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REVIEW

Dental & Craniofacial Research

Regenereation in periodontics

Murtaza Kaderi[1*], Mohsin Ali[2] and Alfiya Ali[3] and Tasneem Kaderi[4]

[1]Department of Periodontics, ACPM Dental College and Hospital, India

[2]Department of Oral and Maxillofacial surgery, Sri Balaji Dental College, India

[3]Priority Dental Care, India

[4]Private Practitioner, India

Abstract

The goals of periodontal therapy are to arrest of periodontal disease progression and to attain the regeneration of the periodontal apparatus. Osseous grafting and Guided tissue regeneration (GTR) are the two techniques with the most extensive documentation of periodontal regeneration. However, these techniques offer limited potential towards regenerating the periodontal tissues. Recent surgical procedures and application of newer materials aim at greater and more predictable regeneration with the concept of tissue engineering for enhanced periodontal regeneration and functional attachment have been developed, analyzed, and employed in clinical practice.

Introduction

A complex group of tissues, the periodontium consists of soft tissues like Gingiva and the periodontal ligament and mineralized tissues in the form of Cementum and the Alveolar bone. These structures support and invest the teeth in the oral cavity. Periodontitis is defined as "an inflammatory disease of the supporting periodontal tissues caused by specific microorganisms or groups of specific microorganisms, resulting in progressive destruction of supporting periodontal tissues with increased probing depth, recession or both [1]." Periodontal disease alters the morphologic features of the alveolar bone in addition to reducing the height. Generally, bony deformities are not uniform. Bone defects could be "supra-bony" or "intra-bony" or a combination of both. Other bone deformities resulting from periodontal disease include osseous craters, reversed architecture, bulbous bone contours, ledges and furcation involvement. These changes often lead to tooth loss [1].

Regeneration of lost periodontal support in appropriate regions remains the primary goal of periodontal therapy. Several periodontal therapeutic modalities have been implicated for periodontal regeneration, involving formation of new bone and new cementum with yet outcomes of these modalities are not very predictable. The character of the bone loss determines the type of surgery indicated along with the prognosis [2].

"Periodontal regeneration is defined histologically as regeneration of the tooth's supporting tissues, including alveolar bone, periodontal ligament, and cementum over a previously diseased root surface." 'Bone fill' is the clinical and histological restoration of mineralized bony tissue in a treated periodontal defect. It does not describe the presence of histologic evidence of new connective tissue attachment [3]. Presently, guided tissue regeneration (GTR) and osseous grafting have been most extensively documented for periodontal regeneration [4]. Some recent advances in the regenerative therapies include the use of: 1) root surface bio-modification; 2) Platelet concentrates; 3) Enamel matrix derivatives; 4) Growth factors; 5) Bone morphogenic proteins and 6) Tissue engineering.

Osseous grafting

Bone replacement grafts like autografts, allografts, xenografts, and alloplasts, are the most widely used substitutes for the correction of a variety of periodontal osseous defects. The rationale for using bone replacement graft materials in periodontal therapy is to enhance the regenerative capacity of bone and achieve new attachment [5]. A list of osseous and non-osseous graft material has been enlisted in figure 1.

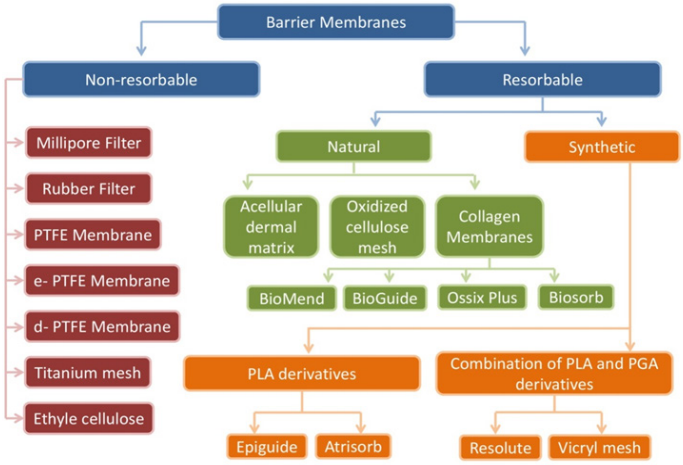

Figure 1. *Classification of Barrier membranes*

Biologic mechanisms which support the use of bone grafts in periodontal regeneration are Osteogenesis, Osteoinduction, Osteoconduction and Osteopromotion.

