REGENERATIVE PERIODONTAL THERAPY

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ABSTRACT: Periodontitis is the one of the most common diseases affecting the oral cavity. It is defined as chronic inflammatory disease affecting the supporting structures of the teeth ultimately leading to tooth loss. There are various treatment modalities ranging from conventional scaling and root planning to surgical therapies. However, all these treatments focus on reducing the inflammation and arresting the disease progression but does not regenerate the lost tissues. Over the past two decades, various regenerative periodontal therapies, such as guided tissue regeneration, enamel matrix derivative, bone grafts, growth factor delivery and the combination of cells and growth factors with matrix-based scaffolds have been developed to target the restoration of lost tooth-supporting tissues. this review highlights various regenerative treatments for the management of periodontitis.

KEYWORDS: periodontal, therapy, regenerative, healing

INTRODUCTION

Periodontium consists of tooth-supporting structures which includes gingiva, cementum, periodontal ligament and alveolar bone. Periodontitis is a chronic inflammatory disease which affects both soft and hard tissues of the oral cavity leading to degradation of periodontal tissues, causing tooth movement and eventually tooth loss. Treatment strategies focus on plaque removal and local inflammation control, such as scaling and root planing and surgical treatments. Those therapies attempt to minimize symptoms and prevent disease progression, but cannot restore the attachment of periodontal tissues to teeth and the original periodontal tissues.(1,2,3)

The goal of regenerative periodontal therapy is the reconstruction of the lost periodontal structures Therefore, the functions of teeth and dentition remain impaired after the treatments. Some regenerative approaches, such as guided tissue regeneration and bone grafts, were developed to achieve periodontal tissue formation. However, clinical outcomes of those approaches are variable and unpredictable. Therefore, it is imperative to develop alternative regenerative strategies to restore the structures and functions of periodontal tissues for periodontitis patients. In this paper, we overview periodontal tissue regeneration strategies.(5,6,7,8,9)

BONE SUBSTITUTES

The application of bone substitutes is based on the assumption that these materials facilitate the regeneration of alveolar bone and root cementum, and create the space needed for the regeneration process. They are divided according to their characteristics as: materials containing bone-forming cells (osteoneogenesis), growth factors (osteoinductivity), or materials serving as a scaffold for bone regeneration (osteoconduction).(10)

DEMINERALISED BONE MATRIX

Demineralized bone matrix (DBM) is bone that has been acid-treated in order to remove the mineral matrix, while maintaining the organic matrix and growth factors such as bone morphogenetic protein (BMP), insulin growth factor (IGF), transforming growth factor (TGF), or fibroblast growth factor (FGF). In proportion, 93% of a DBM is represented with collagen and 5% with growth factors. Since some growth factors are maintained, DBM can show osteoinductive capabilities and osteoconductive properties by the presence of a collagen structure.(11)

PLATELET RICH PLASMA

Platelet-rich plasma (PRP) is generally used as a gel that is easily obtained with the patient's blood. Blood is centrifuged through gradient density, and the resulting blood platelets are mixed with thrombin and calcium chloride. Hence, PRP includes an important concentration of platelets and fibrinogen, as well as growth factors such as platelet derived growth factors (PDGF), vascular endothelial growth factor (VEGF), IGF, and TGF. PRP is expected to show pro-coagulant effects due to platelets; however, there is no evidence in the literature of benefits for the addition of PRP to accelerate bone healing.(12)

BMPs

Bone morphogenetic proteins (BMPs) are osteoinductive growth factors included in the transforming growth factor β (TGF-β) superfamily. They are produced by osteoblasts and are largely involved in the skeletogenic process, enabling ectopic bone formation. BMP play a role in the recruitment of osteoprogenitor cells in bone formation sites. Genetic engineering allows to synthetize recombinant human BMP (rhBMP-2 and rhBMP-7), which can be produced in large quantities and limit risks of contamination.(13)

