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Review

Tissue engineering: Dentin – pulp complex regeneration approaches (A review)

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ABSTRACT

Dental pulp is a highly specialized tissue that preserves teeth. It is important to maintain the capabilities of dental pulp before a pulpectomy by creating a local restoration of the dentin-pulp complex from residual dental pulp. The articles identified were selected by two reviewers based on entry and exit criteria. All relevant articles indexed in PubMed, Springer, Science Direct, and Scopus with no limitations from 1961 to 2016 were searched. Factors investigated in the selected articles included the following key words: Dentin-Pulp Complex, Regeneration, Tissue Engineering, Scaffold, Stem Cell, and Growth Factors. Of the 233 abstracts retrieved, the papers which were selected had evaluated the clinical aspects of the application of dentin-pulp regeneration. Generally, this study has introduced a new approach to provoke the regeneration of the dentin-pulp complex after a pulpectomy, so that exogenous growth factors and the scaffold are able to induce cells and blood vessels from the residual dental pulp in the tooth root canal. This study further presents a new strategy for local regeneration therapy of the dentin-pulp complex. This review summarizes the current knowledge of the potential beneficial effects derived from the interaction of dental materials with the dentin-pulp complex as well as potential future developments in this exciting field.

Contents

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1. Introduction

The dental pulp, confined with the dentin and enamel, is in the center of a tooth and is made of living pulp cells, odontoblasts, immune system cells, neurons, endothelial cells, and the extracellular matrix. It is crucial to preserve the performance of healthy teeth (Avery et al., 2006). The dental pulp consists of blood vessels to deliver nutrients to the tooth, clear waste products, and a neural network to protect against harmful stimuli such as pain through the apical foramen of the tooth. Dendritic cells, macrophages, and T-lymphocytes immunologically protect teeth from microorganisms and other foreign antigens. Pulp cells and odontoblasts play vital roles in the regeneration of dentin damaged by tooth wear or dental care, as a protective physical defense in the removal of exogenous stimuli by depositing tertiary dentin on the pulp chamber surface. Severe pain and pulp tissue ischemia occur with stimulation of inflammatory agents like acute infection or internal pressure in the pulp chamber (Hargreaves et al., 2012). In such circumstances, dentists have to remove an entire pulp using a pulpectomy to rescue patients from the unbearable pain (Bergenholtz et al., 2013). Otherwise, pulp necrosis can occur through ischemia caused by a disruption in blood circulation (Heyeraas and Kvinnsland, 1991).

The main internal part of the tooth underneath the surface enamel layer in the crown is the dentin-pulp complex, involving the whole tooth root covered by a thin layer of cement. The structural integrity and insulative characteristics of the tooth are kept by highly mineralized dentin that encloses the pulp chamber and canals, resulting in vitality of the tooth, and neurovascular supplies exit through limited foramina at the root apices.

Moreover, the pulp has repair mechanisms which may be activated by bleeding to cover the dentin from harmful triggers such as attrition, trauma, and tooth decay. Overall, the dentin-pulp complex is responsible for dental health.

Several factors limit the possibility of pulp tissue regeneration (Smith et al., 2008). The dental pulp has the least collateral blood supply because of the anatomical features of the pulp chamber, and this leads to a disruption in the function of the immune system for infection control (Huang, 2009). Odontoblasts, also as post-mitotic cells, have restricted (or no) ability to proliferate (Arana-Chavez and Massa, 2004). Losses due to superficial caries are caused by stimulating odontoblast cells in promoting their secretory activity, and this leads to dental restorative competence (Smith et al., 2008). Odontoblasts can elaborate reparative (tertiary) dentin under suitable conditions, but it is a poorly organized and mineralized matrix compared with primary and secondary dentin (Nakashima and Akamine, 2005). Bacterial by-products and/or the actual bacteria can be controlled by new dentin to maintain the pulp.