- Osteogenesis is the formation or development of new bone by osteogenic cells contained in the graft.
- Osteoinduction is the chemical process by which molecules contained in the graft (Bone morphogenic proteins) induce the undifferentiated mesenchymal cells to mature into osteoblasts, which in turn form bone.
- Osteoconduction is the physical effect by which the matrix of the graft forms a scaffold that favors host osteoprogenitor cells to penetrate the graft and form new bone.
- Osteopromotion is the property of the material that promotes the de novo formation of the bone.

Amongst the various grafting materials enlisted, only Autogenous grafts possess the osteogenic property. Allografts such as Demineralized Freeze-Dried Bone Allografts (DFDBA) have shown to be osteoinductive whereas Freeze-Dried Bone Allografts (DFDBA), Xenografts and Alloplasts are purely osteoconductive [6-8]. Studies have indicated that graft particle size is an important aspect to be considered while selecting the grafting material. Polson et al. recommended grafting material with particle size of 250-750 µm to be used in periodontal regeneration. Grafts with particles less than the recommended size resorb at a very fast rate and grafts with particle size < 125 µm have been reported to induce a foreign body giant cell response [9-12].

Guided Tissue Regeneration (GTR)

The concept of "compartmentalization" was introduced by Melcher, in 1976. The concept that only PDL cells have the potential to create a new connective tissue attachment has been shown through extensive research. Moreover, results strongly indicate that excluding epithelial cells favors periodontal regeneration [13,14]. GTR procedures were subsequently developed where barrier membranes helped to achieve epithelial exclusion with selective cell repopulation of the periodontal wound, clot stabilization and space maintenance [14]. GTR has been tried using various non-resorbable as well as bioabsorbable membranes. A list of cell-occlusive barriers is shown in figure 2.

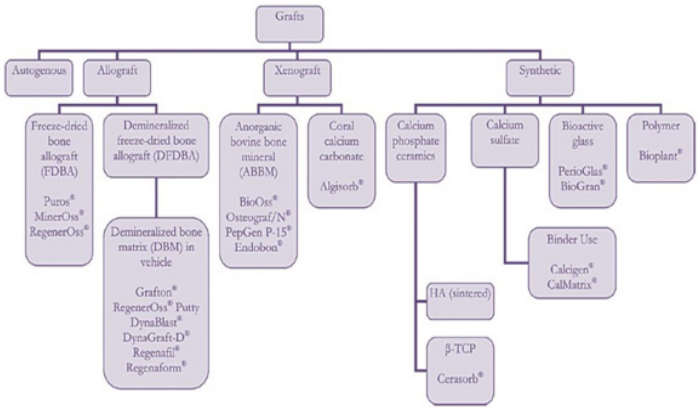

Figure 2. *Classification of Bone replacement grafts.*

Guided tissue regeneration consistently proves to be more effective in improving clinical attachment levels and probing depth reduction in comparison to open flap debridement alone for the treatment of periodontal osseous defects. When a comparison was made with non resorbable membranes, resorbable membranes proved to be equally successful [15,16].

Wang et al. broadly divided the barrier membranes used for GTR into three generations [17]:

First generation membranes

Developed in the 60s and 70s, these membranes were used to accomplish a suitable composition where its physical properties would be similar to the replaced tissue. These include non-bioresorbable membranes such as filter produced from expanded polytetrafluoroethylene (e-PTFE), cellulose acetate (Millipore), titanium reinforced ePTFE, titanium mesh or high-density-PTFE. Disadvantage with these membranes is the requirement for a surgical re-entry to retrieve the membrane.

Second generation membranes

These membranes are bioabsorbable to avoid surgical re-entry. These are either natural or synthetic membranes. Natural membranes provide physiological signals for the induction and preservation of cell machinery and possess an ability to enzymatically degrade through natural pathways. Natural barriers are derived from collagen or chitosan. Synthetic membranes are prepared using polyesters (such as poly(glycolic acid), poly(lactic acid), poly(-aprolactone) and their copolymers). Several complications have been reported with collagen membranes such as early degradation, epithelial down growth along the material and premature loss of material. Although very minimal, there is a risk of transmission of infections and autoimmunization with their use.