HYDROXYAPITITE

Hydroxyapatite (HA) is part of the apatites family, which are crystalline compounds with crystalline hexagonal lattice. HA has the specific formula ($Ca_{10}(PO_4)_6(OH)_2$) and is the primary mineral component of teeth and bones. Thus, HA is extremely biocompatible and does not promote an inflammatory response. Natural HA is porous with a various porosity depending on the bone site that is extracted (for example 65% porosity and pores from 100 to 200 μm for trabecular bone), which allows osteoconductive properties.(14)

SYNTHETIC BONE SUBTITUTE

CALCIUM SULFATE

The first therapeutic success using calcium sulfate ($CaSO_4$) as a bone substitute was reported in 1892. However, this material also called "gypsum" or "plaster of Paris" and has only been FDA accepted in 1996. Calcium sulfate offers many advantages as it presents a structure similar to bone, it is osteoconductive, inexpensive, and available in different forms (hard pellets and injectable fluids). It does not generate allergic reactions. Moreover, calcium sulfate has a crystalline structure that is osteoconductive, onto which bone capillaries and perivascular mesenchymal tissue can invade. Calcium sulfate resorbs rapidly in 1–3 months. This resorption creates porosity while stimulating bony ingrowth.(15,16)

CALCIUM SULPHATE CEMENTS

Calcium phosphate cements (CPCs) were invented in 1986 by Brown and Chow and were FDA approved for the treatment of non-load-bearing bone defect in 1996 (concerning tetracalcium phosphate and dicalcium phosphate dihydrate products). This bioresorbable material can stay in the body for long up to 2 years without resorption, depending on its formulation.(17)

β-TRI CALCIUM PHOSPHATE

β-tri-calcium phosphate (β-TCP) ($Ca_3(PO_4)_2$) has largely been used as a bone substitute for more than 25 years, mainly for orthopedics and dentistry applications, and is considered as the "gold standard" for synthetic bone. It is a biocompatible and bioresorbable material with properties similar to the inorganic phase of bone. β-TCP is osteoconductive.(18,19)

POLYMER BASED BONE SUBSTITUTE

Although natural polymers such as collagen exist and are slightly used alone rather than in combination with HA; for example, this section (synthetic bone substitutes) will be focused on synthetic polymers. They can be nondegradable (like poly(methylmethacrylate) or PMMA) or fully biodegradable, thus allowing a total bone replacement in time (e.g. polylactic acid (PLA)) without remaining foreign bodies. Initially used as graft extenders, researches focus on synthetic polymeric bone substitutes, especially in the field of tissue engineering. Polyesters like poly(ε-caprolactone) (PCL), for example, can be synthetized by mimicking the collagenic matrix, offering a structural porosity and osteoconductive properties.(20,21)

GUIDED TISSUE REGENERATION

The biologic principle of GTR is based on observations indicating that periodontal regeneration occurs when the epithelial and connective tissue cells are selectively excluded from colonizing the root surfaces and the periodontal defects. Following the application of a mechanical barrier, cells from the periodontal ligament and from the alveolar bone will selectively repopulate the artificially created space.(22)

ENAMEL BONE MATRIX

Acellular cementum is the most important tissue for the insertion collagen fibers. It plays the largest role in attaching the tooth to the alveolar socket. Studies by Slavkin and Boyde [2] and Slavkin have shown that proteins, se- creted during tooth development by the Hertwig root sheath, play a crucial role in the formation of acellular root cementum. These proteins, referred to as enamel matrix proteins, constitute the largest proportion of the enamel matrix. They consist of a whole family of proteins, of which 90% are amelogenins, and the remain- ing 10% prolin-rich nonamelogenins, tuftelin and other serum proteins.(22,23,24,25)

EMD positively influences periodontal wound healing in humans. The goal of the current overview is to present, based on the existing evidence, the clinical indications for regenerative therapy with EMD. Surgical periodontal treatment of deep intrabony defects with EMD promotes periodontal regeneration. The application of EMD in the context of non-surgical periodontal therapy has failed to result in periodontal regeneration. Surgical periodontal therapy of deep intrabony defects with EMD may lead to significantly higher improvements of the clinical parameters than open flap debridement alone. The results obtained following treatment with EMD are comparable to those following treatment with GTR and can be maintained over a longer period.(26)

