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Review

The Use of Regenerative Endodontic Procedures for the Treatment of Immature Teeth

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Abstract

Regenerative endodontic procedures (REPs) are a biologically based treatment approach for immature permanent teeth that have been diagnosed with pulp necrosis. The primary objective of REPs is to regenerate the pulp-dentin complex, thereby increasing the tooth's lifespan and restoring its normal function. The success of REPs depends on several factors, including patient age, apical opening size, root development stage, and the presence of infection. Biomaterials used in REPs have also been shown to influence clinical outcomes. Several challenges and limitations still need to be addressed to improve the clinical outcomes of REPs, including disinfection of the root canal, selection of biomaterials, and availability of stem cells. Future research should focus on developing novel disinfection strategies, identifying the ideal biomaterials for REPs, and exploring alternative sources of stem cells. With continued research and development, REPs have the potential to become a viable alternative to traditional endodontic procedures for treating immature teeth with open apices.

Keywords: *endodontic therapy, regenerative endodontics, immature teeth*

Introduction

Dental caries and traumatic injuries can lead to pulp necrosis and arrested root development in immature permanent teeth. Traditional endodontic treatments such as apexification with calcium hydroxide or MTA have been commonly used to promote root end closure, however, they fail to promote continued root maturation, leaving the tooth prone to fracture and decreasing long-term prognosis (1, 2). Regenerative endodontic procedures (REPs) have recently been introduced as an alternative treatment approach for immature teeth with necrotic pulps, allowing for continued root development and maturation (3).

REPs include the use of a biologically based approach to regenerate pulp-like tissue, dentin, and root development in immature teeth with pulpal necrosis (4). These procedures involve a combination of disinfection, placement of a scaffold, and a cell source that provides the necessary material for regeneration (5). The three main types of REPs include pulpal revascularization, pulp regeneration, and reimplantation with stem cells (6).

The pulpal revascularization involves the use of a blood clot to provide a scaffold for the regeneration of pulp-like tissue, dentin, and continued root development. The procedure involves minimal instrumentation of the root canal, followed by disinfection and creation of a blood clot in the pulp chamber. The blood clot acts as a scaffold for the ingrowth of new blood vessels, and the migration and proliferation of host-derived stem cells, leading to the regeneration of pulp-like tissue (7). The pulp tissue formed in this process is different from the original, as it lacks innervation and immune cells, but it has been proven to provide sensory function and promote tooth survival (8). The pulpal revascularization technique has been shown to be successful in treating immature permanent teeth with necrotic pulps, resulting in the formation of new hard tissue, continued root development, and apical closure (9).

The pulp regeneration technique involves the use of stem cells to regenerate pulp-like tissue, dentin, and continued root development. The procedure involves the isolation of dental pulp stem cells (DPSCs) from the patient's own tooth or from a donor tooth and their delivery to the root canal. The DPSCs differentiate into odontoblast-like cells, which secrete dentin-like tissue, promoting continued root development (10). The use of stem cells for pulp regeneration has shown promising results, with studies reporting increased root length, apical closure, and the formation of new hard tissue. However, there are concerns regarding the safety and efficacy of using exogenous stem cells, and further studies are needed to determine the optimal source and delivery method of these cells (11).

Reimplantation with stem cells involves the use of ex vivo cultured stem cells to repopulate the pulp chamber and promote root development. It includes extraction of the affected tooth, removal of the pulp tissue, and ex vivo culture of stem cells derived from the pulp tissue. The cultured cells are then delivered back to the tooth and allowed to repopulate the pulp chamber, promoting the regeneration of pulp-like tissue, dentin, and continued root development (12). Reimplantation with stem cells has been shown to be effective in treating immature permanent teeth with necrotic pulps, with studies reporting increased root length, apical closure, and the formation of new hard tissue. This technique is technically demanding and requires a specialized facility for cell culture, making it less accessible than other REPs (13).

The use of REPs has demonstrated favorable outcomes in the regeneration of pulp-like tissue, dentin, and continued root development (6). Factors that may affect the success of REPs include the age of the patient, the degree of root development, the presence of periapical lesions, and the type and quality of the scaffold and cell source used (14). There are still questions regarding the predictability and long-term outcomes of these procedures (15). This review aims to provide an update on the current knowledge and clinical applications of REPs for the treatment of immature permanent teeth with necrotic pulps.