Third generation membranes

These barriers were developed to provide additional delivery of specific agents such as antibiotics, growth factors and adhesion molecules to aid periodontal regeneration. Third generation barriers include [17] –

- Antimicrobial delivering membranes– Synthetic membranes incorporating amoxicillin or tetracycline are examples of such barriers.
- Bioactive Calcium and Phosphates delivering membranes– These are three-layered membranes which have a porous side (to allow cell in growth) consisting of nano-carbonated hydroxyapatite/collagen/PLGA, a pure PLGA non-porous side (to discourage cell adhesion), and a transitional layer consisting of nCHAC/PLGA.
- Growth Factors delivering membranes-The bioactive molecules incorporated in the membranes include PDGF, IGFI, basic fibroblast growth factor (FGF-2) , TGF-1 , BMP-2, -4, -7 and -12, and enamel matrix derivative (EMD) [17].

Other developments

Recent advances in GTR membranes include Electrospinning (e-spinning) for membrane, functionally Graded Multilayered membranes and the use of Platelet-Rich Fibrin Autologous membrane [17].

Root Biomodification

TIt is well established that periodontal regeneration is not favored by a periodontally diseased root surface. Demineralization modifies the diseased root surface, creates an acceptable surface that can influence events in wound healing. The rationale of applying these agents on the root surface is to remove the smear layer, open and widen the dentin tubules, expose the dentin collagen matrix, induce mesenchymal cell differentiation, extract endotoxins and othertoxic products and accelerate cementogenesis [18].

Recent evidence does not support the adjunctive application of routinely used root biomodification agents i.e. citric acid, tetracycline HCl or EDTA to reduce probing depth or improve clinical attachment levels [19]. Their role in smear layer removal and detoxification has been proved only in in-vitro and animal studies. Recently Angelo Mariotti in a systematic review on efficacy chemical root surface biomodifiers in the treatment of periodontal disease established that chemical modifiers like EDTA, citric acid ortetracycline provides no benefit of clinical significance to regeneration in patients with chronic periodontitis [19]. On the contrary, Fibronectin has been shown to significantly enhance the effects of demineralization with regard to new attachment and enhance cell proliferation from periodontalligament and supra crestal area [20].

Since the last two decades there have been advances in recognition of newer root biomodification agents. Root conditioners such as Laminin, Chondroitin sulphate, polyacrylic acid, sodium hypochlorite, Sodium Deoxy Cholate and Human Plasma Fraction Cohn IV, Formalin, Enzymes (such as Hyaluronidase, Elastase and collagenase), Stannous Fluoride, Growth Factors (such as recombinanthuman platelet-derived growth factor BB) and Lasers (such as Nd: YAG, Er: YAG, Er, Cr:YSGG and Carbon-di-oxide lasers) have been employed with varying histological evidence of regeneration in patients with chronic periodontitis. Most of the research conducted using newer root biomodification agents have been limited to in-vitro studies evaluating their effect on periodontal fibroblast attachment on dentinal root surfaces [21,22].

Platelet Concentrates

Platelets are composed of growth factors and cytokines which play a vital role since they are the key factors for regeneration of the bone. Platelet concentrates [platelet-rich plasma (PRP) and platelet-rich fibrin (PRF)] are routinely used for surgical procedures in medical and dental fields. PRF is a natural fibrin-based biomaterial prepared from blood harvest devoid of anticoagulants without any artificial biochemical modification that allows obtaining fibrin membranes enriched with platelets and growth factors. Advantages of PRF over PRP include [23]:

- Addition of bovine thrombin or other anticoagulants avoided.
- 3-D network-connected trimolecular or equilateral junctions-allows the formation of a fine and flexible fibrin network able to support cytokines enmeshment and cellular migration.
- The 3-D structure gives elasticity and flexibility to the PRF membrane.

Platelet concentrates have come a long way since its first appearance in 1954 to the T-PRF, A-PRF and i-PRF introduced recently. A brief depiction of the recent concept of Low Speed Centrifugation Process (as suggested by Choukroun et al.) is shown in figure 3 [23].

Applications in periodontics: PRF when used as a membrane for guided tissue regeneration has a space making effect which facilitates cell events that are favorable for periodontal regeneration allowing mineralized tissue formation. Evidence indicates that the use of platelet concentrates for the treatment of 3-wall intra-bony defects and mandibular grade II furcation defects in chronic periodontitis patients results in statistically significant improvement in pocket depth reduction and bone fill [24].

