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ЛЕКАРСТВЕННЫЕ СРЕДСТВА И МЕТОДЫ ВНУТРИКАНАЛЬНОЙ ДЕЗИНФЕКЦИИ В РЕГЕНЕРАТИВНОЙ ЭНДОДОНТИИ

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INTRACANAL DISINFECTION AND MEDICAMENTS IN REGENERATIVE ENDODONTICS

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Резюме. Регенеративное эндодонтическое лечение в настоящее время является методом выбора при лечении незрелых постоянных зубовс невитальной пульпой. В статье проведен анализ литературы, касающейся трудностей дезинфекции корневых каналов несформированных постоянных зубов, сделан акцент на требованиях к современным дезинфицирующим средствам, описаны современные подходы и технологии, обеспечивающие качество регенеративного лечения.
Ключевые слова: регенеративное эндодонтическое лечение, реваскуляризация, невитальная пульпа, незрелые зубы.

Resume. Regenerative endodontic treatment is currently the method of choice in the treatment of nonvital immature permanent teeth. The article analyzes the literature concerning the difficulties of root canal disinfection of unformed permanent teeth, emphasizes the requirements for modern disinfectants, describes modern approaches and technologies that ensure the quality of regenerative treatment.
Keywords: regenerative endodontics, pulp revascularization, nonvital pulp, immature teeth.

Introduction. Immature necrotic permanent tooth presents a distinctive challenge. Various treatment modalities have been employed to create hard tissue barrier at the apex, which includes non-vital pulp therapy with calcium hydroxide, apexification with mineral trioxide aggregate, pulp revascularization and regeneration. Regenerative endodontics is a novel modality which involves physiological replacement of the damaged structures of tooth like dentin, root and cells of the pulp-dentin complex [3].

Root canal irrigation and disinfection is One of the most significant stages of root canal therapy, removing infectious microorganisms and microbial components from root canals to preventing re-infection of canals. Various chemical and mechanical methods have been used to reach this purpose. Ethylene-diamine-tetra-acetic acid (EDTA), sodium hypochlorite (NaOCl) and chlorhexidine (CHX) are some of the best-known chemical components for root canal disinfection [6, 9].

In Recent years, the advent of nanomaterials and their ability in targeted drug delivery have led to significant progress in the disinfection of root canal and accessory canals. Nanoparticles showed higher antibacterial potency because they have higher polycationic/polyanionic nature and higher charge density so their interaction with the bacterial cell is higher [7].

Aim: to review new approaches in intracanal disinfection and medicaments in regenerative endodontics of immature permanent teeth.

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Materials and methods. A primary search were performed within articles of the last ten years using PubMed and Google Scholar search motors and a total of 50 articles were recognized. The search was conducted by using these keywords: "polymers", "nanoparticles", "polymeric nanoparticles", "root canal disinfection", and "regeneration". Then, the studies were classified in the following order: root canal irrigation and disinfection, obturating materials, root-repair materials, regenerative endodontics therapy.

Results and their discussion. Pulp necrosis in immature teeth due to caries, dental trauma or developmental aberrations poses severe challenges to the dental practitioner. Short roots, thin, fracture-prone dentine walls and wide root canals and apices do not present ideal conditions for conventional root canal treatment. The classic apexification procedure established more than 40 years ago consists of long-term intracanal medication with calcium hydroxide to stimulate the formation of a calcified barrier at the apical foramen. Due to the weakening effect of calcium hydroxide on the thin dentine walls and the resulting high incidence of root fracture (Andreasen et al.2006), this procedure is not advocated any more.

Current treatment protocols recommend the placement of an MTA-plug to close the apical foramen followed by filling of the root canal with gutta-percha. Although MTA induces a mineralized barrier apically, further root formation cannot be expected, and susceptibility to root fractures due to thin canal walls and poor root-crown ratio remains [6]. Revitalization procedures in immature teeth after pulp necrosis have become part of the endodontic treatment spectrum and should be considered as an alternative to apexification [7].

Analysis of the literature over the past decade has shown that the degree of root canal disinfection determines the success of endodontic treatment. The problems of endodontic disinfection of immature permanent teeth in children are:

- disinfection resistance is found more in teeth in comparison with soft tissues, this is mostly because of Tubular structure of dentin and presence of biofilm culture communities;
- more numerous and faster bacterial growth can be found more in the coronal part of the canal in comparison with middle and apical part;
- limitations in mechanical debridement in large canals;
- bacterial resistance against antibiotics [10].

Regenerative endodontic procedures/treatment is biologically-based approach, which is synonymously referred to as "revascularization" in the literature, aims at the (re)generation of pulp-like tissue inside the root canal after inducing an influx of stem cells from the apical papilla. It results not only in a resolution of pain and inflammation, but also in healing of periapical lesions.

A significant effect of persistent or postoperative infection on the healing process in regenerative endodontic treatment is due to the following reasons:

1. The perpetuation of inflammation in the area
2. Decrease in the migration ability of stem cells
3. Stem cell differentiation changes (stem cells differentiate into osteoblast instead of odontoblast) [2].

Immature permanent teeth compared to mature ones have difficulties in bacterial disinfection due to deeper penetration of bacteria into the tubules of immature teeth, more

difficult eradication due to the complex anatomic structure of immature teeth, as well as thin walls of immature teeth lead to limited mechanical debridement of root canals.

