmed by several other authors ⁽⁴⁰⁾. Negm reported that more than 85% of cases were with the complete pain relief after one hour, and more than 93% were free of pain 24 hours after the treatment ⁽⁴¹⁾.

Septomixine forte

Septomixine forte is composed of two antibiotics: neomycin sulfate and polymixyn B sulfate.

None of them can be considered convenient for the use against the common endodontic bacteria, because of their inadequate spectrum of activity ⁽³⁶⁾. Neomycin is bactericidal for Gram negative bacteria, but is ineffective against *Bacteroides*. Polymixyn B is not efficient against Gram positive bacteria. Tang et al. ⁽⁴²⁾ have shown that usual once weekly use of Septomixine forte was not successful in growth inhibition of residual bacteria between the appointments. By the addition of an anti-inflammatory agent (glucocorticoid) 0.05% dexamethasone, the efficacy of Septomixine forte was increased.

Triple antibiotic paste (3-MIX MP)

The most commonly used is the combination of three antibiotics. Sato et al. were the first that use triple antibiotic paste, containing metronidazole, ciprofloxacin and minocycline ⁽⁴³⁾. The commercial name of the paste is 3-MIX MP.

Metronidazole is nitroimidazole derivative, selectively toxic to anaerobic bacteria. It also shows wide spectrum of antimicrobial activity against protozoa and anaerobic bacteria. Presence of some redox proteins reduce nitro group of metronidazole producing intracellular free radicals which damage bacterial DNA and rapid cell death (44).

Minocycline is polysynthetic tetracycline derivative and acts primarily as bacteriostatic, by binding to 30s ribosome with consequent inhibition of protein synthesis in sensitive bacteria. It possesses broad activity spectrum against Gram positive and Gram negative bacteria.

Ciprofloxacin is a synthetic fluoroquinolone derivative with rapid bactericidal effect. Bactericidal effect is probably due to cellular DNA damage. It is effective against Gram negative bacteria, while its action against Gram positive bacteria is limited. Many of Gram negative bacteria are resistant to ciprofloxacin. In the case of mixed infections, it is often combined with metronidazole. Metronidazole and ciprofloxacin may generate fibroblasts, representing thus favourable effect in regenerative processes ⁽⁴⁵⁾. It has also been shown that each of the three antibiotics used singly are not fully effective in the elimination of bacteria, while their combination results in the complete eradication. Hoshino et al. ⁽⁴⁶⁾ recommended the mixture of metronidazole (500 mg), minocycline (100 mg) and ciprofloxacin (200 mg) in ratio of 1:1:1 for 3MIX formulation.

CONCLUSION

The aim of endodontic teeth treatment with pulp necrosis and periapical infection is the elimination of microorganisms from the root canal system. The choice of intracanal medicament to be used during the endodontic treatment depends on diagnosis and the state to be treated. Along with chemomechanic preparation, the use of sodium hypochlorite as irrigant is recommended, with the volume of 2.5 ml/canal, while for the final flushing the volume of 5-10 ml is required. In the case of recurrent infection, in addition to NaOCl solution, 2% chlorhexidine solution is used as flushing agent. In periapical periodonttis, the majority of authors

recommend calcium hydroxide as intraflushing canal medicament. However, calcium hydroxide cannot be universal agent, since it is not equally effective against all bacteria present in the infected root canal. Chlorhexidine gel 2% is recommended as a second choice. In the control of pain and inflammation, antibiotic paste combined with glucocorticoid is recommended. In order to provide new, more effective single or combined medicament for the treatment of infected root teeth canal, instead of currently used with their advantages and disadvantages, further clinical and fundamental studies are necessary.

Sažetak

Bakterije imaju glavnu ulogu u razvoju nekroze zubne pulpe i periapikalnih oboljenja. Eliminacija patogene mikroflore iz sistema kanala korena zuba je osnovni cilj endodontske terapije. Prihvaćeni postupci u endodontskom tretmanu u eliminaciji infekcije uključuju debridman kanala korena sa instrumentacijom, irigaciju sa dezinfekcionim rastvorima kao što su natrijum hipohlorit (NaOCl) i hlorheksidin (CHX) i primenu nekog intrakanalnog medikamenta sa antimikrobnim dejstvom. Izbor interkanalnog medikamenta zavisi od tačne dijagnoze, stanja koje se tretira kao i poznavanje mikroorganizama koji su izazvali infekciju i mehanizama njihovog rasta i preživljavanja. Obično korišćeni medikamenti su preparati Ca(OH)₂ i antibiotske paste. Svi preparati imaju prednosti i nedostatke, ali dalja istraživanja su potrebna da bi se izabrali preparati najefikasniji u lečenju inficiranog kanala korena zuba.