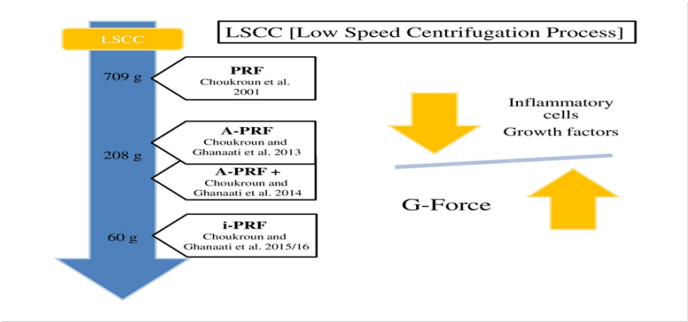

Figure 3. *Development of solid and injectable PRFs following the low-speed centrifugation concept (LSCC).*

Enamel Matrix Derivatives

TThe enamel matrix derivatives mainly consist of amelogenin, i.e. expressed in human teeth between the peripheral dentin and the developing cementum during root formation. Histologic evidence demonstrates that EMD, used on previously periodontally affected root surfaces induces new cementum, PDL, and alveolar bone formation. A recent systematic review showed that EMD significantly improved CAL gain in intra-bony defects compared with a control. In the treatment of furcations, evidence shows significantly greater reduction in horizontal furcation depth and less recession and postoperative complications after the use of EMD [25].

Growth Factors

A range of growth and differentiation factors (GDFs) – such as platelet derived growth factor (PDGF),acidic and basic fibroblast growth factors (a/bFGF), and bone morphogenetic proteins (BMPs) have been assessed for their potential to support periodontal wound healing and regeneration. Human histological research has shown periodontal regeneration in intrabony defects treated with either GDF5 or rhPDGF-BB on abeta-tricalcium phosphate(b-TCP) carrier while the combination of rhPDGF-BB and DFDBA resulted in robust and consistent periodontal regeneration [26].

Tissue Engineering

With the advances in molecular and cellular biology, periodontal research has incorporated tissue engineering principles for comprehending the processes involved in periodontal healing. The use of tissue engineering has been employed for periodontal regeneration to achieve a more reliable and predictable regeneration

of periodontal tissues. Three basic components of periodontal tissue engineering include appropriate signals, cells and scaffolds that target the tissue defect. Cells provide the machinery for new-tissue growth and regeneration. Signaling factors modulate cellular activity and provide stimuli to cells to differentiate toward developing tissues. Finally, scaffolds guide and form a template structure three dimensionally to facilitate the above processes critical for tissue engineering [4] (Figure 4).

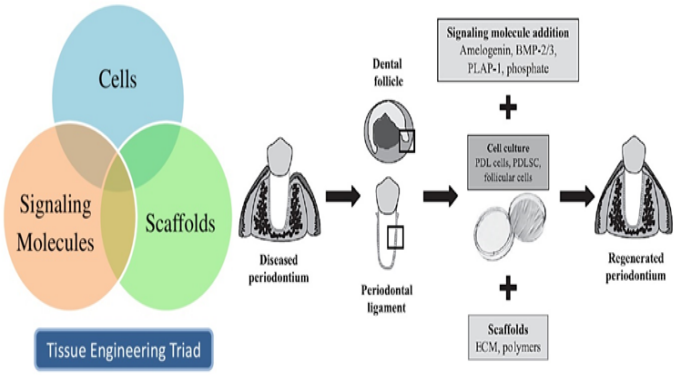

Figure 4. *Schematic illustration of elements necessary in periodontal tissue engineering.*

Conclusion

The periodontal therapy aims to reduce or eliminate tissue inflammation induced by bacterial plaque and its by-products, correct defects or anatomical problems caused by the disease process, and regenerate periodontal tissues lost as a consequence of disease progression. Through continuing efforts our understanding of periodontal regeneration biology has progressed and through this we can also expect developments in biologic and materials sciences, providing newer guided tissue regenerative materials and delivery systems. Further, establishing a scientifically sound, evidence-based rationale is critical to the ultimate success of regenerative therapies.

