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REVIEW ARTICLE

Recent considerations in regenerative endodontic treatment approaches

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Abstract *Background/purpose:* Regenerative approaches in endodontics are considered in two concepts. One is a revascularization approach to achieve continued apical formation while the other involves the pulp/dentin regeneration via tissue engineering technology. Recently, some case reports have shown that infected immature teeth can be treated by revascularization approach. However, there is still no standardized treatment protocol for this procedure. The purpose of this review article was to evaluate the effects of regenerative endodontic treatment for necrotic immature permanent teeth and to discuss recent treatment approaches.
Materials and methods: Articles published in dental journals from January 2001 to August 2013 were searched using the following keywords: immature permanent teeth OR immature teeth OR pulp revascularization OR pulp revitalization OR regenerative endodontics by using electronic databases (MEDLINE using the PubMed search engine, Embase, Scopus, and Cochrane Central Register of Controlled Trials).
Results: The regenerative endodontic treatments with various methods and materials result in a significant increase in root length and dentinal wall thickness. Stimulation of stem cells in apical root canal system is required to induce tissue formation and continued root development. Alternative disinfection materials and protocols are required.
Conclusion: Although the regenerative treatment approaches have good clinical outcomes in the majority of case reports, the outcomes are unpredictable. Since the current clinical protocols for regenerative endodontics do not fully fulfill the triad of tissue engineering ((growth factors, scaffold and stem cells), further translational studies are required to achieve more pulp- and dentin-like tissue in the root canal system to achieve pulp regeneration.

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Introduction

The main goal of root canal treatment is the prevention or treatment of apical periodontitis.[1] For the treatment of immature permanent teeth, the goal is to restore the original physiologic structures and functions of the pulp–dentin complex. However, treating necrotic immature teeth has always been a clinical challenge for several reasons.[2] It is difficult to achieve an appropriate apical seal with an open apex by using conventional root canal treatment. In addition, the discontinued development of dentinal walls after pulp necrosis can cause thin dentinal walls that make the tooth more prone to fracture.

One-visit apexification that is performed by placing an apical barrier by using mineral trioxide aggregate (MTA) is an alternative to conventional long-term calcium hydroxide [$Ca(OH)_2$] therapy and may shorten the treatment time between the patient's first appointment and the final restoration.[3] The survival rate of MTA apexification is greater than that of $Ca(OH)_2$ apexification.[4] Mineral trioxide aggregate is effective in supporting the formation of new hard tissue in the apical area of the affected immature necrotic teeth; however, the risk of future fracture may remain because the root width will not increase in MTA apexification-treated teeth.[4]

Regenerative approaches in endodontics comprise two clinical concepts. One concept involves a revitalization approach to achieve tissue regeneration. In this method, new living tissue is expected to form in the cleaned canal space, thereby allowing continued root length and thickness. The other concept is the active pursuit of pulp and dentin regeneration via tissue engineering technology to implant or re-grow pulp tissue. The technology is in its infancy, but it potentially allows immature pulpless teeth to continue growing and maturing. With this understanding, it may be that apexification will become less needed in years to come.

Revascularization is a valuable treatment in immature necrotic teeth. Procedures attempting to preserve the remaining dental pulp stem cells and the mesenchymal stem cells of the apical papilla (SCAPs) can result in root canal revascularization and the completion of root maturation.[5] Stem cells generally remain in a quiescent state to protect their proliferative potentials *in vivo*.[6] Quiescent stem cells may be activated by microenvironmental changes such as tissue injury or disease.[7] In the presence of apical periodontitis, the root canal lumen is probably devoid of vital tissues. However, traces of pulpal tissue may survive apically, even in the presence of a large periapical lesion.[8,9]

The key procedures of the regenerative protocol are minimal or no instrumentation of the canal while relying on a gentle but thorough irrigation of the root canal system. The disinfection is augmented with intracanal medication, and the treated tooth is sealed with MTA and glass ionomer/resin cement at the completion of the treatment. Periodical follow-ups will take place to observe any continued maturation of the root.[10]

To date, pulp revascularization is reported as a promising approach for treating immature permanent teeth. By contrast, there are some drawbacks and variables in relation to this treatment approach.[11,12] The purpose of this article was to review the recent literature and to evaluate recent treatment approaches to guide clinicians in using regenerative endodontic procedures in clinical endodontics.

Materials and methods

Articles concerning pulp revascularization published in dental journals from January 2001 to October 2013 were searched using the following keywords: "immature permanent teeth", "immature teeth", "pulp revascularization", "pulp revitalization", or "regenerative endodontics". The electronic databases that use MEDLINE were the PubMed search engine (http://www.ncbi.nlm.nih.gov/sites/pubmed), Embase (http://www.embase.com), Scopus (http://www.scopus.com), and Cochrane Central Register of Controlled Trials (http://www.cochrane.org). The data obtained from the clinical case series and case reports are summarized in Table 1.[4,9,11,12,19,20,23–27,30,31,49] The percentages of the treatment factors are evaluated in Table 2.

Results

Dental caries (12.9%), trauma (33.8%), and dens evaginatus (25.9%) were the potential causes of necrotic pulp of immature teeth, that lead to the cessation of root formation. Premolars were the most affected and treated teeth (59.6%). Sodium hypochlorite (2.5–6%) has been used for irrigation and disinfection during regenerative endodontic therapy. Calcium hydroxide and triple antibiotic paste are mostly used as intracanal medicaments. Regenerative endodontic procedures potentially allow the thickening of the dentinal walls (76%) and lengthening of the root canals (54%).

Discussion

Factors causing pulp necrosis in immature teeth

Dental caries, trauma, and anomalous tooth morphology (i.e., dens evaginatus) cause pulp necrosis of immature teeth and thereby cause the cessation of root formation. Eradication of bacteria from the pulp canal has a key role in successful revascularization because revascularization halts in the presence of infection.[13]

Premolars are the most affected and treated teeth. This may be related to the prevalence of dens evaginatus in this tooth type. Dens evaginatus is an uncommon dental anomaly that presents by protrusion of a tubercle from the occlusal surfaces of the posterior teeth or lingual surfaces of the anterior teeth. It occurs primarily in Asian people.[14] It is also called central cusp in premolars.[14] The greatest disadvantage of dens evaginatus is that it makes the tooth more susceptible to pulp exposure caused by wear or fracture, and therefore leads to pulpal complications soon after eruption. In addition, because dental trauma mostly occurs in the anterior dental region and the upper incisors are more protracted than the other teeth, these tooth types most often have necrotic dental pulp.[15]