Dentin with its tubular structure has a strong relationship with pulp tissue through the odontoblastic process (Smith et al., 2008). However, factors causing harm to teeth, such as trauma, deep cavity preparation, or severe caries lesions (Mjör, 2009), overcome the odontoblasts, possibly creating irreversible infection (pulpitis) or necrosis in the dental pulp (Smith et al., 2008). Routine endodontic therapy is usual under such conditions, but there are some shortcomings here despite the positive outcomes (Huang, 2009), namely, the loss of a remarkable level of dentin resulting in a poor survival rate for teeth (Demarco et al., 2005). This especially occurs with dental trauma in young patients with immature teeth, a frequent incidence in clinical dental practices.

At present, non-invasive techniques and maximum conservation of tooth structure are the current dental treatments. The risk of pulp exposure and subsequent enhanced reparative potential can be decreased by the differentiation between heavily infected outer carious dentin and demineralized affected inner dentin (Dyes, 2000). Clinical and laboratory techniques classify various layers of dentin caries lesions (Anderson et al., 1985; Fusayama and Terachima, 1972), despite conflict or overlap in outcomes; thus, the nature and changes of such lesions should be made clear.

Dental caries and trauma trigger cellular and molecular responses in the pulp which can appear as inflammatory and/or regenerative events at both tissue and cellular levels. The defense response increases initially for managing the infection and healing wounds in the pulp like any other injured tissue in the body (Bjørndal and Darvann, 1999; Bjørndal et al., 1998). This study shows a new strategy for local regeneration therapy of the dentin-pulp complex from residual dental pulp following a pulp amputation to avoid pulpectomy. The pulp amputation treatment occurs after the removal of damaged coronal pulp tissue and the watering of the root canal orifice with chemical reagents. Calcium hydroxide-based materials or mineral trioxide aggregate (MTA) are applied to the root canal orifice to promote the formation of dentin bridges to preserve root pulp (Bergenholtz et al., 2013; Lee et al., 2015; Nosrat and Nosrat, 1998; Reston and de Souza Costa, 2009). Nevertheless, after a pulp amputation, layers of necrotic tissue are observed at an interface between the residual root pulp and the dentin bridge (Bergenholtz et al., 2013). The recently established dentin bridge through pulp amputation has poor ability to conserve the residual root pulp because of its porous hard tissue with a low degree of calcification (Leye Benoist et al., 2012). It is noteworthy that the pulp amputation itself never causes the regeneration of pulp or dentin which was lost in the coronal portion. Only vital pulp can lead to the regeneration of dentin; however, the regeneration of pulp tissue is difficult, because the tissue is recapped in dentin with no collateral blood supply except from the root apical meristem. Efforts have already begun to achieve pulp tissue regeneration. The regeneration of pulp and dentin has been developed using modern tissue engineering concepts and the discovery of dental stem cells. Moony and Rutherford conducted one of the first attempts to test pulp tissue engineering (Bohl et al., 1998; Buurma et al., 1999; Mooney et al., 1996; Yen and Sharpe, 2008; Young et al., 2005b, 2002). They stopped working because of failing to isolate and identify the pulp stem cells, which potentially may differentiate into odontoblast. Pulp tissue should be regenerated with a suitable performance, for example, the ability to construct dentin to repair the lost structure. Researchers have demonstrated that the obtained pulp cells can differentiate into odontoblast-like cells and produce a dentin-like mineral structure in vitro (About et al., 2000; Tsukamoto et al., 1992). Gronthos et al. demonstrated the in vivo generation of dentin from pulp cells and observed pieces of human pulp/dentin complex formed ectopically in immunocompromised mice (Gronthos et al., 2000). This finding was a start to further reviewing the stem cell-based regeneration of pulp/dentin in clinical uses.

The dental root canal system is often difficult to debride because of challenges in the treatment of immature permanent teeth using pulpal necrosis. Furthermore, there is a high risk of subsequent fracture in the thin dentinal walls (Cvek, 1992), resulting in a restorative dilemma in young patients with a growing craniofacial skeleton

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