References

1. Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. *Lancet*. 2005; 366: 1809-1820.
2. Wang HL, Greenwell H, Fiorellini J, Giannobile W, Offenbacher S, et al. Periodontal regeneration. *J Periodontol*. 2005; 76: 1601-1622.
3. American Academy of Periodontology. Glossary of Periodontal Terms. Chicago: American Academy of Periodontology; 2001.
4. Benatti BB, Silvério KG, Casati MZ, Sallum EA, Nociti Jr FH. Physiological features of periodontal regeneration and approaches for periodontal tissue engineering utilizing periodontal ligament cells. *J Biosci Bioeng*. 2007; 103: 1-6.
5. Garrett S, Bogle G. Periodontal regeneration with bone grafts. *Curr Opin Periodontol* 1994: 168–177.
6. Mellonig J, Bowers G, Bailey R. Comparison of bone graft materials. I. New bone formation with autografts and allografts: A histological evaluation. *J Periodontol.* 1981; 52: 297-302.
7. Moore WR, Graves SE, Bain GI. Synthetic bone graft substitutes. *ANZ J Surg*. 2001; 71: 354-361.
8. Mellonig JT. Autogenous and allogeneic bone grafts in periodontal therapy. *Crit Rev Oral Biol Med* 1992; 3: 333-352.
9. Nabers CL, O'Leary TJ. Autogenous bone transplants in the treatment of osseous defects. *J Periodontol* 1965; 36: 5-14.
10. Yukna RA. Clinical evaluation of coralline calcium carbonate as a bone replacement graft material in human periodontal osseous defects. *J Peridontol*. 1994; 65: 177-185.
11. Polson AM. Periodontal regeneration – Current status and directions. Quintessence Publishing Co, Inc. 1994.
12. Nyman S, Lindhe J, Karring T, Rylander H. New attachment following surgical treatment of human periodontal disease. *J Clin Periodontol*. 1982; 9: 290-296.
13. Gottlow J, Nyman S, Karring T, Lindhe J. New attachment formation as the result of controlled tissue regeneration. *J Clin Periodontol*. 1984; 11: 494-503.
14. Schultz AJ, Gager AH. Guided tissue regeneration using an absorbable membrane (polyglactin 910) and osseous grafting. *Int J Periodontics Restorative Dent.* 1990; 10: 8-17.
15. Laurell L, Falk H, Fornell J, Johard G, Gottlow J. Clinical use of a bioresorbable matrix barrier in guided tissue regeneration therapy. Case series. *J Periodontol.* 1994; 65: 967-975.
16. Wang HL, MacNeil RL. Guided tissue regeneration. Absorbable barriers. *Dent Clin North Am*. 1998; 42: 505-522.
17. Register AA. Bone and cementum induction by dentin demineralized in situ. *J Periodontol*. 1973; 44: 49-54.
18. Mariotti A. Efficacy of chemical root surface modifiers in the treatment of periodontal disease. A systematic review. *Ann Periodontol Dec*. 2003; 8: 205-226.
19. Caffesse RG, Nasjleti CE, Anderson GB, Lopatin DE, Smith BA, et al. Periodontal healing following guided tissue regeneration with citric acid and fibronectin application. *J Periodontol*. 1991; 62: 21-29.
20. Willey R, Steinberg AD. Scanning electron microscopic studies of root dentin surfaces treated with citric acid, elastase, hyaluronidase, pronase and collagenase. *J Periodontol*. 1984; 55: 592-596.
21. Dilsiz A, Aydin T, Canakci V, Cicek Y. Photomedicine and Laser Surgery. 2010; 28: 337-343.
22. Miron RJ, Choukroun (2017) Platelet Rich Fibrin in Regenerative Dentistry: Biological Background and Clinical Indications. John Wiley & Sons.
23. Castro AB, Meschi N, Temmerman A, Pinto N, Lambrechts P, et al. Regenerative potential of leucocyte- and platelet-rich fibrin. Part A: intra-bony defects, furcation defects and periodontal plastic surgery. A systematic review and meta-analysis. *J Clin Periodontol*. 2017; 44: 67-82.
24. Koop R, Merheb J, Quirynen M. Periodontal regeneration with enamel matrix derivative in reconstructive periodontal therapy: a systematic review. *J Periodontol*. 2012; 83: 707-720.
25. Stavropoulos A, Wikesjö UME. Growth and differentiation factors for periodontal regeneration: a review on factors with clinical testing. *J Periodont Res*. 2012; 47: 545-553.

Correspondence: Dr. Murtaza Altaf Kaderi, Department of Periodontics, ACPM Dental College and Hospital, 1509, Agra Road, Dhule – 424001,Maharashtra, India, E-mail: dr.murtazakaderi@gmail.com

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