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Methodology

In this study, a thorough literature search was conducted on April 18, 2023, in the Medline and Cochrane databases, utilizing medical topic headings (MeSH) and relevant terms available in the database. The study primarily included articles published between 2000 and 2023. To ensure comprehensive coverage, a manual search of publications was also conducted using Google Scholar, with the reference lists of previously identified papers as a starting point. The study aimed to extract valuable information from papers discussing scientific evidence on regenerative endodontic procedures for the treatment of immature teeth. No limitations were imposed on the type of publication, participant age, language, or publication date.

Discussion

Dental pathologies affecting the pulp and periapical region are commonly encountered in clinical practice, resulting from caries, trauma, or dental anomalies. Root canal treatment (RCT) is the established treatment option for managing endodontic diseases in fully developed permanent teeth, with excellent clinical outcomes. Immature permanent teeth with pulp necrosis are traditionally managed using apexification procedures (16). The objective of endodontic therapy is to eliminate pulp and periapical inflammation/infection while preserving the tooth. Nonetheless, these treatment procedures involve the removal of pulp and dentin tissues, which compromises the dentin's strength, immunological response, and proprioceptive functions, leading to an increased risk of reinfection and tooth fracture (17). The restoration of vital pulp and the restoration of the biological function of teeth have emerged as the primary objectives of modern endodontics.

The goal of endodontic treatment is to remove the infected or inflamed pulp tissue, clean and shape the root canal, and fill it with a biocompatible material. In immature teeth, traditional endodontic procedures may lead to root stunting, thinning of the dentinal walls, and root fractures. Regenerative endodontic procedures (REPs) have been introduced as an alternative to traditional endodontic procedures. REPs aim to restore the function and vitality of immature teeth by promoting the regeneration of the pulp-dentin complex (11, 18).

REPs involve the use of tissue engineering principles to regenerate the pulp-dentin complex in immature teeth with open apices. REPs aim to promote the regeneration of pulp tissue, which leads to root elongation and thickening, and dentin deposition, which enhances the structural integrity of the tooth. REPs involve the use of a triad of strategies, including disinfection, biomaterials, and stem cells (3).

REPs are recommended for cases that fulfill specific criteria, which include: (a) the presence of necrotic permanent teeth with incomplete root formation, regardless of the existence of periradicular lesions; (b) the final restoration not requiring a post/core; (c) patients/parents who can adhere to the treatment requirements; and (d) patients without allergies to the medicaments or antibiotics used in the procedure. However, certain cases may not be appropriate for REPs, such as teeth immediately replanted after avulsion, cases with inadequate tooth isolation, teeth requiring post restoration due to extensive coronal tissue loss, or teeth with endodontic-periodontal lesions (14).

When dealing with immature permanent teeth, the diameters of the apices typically exceed the size of the largest files, presenting a challenge for mechanical instrumentation. Furthermore, mechanical preparation may compromise the already fragile and thin dentin wall of the roots. The ESE statement and the most recent AAE guideline do not recommend mechanical instrumentation. However, avoiding mechanical instrumentation may allow bacterial biofilm to persist in dentinal tubules, resulting in failed REPs. Therefore, minimal instrumentation should be considered in REPs. The canal walls should be gently brushed circumferentially with endodontic instruments such as larger-sized K files and Hedström files to disrupt the bacterial biofilm, without aggressively removing dentin (14).

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Disinfection of the root canal is a crucial step in REPs. The root canal of immature teeth with open apices may contain necrotic tissue, bacteria, and their by-products, which may hinder the regeneration of pulp tissue. Disinfection of the root canal is achieved through the use of irrigants, such as sodium hypochlorite (NaOCl) and chlorhexidine (CHX), and antibiotics, such as metronidazole (MET) and ciprofloxacin (CIP) (19). NaOCl is the most frequently applied irrigant in REPs due to its excellent antimicrobial activity and tissue-dissolving properties. However, the use of NaOCl in REPs has been associated with root resorption and cytotoxicity to stem cells (20). CHX has been suggested as an alternative irrigant to NaOCl due to its broad-spectrum antimicrobial activity and low cytotoxicity to stem cells. MET and CIP have been used as antibiotics in REPs due to their excellent antibacterial activity against anaerobic bacteria commonly observed in the root canal of immature teeth (21).

Biomaterials used in REPs serve as a scaffold for the regeneration of pulp tissue and the deposition of dentin. The ideal biomaterial for REPs should be biocompatible, osteoconductive, and osteoinductive (22). Commonly used biomaterials in REPs include platelet-rich plasma (PRP), blood clot, collagen scaffolds, and mineral trioxide aggregate (MTA) (23).

