PULP THERAPY

Dental pulp therapy advances

BACKGROUND

Dental pulp supports tooth vitality by supplying essential factors and plays a key role in tooth maintenance. When sound dentin, which surrounds dental pulp, is lost because of tooth wear, fracture, or caries, odontoblasts or odontoblast-like cells repair the tooth. If dental caries or tooth fractures progress, the dental pulp can become infected and inflamed, increasing the internal pressure of the pulp chamber and causing pulp ischemia and severe pain. Pulpectomy can be done to avoid impaired blood circulation, pulp necrosis, and periapical disease. It's possible that many root canal treatments and tooth extractions could be avoided with proper direct pulp capping or pulp regeneration therapy. The current perspectives on direct pulp capping and dentin-pulp complex regeneration were presented along with novel approaches for dental pulp preservation and regeneration therapies.

DIRECT PULP CAPPING TRENDS

Direct pulp capping or pulpotomy is carried out to avoid pulp depth. The exposed vital pulp is covered with dental materials to facilitate the formation of reparative dentin. The ideal pulp capping material should adhere to tooth substrate, maintain a good seal, be insoluble in tissue fluids, maintain dimensional stability, and be nonresorbable, nontoxic, noncarcinogenic, nongenotoxic, and radiopaque. In addition, biocompatibility and bioactivity are desirable. None of the materials currently available satisfies all of these desirable properties. The most widely used materials for direct pulp capping are calcium hydroxide and mineral trioxide aggregate (MTA), but newer agents are being developed (Figure 1).

Calcium Hydroxide

Calcium hydroxide is the traditional 'gold standard' for direct pulp capping materials and has a long history of use. It offers antibacterial properties and induces necrosis and mineralization directly beneath the material. It can be of the one-paste nonsetting type or the curable 2-paste system. Although both offer highly desirable properties, both also have drawbacks.

MTA

MTA is widely used as a direct pulp capping material with antibacterial activity. It also has greater sealing ability, lower solubility, higher physical strength, and greater stability than calcium hydroxide. MTA can be used in a moist environment, prevents bacterial infiltration, and creates a thicker dentin bridge formation with reduced inflammatory response, less hyperemia, and less necrosis than calcium hydroxide.

MTA also has the disadvantages of discoloration, toxic elements, higher cytotoxicity when freshly mixed, high pH during setting, poor handling, long setting time, and a requirement for sufficient moisture during hardening. Improved MTA/calcium silicate materials have been developed to overcome these disadvantages. Among these are light-curable resin-modified calcium-silicate–based materials. Although they offer immediate light-polymerization, prevention of material washout, and superior physical properties, they appear to be more cytotoxic than resin-free calcium silicates/MTA. Further study is needed.

Bioactive Glass-based Cement

Bioactive glasses show the clinical ability to bond with bone by forming a hydroxyapatite layer on the surface and are used in orthopedic surgery for bone engineering. A bioactive glass–based cement with hydroxyapatite-like precipitation on the surface of the hardened cement, stable pH level, and biocompatibility without cytotoxic effects has been developed. This cement can induce reparative dentin formation on the surface of exposed dental pulp when used for direct pulp capping. An improved version is under development.

Future materials for direct pulp capping

A novel therapy is expected to induce wound healing and dentinogenesis similar to the natural processes. Bone morphogenetic protein (BMP)-2 has been approved for clinical use. Among its properties is the ability to induce the differentiation of dental pulp stem cells into odontoblasts. Other members of the same Transforming growth factor (TGF)-β superfamily have been identified as important factors that induce dentinogenesis.

Heat shock proteins (HSPs) and cell-cycle arrest can accumulate and induce cellular resistance to various stimuli. HSPs may offer useful biological molecules in the role of a pretreatment agent for direct pulp capping.

Macromolecular translocation inhibitor II (MTI-II) peptide anti-inflammatory drug (MPAID) may regulate the inflammatory response and maintain a protective dental pulp response. Anti-inflammatory agents similar to MPAID may be candidates for direct pulp capping or pretreatment roles.