The degree of disinfection determines the success of the treatment [9]. Disinfection in regenerative endodontic procedures (REP): can be performed in two ways irrigation with antiseptic solutions and the use of intracanal medications. There are several requirements for the ideal Irrigants for use in REP: chemical destruction of bacteria, removal of disturbed biofilms, detoxification of bacterial antigens, removal of intracanal medications.

Sodium hypochlorite (NaOCl) is the most common solution for disinfection of the root canal system. It is an alkaline material with a PH of 10.9 to 12, has excellent bactericidal effectiveness, the ability to dissolve tissues and effective hemostatic agent in local application [8]. Usage of high Concentration NaOCI in REPs have different effects:

1. Direct effects: decrease stem cell survival, decrease attachment and differentiation of stem cells.

2. Indirect effects: decrease Carbon and nitrogen content in dentin and leads to its demineralization due to clastic effect on dentin, decrease of odontoblastic differentiation and decrease dentin-derived growth factors [5, 8].

Therefore, the Optimal concentration of NaOCl in REPs is 1.5% NaOCl concentration which doesn’t change in odontoblastic differentiation.1.5% NaOCl is optimal for its dissolution and disinfecting capabilities followed by 17% EDTA as a final irrigant to promote stem cell survival, attachment and differentiation. Usage of EDTA as the final irrigant partially reversed the detrimental effects of NaOCl. General objectives and considerations for use of intracanal antimicrobial agents in RET cases are broad spectrum, biocompatible and anti-inflammatory action, minimal effect on dentin matrix proteins, reduced discoloration of enamel and dentin and specific efficacy to patient's own microflora [5, 10].

The most common intracanal medication used in REP was the triple antibiotic paste (TAP), originally developed by Hoshino et al. 1996. The paste disinfects dentin infected with Escherichia coli, is effective against a wide range of pathogens in necrotic teeth, but cannot kill all culturable bacteria. TAP consists of 3 antibiotics: Metronidazole (toxic to anaerobes and effective against protozoa), Ciprofloxacin is bactericidal, effective against Gram-negative bacteria and limited effective against Gram-positive bacteria, but many anaerobic bacteria are resistant to Ciprofloxacin; Minocycline has a bacteriostatic effect and strong anti-inflammatory effect, active against Gram-positive and Gram-negative bacteria, increases Interleukin-10, improves revascularization [1].

The Second intracanal medicament in a clinical case of REP is double antibiotic paste (DAP), it is composed of Ciprofloxacin and Metronidazole [lwaya et al. in 2001]. This medication has significant direct antibacterial effects regardless of the bacterial biofilms at 5 mg/mL. At 1 mg/mL there are significant decrease in amount of E. faecalis and P. intermedia biofilms but no significant decrease in viability, proliferation and mineralization of dental pulp stem cells. It is optimal for antibacterial properties against endodontic pathogens. DAP + EDTA combination have significant increase in dental pulp stem cells attachment compared to treatment with the DAP alone. Therefore, residual antimicrobial effect on dentin in 5 mg/mL is more than 1 mg/mL [1, 5].

One of the new approaches in REPs is usage of antibiotic-eluting fibers as drug delivery systems. Nanofibers can be manufactured from a variety of natural polymers which include: chitosan, fibronectin, gelatin, collagen and silk as well as from artificial polymers such as poly lactic acid (PLA), poly glycolic acid (PGA) and poly lactic-co-glycolic acid (PLGA).

Often, polymer combinations or different additives are used to finely tune mechanical and drug loading/releasing properties of resulting nanofibers. Use of natural compounds such as Propolis which has good antimicrobial and anti-inflammatory properties and well-known antifungal and antimicrobial activity. Mesoporous Bioactive Glass is a drug delivery system which is used especially for guided bone regeneration in periodontal tissue has an antibacterial action against E. faecalis biofilm and leaching effect of silver ions. Chitosan is a natural compound used as a drug carrier with inherent antimicrobial action and excellent wound dressing material, Biocompatible, degradable and nontoxic effect. Use of antibiotic-eluting fibers as drug delivery systems has more cell-friendly effect because of its minimal cytotoxicity, it increases (9x) proliferation of stem cells compared with pure TAP. Lower content of antibiotics within the fibers leads to well- controlled release of antibiotics. Minimal remaining drug in each fiber has minimal risk of sustained antimicrobial action, minimal tooth discoloration of TAP-eluting nanofibers when compared with TAP and significant antimicrobial effect compared with pure TAP [1, 4, 8].

Conclusion: the degree of disinfection determines the success of the treatment nonvital immature permanent teeth. 1.5% NaOCl concentration doesn't change in odontoblastic differentiation. Use of EDTA as the final irrigant partially reversed the detrimental effects of NaOCl.1.5% NaOCl is optimal for its dissolution and disinfecting capabilities followed by 17% EDTA as a final irrigant to promote stem cell survival, attachment and differentiation. In regenerative endodontic treatment use of antibiotic-eluting fibers as drug delivery systems which is composed of nanofibers increase 9 times proliferation of stem cells compared with pure TAP, well- controlled release of antibiotics during the procedure and minimal tooth discoloration of TAP-eluting nanofibers when compared with TAP can improve the quality of treatment.

There have been significant changes in the clinical treatment of infected immature permanent teeth over the years. Although the new treatment approach can sometimes be challenging and the outcome of the revascularization procedure is still somewhat unpredictable, new modifications of regenerative endodontic therapy make it the method of choice for the treatment of infected permanent immature teeth.

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