REFERENCES

- 1. Bergenholtz G. Pathogenic mechanisms in pulpal disease. J Endod 1990; 16: 98-101.
- 2. Hahn CL, Best AM, Tew JG. Cykotine induction by Streptococcus mutans and pulpal pathogenesis. Infect Immun 2000; 68: 6785-6789
- 3. Bergenholtz G, Horsted-Bindslev P, Reit C. Textbook of Endodontology. Second edition. Wiley-Blackwell; 2010.
- 4. Schafer E. Irrigation of the root canal. Endo 2007; 1(1): 11-27.
- 5. Siqueira J, Rocas I. Bacterial Pathogenesis and Mediators in Apical Periodontitis. Braz Dent J 2007; 18(4): 267-280.
- 6. Peciuliene V, Maneliene R, Balcikonyte E, Drukteinis S, Rutkunas V. Microorganisms in root canal infections: a review. Stomatologija, Baltic Dental and Maxillofacial Journal 2008; 10: 4-9.
- 7. Rolph HJ, Lennon A, Riggio MP et al. Molecular identification of microorganisms from endodontic infections. J Clin Microbiol 2001: 39: 3282-9.
- 8. Barbosa CAM, Goncalves RB, Siqueira JF, De Uzeda M. Evaluation of the antibacterial activities of calcium hydroxide, chlorhexidine, and camphorated paramonochlorophenol as intra canal medicament. A clinical and laboratory study. JEndodon 1997; 23: 297-299.
- 9. Sedgley C. Root canal irrigation—A historical perspective. J Hist Dent. 2004; 52: 61–5.
- 10.Zehnder M. Root canal irrigants. J Endod 2006; 32: 489-398.

- 11. McDonnell G, Russell D. Antiseptics and disinfectans: activity, action and resistance. Clin Microbial Rev 1999; 12:147-179.
- 12. Silva IA, Leonardo MR, Assed S, Tanomary Filho M. Histological study of the effect of some irriganting solutions on bacterial endotoxin in dogs. Braz Dent J 2004; 15: 109-114.
- 13. Yamada RS, Armas A, Goldman M, Lin PS. A scanning electron microscopic emparasion of a high volume final flush with several irrigating solutions. Part 3. J Endod 1983; 9: 137-142.
- 14. Viana ME, Gomes BP, Berber VB, Zaia AA, Ferraz CC, de Souza-Filho Fl. In vitro evaluation of the antimicrobial activity of chlorhexidine and sodium hypochlorite. Oral Surg. Orall med. Oral Pathol. Oral Radiol. Endod 2004; 97: 79-84.
- 15. Peciuliene V, Reynaud A, Balciuniene I, Haapasalo M. Isolation of yeasts and enteric bacteria in root filled teeth with chronic apical periodontitis. Int EndodJ 2001; 34: 429-434.
- 16. Spratt DA, Pratten J, Wiklson M, Gulabivala K. An in vitro evaluation of the antimicrobial efficiacy of irrigants on biofilms of root canal isolates. Int Endod J 2001; 34: 300-307.
- 17. Dunavant TR, Pratten J, Glickman GN, Solomon ES, Honeyman AL. Comparative evaluation of endodontic irrigants against Enterococus faecalis biofilms. J Endod 2006; 32: 527-531.
- 18. Siqueira JF, Rocas IN, Santos SR, Lima KC, Magalhaes FA, de Uzeda M. Efficacy of instrumentation techniques and irrigation regiments in reducing the bacterial population within root canal. J Endod 2002; 28: 181-184.

- 19. Chang YC, Huang FM, Tai KW, Chou MY. The effect of sodium hypochlorite and chloehexidine on cultured human periodontal ligament cells. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001; 92: 446-450.
- 20. Sirtes G, Waltimo T, Schaetzle M, Zehnder M. The effects of temperature on sodium hypochlorite short term stability, pulp dissolution capacity, and antimicrobial eficacy. J Endod 2005; 31: 669-671.
- 21. Hulsmann M, Hahn W. Complications during root canal irrigation: literature review and case reports. Int Endod J 2000; 33: 186-193.
- 22. Gomes BPFA, Souza SFC, Ferraz CCR, et al. Effectiveness of 2% chlorhexidine gel and calcium hydroxide against Enterococcus faecalis in bovine root dentine in vitro. Int Endod J 2003;36:267-275.
- 23. White RR, Janer LR, Hays GL. Residual antimicrobial activity associated with a chlorhexidine endodontic irrigant used with sodium hypochlorite. Am J Dent 1999; 12: 148-150.
- 24. Zamany A, Safavi K, Spangberg LS. The effect of chlorhexidine as an endodontic disinfectant. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003; 96: 1290-1294.
- 25. Dametto FR, Ferraz CC, Gomes BP, Zaia AA, Teixeira FB, de Souza-Filho FJ. In vitro assessment of the immediate and prolonged antimicrobial action of chlorhexidine gel as an endodontic irrigant against Enterococcus faecalis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2005;99(6):768–72.
- 26. Dammaschke T, Schneider U, Stratmann U, Mokrys K, Yoo JM, Schafer E. Effect of root canal dressings on the repair of