DENTIN-PULP COMPLEX REGENERATION

Regeneration After Pulpotomy

In pulpotomy, coronal pulp is amputated surgically, then the remaining root pulp surface is treated using a medicament such

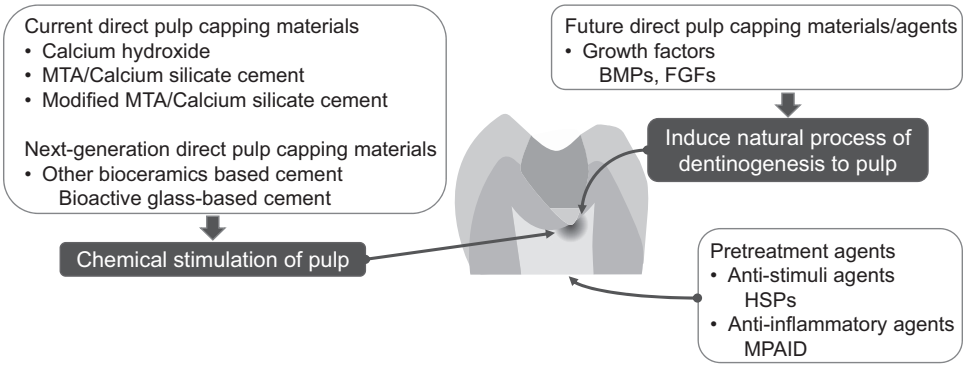

Figure 1. Current and future direct capping materials/agents. Current direct pulp capping is the reaction of dental pulp to the chemical stimulation. Ideal direct pulp capping materials/agents induce dentinogenesis similar with natural biological process to pulp. Application of anti-stimuli and/or anti-inflammatory agents in combination with the direct pulp capping materials/agents will be effective. (Courtesy of Morotomi T, Washio A, Kitamura C: Current and future options for dental pulp therapy. *Jpn Dent Sci Rev* 55:5-11, 2019.)

as calcium hydroxide or MTA to promote the formation of a dentin bridge. Current pulpotomy never leads to the regeneration of the dentin-pulp complex lost coronally. Tissue regeneration requires the induction of stem cells and capillary networks, the delivery system of growth factors, and scaffolds for cell proliferation and differentiation. After pulp amputation, dental pulp stem cells and capillaries may be induced from residual root pulp tissues and a closed space prepared using adhesive materials. Choice of growth factor, delivery system of the growth factor, and suitable scaffolding to induce the stem cells and blood vessels from the residual pulp are critical components of this process.

The controlled release of fibroblast growth factor (FGF)-2 from gelatin hydrogels can induce the regeneration of angiogenesis, bone, periodontal tissues, and other tissues. Collagen is a primary macromolecular constituent of the dentin extracellular matrix (ECM) and offers excellent biocompatibility and an extensive history of use. Studies suggest that combining FGF-2, gelatin hydrogels, and scaffolds may lead to the local regeneration of the dentin-pulp complex after pulpotomy. Some problems remain, such as lack of an ideal structure with dentinal tubules and insufficient quantity to protect dental pulp or withstand bite forces. BMP-2 may be able to induce in vivo dentin formation, along with other growth factors involved in dentinogenesis. Platelet-rich plasma (PRP) is another candidate and enhances the differentiation of odontoblastic cells and alkaline phosphatase activity. Some combination of factors may prove able to induce local regeneration of ideal dentin-pulp complex.

In addition to collagen, several natural polymers and synthetic polymers can be used for therapy. Hyaluronic acid (HA) plays an important role in maintaining morphologic organization and anti-inflammatory effects and may be well-suited for tissue engineering material. HA sponge has provided ideal properties for scaffold construction useful for dentin-pulp complex regeneration.

Regeneration of Non-vital Teeth

A clinical protocol for root revitalization/revascularization of non-vital immature permanent teeth has been developed. However, the hard tissue produced is not like dentin but rather like cementum and periodontal ligament connective tissues. This protocol could not lead to regeneration of the dentin-pulp complex. Suitable scaffolds and growth factors are needed to induce the differentiation of dental pulp cells containing odontoblasts. In addition, dentin formation is needed to apply into the root canal.

Two major strategies have been developed to achieve entire dental pulp regeneration for non-vital mature permanent teeth. These include the cell homing strategy and the cell transplantation strategy. The cell homing strategy requires the induction of stem/progenitor cells from periapical tissue around the apical area of the root. Scaffolds impregnated with growth factors are injected into root canals to induce the migration, proliferation, and differentiation of endogenous stem progenitor cells around the root apex through an enlarged apical foramen. This method may be more readily accomplished in a clinical setting than the cell transplantation strategy.