COMBINATION THERAPY

Several experimental and clinical studies have shown that the success of regenerative periodontal therapy is limited by the available space under the mucoperiosteal fl ap. Particularly in noncontained intrabony defects, which due to their anatomy cannot ensure suffi cient support for a bioresorbable membrane, the application of various combination therapies has been proposed. Despite the fact that combination approaches have not yet been proven to yield clear advantages over the use of single materials, they appear to be benefi cial in the treatment of wide intrabony defects.(27)

FACTORS INFLUENCING REGENERATIVE PERIODONTAL THERAPY

1. Patient-related factors
2. Morphology of the periodontal defect
3. Flap design
4. Suturing techniques/fl ap adaptation
5. Postoperative protocol(28)

CONCLUSION

The success of periodontal regeneration not only involves the experience and skills of the clinicians but also depends on variety of factors from the selection of the suitable regenerative materials and techniques to the dental armamentarium. A variety of surgical techniques and products for regeneration have been available with substantial research evidence reporting on their efficacy. The clinician should make their choice for the best suitable regenerative modality based on general and site specific factors and with respect to the natural healing events occurring post operatively.

REFFERENCE

1. Health U.S.D.o., Human S. NIH Publication; 2000. Oral Health in America : A Report of the Surgeon General; pp. 155–188
2. Deas D.E. Scaling and root planing vs. conservative surgery in the treatment of chronic periodontitis. *Periodontol.* 2000;71(1):128–139. 2016.
3. Graziani F. Nonsurgical and surgical treatment of periodontitis: how many options for one disease? *Periodontol.* 2000;75(1):152–188. 2017.
4. Smiley C.J. Evidence-based clinical practice guideline on the nonsurgical treatment of chronic periodontitis by means of scaling and root planing with or without adjuncts. *J. Am. Dent. Assoc.* 2015;146(7):525–535.
5. John M.T. Network meta-analysis of studies included in the Clinical Practice Guideline on the nonsurgical treatment of chronic periodontitis. *J. Clin. Periodontol.* 2017;44(6):603–611.
6. Villar C.C., Cochran D.L. Regeneration of periodontal tissues: guided tissue regeneration. *Dent. Clin.* 2010;54(1):73–92
3. Kao R.T., Nares S., Reynolds M.A. Periodontal regeneration - intrabony defects: a systematic review from the AAP Regeneration Workshop. *J. Periodontol.* 2015;86(2 Suppl):S77–S104
4. Lin Z., Rios H.F., Cochran D.L. Emerging regenerative approaches for periodontal reconstruction: a systematic review from the AAP Regeneration Workshop. *J. Periodontol.* 2015;86(2 Suppl):S134–S152
6. Li F. Evaluation of recombinant human FGF-2 and PDGF-BB in periodontal regeneration: a systematic review and meta-analysis. *Sci. Rep.* 2017;7(1):65. [
7.Tobias T. Hägi, Dr med dent1/Oliver Laugisch, Dr med dent1/Aleksandar Ivanovic, Dr med dent1/ Anton Sculean, Prof Dr med dent, Dr hc mult, MS2. Regenerative periodontal therapy
8.Axelsson P, Nystrom B, Lindhe J. The long-term effect of a plaque control program on tooth mortality, caries and periodontal disease in adults. Results after 30 years of maintenance. J Clin Periodontol 2004: 31: 749–757.
9. Tilkeridis K, Touzopoulos P, Ververidis A, et al. Use of demineralized bone matrix in spinal fusion. *World J Orthop* 2014; 5(1): 30–37.
10.Lindhe J, Nyman S. Long-term maintenance of patients treated for advanced periodontal disease. J Clin Periodontol 1984: 11: 504–51.
11. Albanese A, Licata ME, Polizzi B, et al. Platelet-rich plasma (PRP) in dental and oral surgery: from the wound healing to bone regeneration. *Immun Ageing* 2013; 10: 23.