PRP is a concentrated suspension of autologous platelets in plasma, which contains various growth factors, such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF). PRP has been shown to enhance the regeneration of pulp tissue and dentin deposition in REPs (24). Blood clot is another biomaterial commonly used in REPs. It also contains various growth factors, such as PDGF, TGF-β, and insulin-like growth factor (IGF), which promote the regeneration of pulp tissue and dentin deposition. However, obtaining a blood clot is challenging, and it does not possess all the desirable characteristics of an ideal scaffold, such as ease of delivery, favorable mechanical properties, manageable biodegradability, and the ability to integrate growth factors (23).

Collagen scaffolds have also been used as a scaffold for the regeneration of pulp tissue in REPs. Collagen scaffolds provide a biocompatible environment for the growth and differentiation of stem cells into pulp tissue and dentin (25). MTA is a biocompatible cement that has been used in REPs due to its excellent sealing properties and osteoinductive activity (26).

Stem cells play a crucial role in the regeneration of pulp tissue and dentin in REPs. Stem cells can differentiate into odontoblasts and pulp cells, which promote the deposition of dentin and the regeneration of pulp tissue. Stem cells used in REPs include dental pulp stem cells (DPSCs), stem cells of the apical papilla (SCAPs), periodontal ligament stem cells (PDLSCs), inflammatory periapical progenitor cells (iPAPCs) and bone marrow stem cells (BMSCs) (27).

DPSCs are multipotent stem cells found in the dental pulp. DPSCs have been shown to differentiate into odontoblasts and pulp cells, which promote the deposition of dentin and the regeneration of pulp tissue. DPSCs have been used in REPs with good clinical outcomes (14).

SCAPs were initially identified in the apical tissue in 2006 and have since been found to possess proliferation and odontogenic differentiation capabilities that aid in root development. Given their proximity to the tooth apices and these qualities, SCAPs are considered the most auspicious stem cell source for REPs (28).

The vasculature within apical granulomatous tissues is the primary location for the presence of iPAPCs, which makes them a significant prospective source of stem cells for REPs (29). Studies have demonstrated the ability of PDLSCs and BM-MSCs to differentiate into pulp cells and odontoblasts, which facilitate the formation of dentin and the regeneration of pulp tissue. In fact, they have been successfully employed in REPs, yielding favorable clinical results (6).

REPs have shown promising clinical outcomes in the treatment of immature teeth with open apices. Studies have reported increased root length and

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thickness, apical closure, and absence of signs and symptoms of infection. A systematic review and meta-analysis of 17 studies reported a success range from 50% to 98% and the survival rates were between 94% and 100% (30).

The success of REPs depends on several factors, including the age of the patient, the size of the apical opening, the stage of root development, and the presence of infection. Younger patients with larger apical openings and less severe infection have been reported to have better outcomes with REPs (14).

Biomaterials used in REPs have also been shown to influence clinical outcomes. A systematic review and meta-analysis of 32 studies involving treated with REPs reported a success rate for teeth treated with MTA higher than for teeth treated with other biomaterials (9).

REPs still face several challenges and limitations that need to be addressed to promote wider clinical application. Disinfection of the root canal remains a significant challenge. The root canal of immature teeth with open apices may contain complex microbial communities that are difficult to eliminate. The use of irrigants and antibiotics has been shown to have limited success in eliminating all microbial communities (14).

The selection of biomaterials for REPs also remains a challenge. There is a lack of consensus on the ideal biomaterial for REPs. The choice of biomaterials depends on several factors, including their biocompatibility, osteoinductive and osteoconductive properties, handling characteristics, and cost-effectiveness (30).

The availability of stem cells is another limitation of REPs. The collection and isolation of stem cells from dental pulp and bone marrow can be challenging and time-consuming. The use of alternative sources of stem cells, such as induced pluripotent stem cells (iPSCs), is being investigated as a potential solution to this limitation (6).

Conclusion

Regenerative endodontic procedures (REPs) have promising clinical outcomes for treating immature teeth with open apices by promoting pulp tissue regeneration and dentin deposition. Success of REPs depends on various factors, such as patient age, apical opening size, root development stage, and presence of infection. However, disinfection of the root canal, selection of biomaterials, and stem cell availability pose limitations. Further research on novel disinfection strategies, ideal biomaterials, and alternative stem cell sources is needed to optimize the clinical outcomes of REPs.

Disclosure

Conflict of interest

There is no conflict of interest

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Data availability

Data that support the findings of this study are embedded within the manuscript.

Author contribution

All authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

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