The cell transplantation strategy is believed to offer the potential for a high success rate in dentin-pulp complex regeneration. An essential component is the establishment of stem cell sources. Dental pulp stem cells (DPSCs) exhibit the ability to form ectopic human dentin-pulp complex-like structures. In addition, stem cells from human exfoliated teeth (SHEDs), periodontal ligament stem cells (PDLSCs), stem cells from apical papilla (SCAPs), and dental follicle progenitor cells (DFPCs) are also potentially suitable cell sources for this use. Bone-marrow–derived mesenchymal cells (BMSCs), human bone marrow stromal cells (HMSCs), and adipose tissue–derived mesenchymal stem cells (ADMSCs) are alternative source candidates, as are induced pluripotent stem (iPS) cells. To ensure that a sufficient number of cells are available, a dental stem cell blanking system is essential.

Clinical Significance

With the developments in biological factors and biomaterials, new pulp capping agents and regeneration strategies are becoming likely in the near future. The treatment options discussed will change endodontic therapies and improve patients' quality of life.

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SLEEP MEDICINE

Links between periodontal disease, sleep apnea, COPD, and xerostomia

BACKGROUND

Relationships between oral and systemic disease are often found to exist, with several associations between systemic health and periodontal disease (PD). Among the systemic disorders with possible associations with PD are obstructive sleep apnea (OSA), chronic obstructive pulmonary disease (COPD), and xerostomia. The links may involve shared risk factors, treatment responses, or causation. The possible causal relationships between PD and OSA, COPD, and xerostomia were outlined.

CHARACTISTICS OF PD

PD affects the supporting structures of the teeth and is based on disruption of the balance in the oral biofilm. The oral cavity provides a warm, humid environment well-pleasing to harmful aerobic and anaerobic bacteria. These organisms can enter the bloodstream, resulting in bacteremia, which causes an inflammatory response. The inflammation factor has already been linked to cardiovascular disease, diabetes, stroke, preterm birth, cancer, and renal failure.

POSSIBLE LINKS TO OSA

OSA causes disordered breathing related to partial or complete collapse of the upper airway during sleep. This results in hypopnea or apnea. The minimum requirement for a diagnosis of OSA is at least an average of 5 episodes per hour of having airflow cessation. These episodes result in fragmentation of sleep, increased sympathetic activity, and decreased blood oxygen saturation. Risk factors include age, obesity, and craniofacial abnormalities that lead to nasal obstruction and mouth breathing.

The link between OSA and PD is postulated to be a bidirectional cause-effect relationship through the mediator of systemic inflammation. The comorbidity of PD and OSA may result from their overlap in inflammatory responses, with both disorders associated with increased levels of systemic inflammatory markers. However, PD may also contribute to OSA through the aspiration of periodontal pathogens into the lungs, which causes a local inflammatory infection, decreased expiratory lung function, and ultimately can lead to OSA. Even healthy individuals aspirate a small amount of saliva, which in persons with PD would contain pathogens that could harm the airways. Patients with OSA or snoring have a 7 times greater risk for swallowing disorders than healthy persons, so OSA patients are at higher risk for aspirating harmful periodontal pathogens when PD is present. Then, during apnea, the upper airway collapses on inhalation, increasing the pressure needed to reopen the closed airway. With compromised lung function, the individual's ability to overcome an apneic episode is suppressed.

POSSIBLE LINKS TO COPD AND XEROSTOMIA

COPD

In COPD, patients experience a chronic obstruction of airflow and excess production of sputum as a result of chronic bronchitis-increased mucosa in the airway and emphysema-distention of airspaces distal to the terminal bronchiole. As a result, they experience alveolar septa compromise. Risk factors for COPD include smoking history and age.

PD can be a comorbid condition with COPD because of their shared risk factors, inflammatory markers, and decreased lung function. Aspiration of saliva into the lungs is common during sleep, and both high levels of periodontal pathogens and increased inflammatory cytokine levels are found in PD patients compared to healthy persons, making it likely that these