12. Friedlaender GE, Perry CR, Cole JD, et al. Osteogenic Protein-1 (Bone Morphogenetic Protein-7) in the treatment of tibial nonunions: a prospective, randomized clinical trial comparing rhOP-1 with fresh bone autograft. *J Bone Joint Surg Am* 2001; 83-A(Suppl. 1 Pt2): S151–S158.
13. Xie J, Baumann MJ, McCabe LR. Osteoblasts respond to hydroxyapatite surfaces with immediate changes in gene expression. *J Biomed Mater Res A* 2004; 71(1): 108–117.
14. Campana V, Milano G, Pagano E, et al. Bone substitutes in orthopaedic surgery: from basic science to clinical practice. *J Mater Sci: Mater Med* 2014; 25: 2445–2461.
15. Ziran BH, Smith WR, Morgan SJ. Use of calcium-based demineralized bone matrix/allograft for nonunions and posttraumatic reconstruction of the appendicular skeleton. *J Trauma* 2006; 63: 1324–1328.
16. Burguera EF, Xu HHK, Weir MD. Injectable and rapid-setting calcium phosphate bone cement with dicalcium phosphate dihydrate. *J Biomed Mater Res B Appl Biomater* 2006; 77(1): 126–134.
17. Afifi AM, Gordon CR, Pryor LS, et al. Calcium phosphate cements in skull reconstruction: a meta-analysis. *Plast Reconstr Surg* 2010; 126(4): 1300–1309.
18.Gaasbeck RDA, Toonen HG, van Heerwaarden RJ, et al. Mechanism of bone incorporation of TCP bone substitute in open wedge tibial osteotomy in patients. *Biomaterials* 2005; 26: 6713–6719.
19. Koerten HK, van der Meulen J. Degradation of calcium phosphate ceramics. *J Biomed Mater Res* 1999; 44: 78–86.
20. Wagner Q, Offner D, Idoux-Gillet Y, et al. Nanostructured implant combining mesenchymal cells and VEGF nanoparticles for enhanced engineered tissue vascularization. *Nanomedicine* 2016; 11: 2419–2430.
21. Eap S, Ferrand A, Palomares CM, et al. Electrospun nanofibrous 3D scaffold for bone tissue engineering. *Biomed Mater Eng* 2012; 22(1–3): 137–141.
22 Slavkin HC: Towards a cellular and molecu- lar understanding of periodontics: cemento- genesis revisited. J Periodontol 1976;47:249– 255.
23. Brookes SJ, Robinson C, Kirkham J, Bonass WA: Biochemistry and molecular biology of amelogenin proteins of developing dental enamel. Arch Oral Biol 1995;40:1–4.
24. Emdogain in regenerative periodontal therapy. A review of the literature.Anton Sculean, Péter Windisch, Ferenc Döri, Tibor Keglevich, Balint Molnár, István Gera, Fogorvosi szemle 100 (5), 220-32, 211, 2007.
25. Harrel SK. A minimally invasive surgical approach for peri- odontal regeneration: surgical technique and observa- tions. J Periodontol 1999: 70: 1547–1557.
26.Harrel SK, Rees TD. Granulation tissue removal in routine and minimally invasive procedures. Compend Contin Educ Dent 1995: 16: 960, 962, 964 passim.
26. Karring T, Nyman S, Gottlow J, Laurell L. ZDevelopment of the biological concept of guided tissue regeneration–ani- mal and human studies. Periodontol 2000 1993: 1: 26–35.
27. Cortellini P, Tonetti MS. Clinical and radiographic out- comes of the modified minimally invasive surgical tech- nique with and without regenerative materials: a randomized-controlled trial in intra-bony defects. J Clin Periodontol 2011: 38: 365–373.
28.Linghorne WJ. The sequence of events in osteogenesis as studied in polyethylene tubes. Ann N Y Acad Sci 1960: 85: 445–460.