- inflamed periapical tissue. Acta Odont Scand 2005; 63: 143-152.
- 27. Tanomaru Filho M, Leonardo MR, Silva LAB, Anibal FF, Facciplo LH. Inflammatory response to different endodontic irrigation solutions. Int Endod J 2002; 35: 735-739.
- Naenni N, Thoma K, Zehnder M. Soft tissue dissolution capacity of currently used and potential endodontic irrigants. J Endod 2004; 30: 785-787.
- 29. Siqueira JF Jr, Lopes HP. Mechanisms of antimicrobial activity of calcium hydroxide: a critical review. Int Endod J 1999; 32: 361-369
- 30. Rehman K, Saunders WP, Foye RH, Sharkey SW. Calcium ion diffusion from calcium hydroxide-containing materials in endodontically-treated teeth: an in vitro study. Int Endod J 1996; 29: 271-279.
- 31. Tang G, Samaranayake LP, Yip H-K. Molecular evaluation of residual endodontic micro-organisms after instrumentation, irrigation and medication with either calcium hydroxide or Septomixine. Oral Dis 2004; 10: 389-397
- 32. Siqueira JF Jr, Lopes HP. Mechanisms of antimicrobial activity of calcium hydroxide: a critical review. Int Endod J 1999; 32: 361-369
- 33. Sundqvist G, Figdor D, Persson S, Sjögren U. Microbiologic analysis of teeth with

- failed endodontic treatment and the outcome of conservative re-treatment. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998; 85: 86-93.
- 34. De Souza CAS, Teles RP, Souto R, Chaves MAE, Colombo APV. Endodontic therapy associated with calcium hydroxide as an intracanal dressing: microbiologic evaluation by the checkerboard DNA-DNA hybridization technique. J Endod 2005; 31: 79-83.
- 35. Waltimo TMT, Sirén EK, Orstavik D, Haapasalo MO. Susceptibility of oral Candida species to calcium hydroxide in vitro. Int Endod J 1999; 32: 94-98.
- 36. Abbott PV, Hume WR, Pearman JM. Antibiotics and endodontics. Aust Dent J 1990; 35: 50-60
- 37. Abbott PV. Medicaments: aids to success in endodontics. Part 1. A review of literature. Aust Dent J 1990;35:438-448.
- 38. Abbott PV, Heithersay GS, Hume WR. Release and diffusion through human tooth roots in vitro of corticosteroid and tetracycline trace molecules from Ledermix paste. Endod Dent Traumatol 1988;4:55-62.
- 39. Ehrmann EH, Messer HH, Adams GG. The relationship of intracanal medicaments to postoperative pain in endodontics. Int Endod J 2003;36:868-875.
- 40. Ehrmann EH. The effect of triamcinolone with tetracycline on the dental pulp and apical periodontium. J Prosthet Dent 1965; 15: 144-152.

- 41. Negm MM. Intracanal use of a corticosteroid-antibiotic compound for the management of post-treatment endodontic pain. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001:92:435-439.
- 42. Tang G, Samaranayake LP, Yip H-K. Molecular evaluation of residual endodontic micro-organisms after instrumentation, irrigation and medication with either calcium hydroxide or Septomixine. Oral Dis 2004;10:389-397.
- 43. Ahmed N, Neelakantan P. Antiseptics and antibiotics used in regenerative endodontics. International Journal of Pharmaceutical and Clinical Research 2013; 5(4): 141-144.
- 44. Tripathi KD. Essentials of Medical Pharmacology. 5th edition, New Delhi, 1985.
- 45. Ramamurthy NS, Rifkin BR, Greenwald RA, XuJW, Liu Y, Turner G, et al. Inhibition of matrix metalloproteinase-mediated periodontal bone loss in rats: A comparison of 6 chemically modified tetracyclines. J Periodontol 2002; 73(7): 726–734.
- 46. Hoshino E, Kurihara-Aando N, Sato I, Uematsu H, Sato M, Kota K, et al. In-vitro antibacterial susceptibility of bacteria taken from infected root dentine to a mixture of ciprofloxacin, metronidazole and minocycline. Int Endod J 1996; 29(2):125–130.