REGENERATION IN PERIODONTAL SURGERY: A REVIEW

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ABSTRACT

The ultimate goal of periodontal therapy is the regeneration of the tissues destroyed as a result of periodontal disease**.** Clinical and histologic evidence of periodontal regeneration has been shown for multiple regenerative therapies, including bone replacement grafts, guided tissue regeneration, and biologics, when used alone or in combination. Regenerative therapies improve periodontal health, as evidenced by gain in clinical attachment level, reduction in probing depth, and gain in radiographic bone fill. Bonegrafting has become a valuable mainstream clinical procedure in today's era of dentistry in variety of reconstructive applications.The regeneration industry may encourage the use of allograft and alloplasts which may serve as an implement to simple wound healing. This review is an assessment of the clinical use of various regenerative tools specifically bone replacements and membranes. The future of the regeneration may depend on the merging of various technologies and biological concepts. Including the possible use of biological barriers, various bone and periodontal growth inducers and artificial matrices that will attract or carry the cells necessary for regeneration

Keywords: Alveolar bone loss, Bone graft, Barrier membrane, Regeneration, Growth factors.

INTRODUCTION

Regeneration can be defined as the reproduction or reformation of organs or tissue that have been lost or injured as a result of a wound or infection. Regenerative periodontal procedure involves the creation of new alveolar bone, cementum, and periodontal ligament. Most periodontal practices focus on prevention of disease, initiation and corrective surgical treatment to eliminate deep pockets. Regeneration is distinct from tissue repair and is characterized by replacement of the damaged tissues with something that may be inferior to the original tissues both structurally and functionally.[1]

Eliminating bacteria and regenerating bone and supporting tissues helps in reducing pocket depth and repair damage caused by progression of periodontal disease. Over the last decade different modalities of regenerative treatment have been used and clinically

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applied. The positive effects of bone grafts and bone substitute on the outcome of periodontal regenerative procedures are well documented. At the present time, periodontists favor the bone as grafting material which has shown clinical effectiveness, functional periodontal repair, apparent bone defect fill and pocket reduction to manageable levels.

Periodontal Debridement

The removal of periodontal pathogenic bacteria, mineralized deposits on the root surface and infected cementum containing associated toxins is one of the most predictable methods achieved either by non surgical or surgical debridement leading to stable periodontal healing[2]. A study had shown that surgical debridement of intra-osseous defects leads to an increase in periodontal attachment of about 2.5mm with variable amount of bone filling.[3]

Historical Perspective

Hegdus attempted the use of bone grafts for the reconstruction of bone defects produced by periodontal disease[4]. Subsequent to their report and for the next several decades, the evolution of xenografts of various types became the main focus of attention. Buebe and Silvers used boiled cow bone powder to successfully repair intra-bony defects in humans[5]. Melcher used anorganic bone in bovine bone in bone defects with a minimum follow-up of 3 years. He felt that protracted sequestration and slow resorption mitigated against the use of organic bone[6]. Scopp et al. used Boplant bovine bone and reported pocket depth reduction at 6 months[7]. Older reported good results by measuring by probing depth reduction and increasing radiographic density[8].The widespread clinical use that followed these reports resulted in routine rejection and failure[9]. The considerations that govern the selections of a material have been defined as biological acceptability, predictability, clinical feasibility, minimal post operative sequelae, patient acceptances. It is difficult to find a material with all these characteristics, and to date there is no ideal material or technique. Various graft materials have been developed and tried in many forms.

Grafting materials

Bone regeneration can be accomplished through three different mechanisms: osteogenesis, osteoinduction, and osteoconduction. Osteogenesis is the formation and development of bone, even in the absence of local undifferentiated mesenchymal stem cells. Osteoinduction is the transformation of undifferentiated mesenchymal stem cells into osteoblasts or chondroblasts through growth factors that exist only in living bone. Osteoconduction is the process that

provides a bio-inert scaffold, or physical matrix, suitable for the deposition of new bone from the surrounding bone or encourages differentiated mesenchymal cells to grow along the graft surface [10].

All grafting materials have one or more of these three mechanisms of action. The mechanisms by which the grafts act are normally determined by their origin and composition. The primary types of bone graft material are autogenous bone, allografts, xenografts and alloplasts. Autogenous bone harvested from the patient forms new bone by osteogenesis, osteoinduction, and osteoconduction. Allografts harvested from cadavers have osteoconductive and possibly osteoinductive properties, but they are not osteogenic. Xenografts/ alloplasts are typically only osteoconductive.

Autogenous Bone Graft

Autogenous grafts are those obtained from a remote location within the same host and are considered the gold standard bone replacement graft. These grafts are obtained intraorally from the extraction sockets, edentulous ridges, ramus, symphysis, tuberosity, or the surrounding buccal plate They are osteogenic, osteoconductive and osteoinductive. There is no risk of host rejection or disease transmission. But its major disadvantages are procurement morbidity, limited availability and high cost. There are several types of bone graft that have been or are being used clinically. They include cortical bone chips, osseous coagulum, bone blend, intraoral and extra oral cancellous bone, and marrow.

Cortical bone chips

The modern day use of periodontal bone grafts can be traced to the work of nabers and O' Leary[11]. They reported that the use of cortical bone removed during osteoplasty and osteoctomy from sites when the surgical areas could be used successfully to increase in bone height. According to Langer et al. suggests that this type of graft is still in use and may result in bone fill with decreased probing depth[12]. From Zayer and Yukna point of view the cortical chips due to their relative large particle size and potential for sequestration were replaced by osseous coagulum and bone blend[13].

Osseous coagulum and bone blend

The need of progenitors, blood supply and morphogens has encouraged the use of autogenous osteogenic tissue for grafting. For example osseous coagulum and bone blend has been and still is used to achieve bone filling in periodontal and osseous defects[14].The rationale for the use of their mixture as well as blood and osteogenic cells is to supply progenitors and morphogens to the wound site and promote stable clot formation.

Iliac autografts

The use of fresh and preserved iliac cancellous marrow bone has been extensively investigated. This material has been used by orthopedic surgeons for years data from human and animals studies support its use and the technique have prove successful in bone defects and in furcations[15].The advantages of using autogenous grafts are that these grafts are osteogenic, prevent disease transmission, and are cheap. However, they do require a second surgical site at the donor site. Schallhorn used iliac crest grafts in the treatment of infrabony defects and reported up to a 4-mm gain in bone height[15]. However, reports of root resorption, postoperative infection, exfoliation, sequestration, made this treatment option less favorable[16]. The fact that that intraoral autogenous grafts resulted in similar outcomes to bone obtained from extra oral sources made this a more favorable approach for the management of small defects. Several groups have shown that this approach may result in true periodontal regeneration with new cementum formation[17].

Bone Allografts

Allografts consist of tissue transferred from one individual to another genetically dissimilar individual of the same species. The main benefit of allograft bone is the avoidance of a secondary donor site, reduced surgical time, decreased blood loss, decreased host morbidity and unlimited supply of graft material. However, allografts are not osteogenic and bone formation usually takes longer and results in less regeneration than autogenous grafts. With allografts, concerns have been raised regarding the possibility of disease transmission through grafting; however, with meticulous donor screening and specimen processing, the risk is extremely low. Freeze-drying and the Tutoplast® process are two commonly used sample processing methods that can further reduce the risk of disease transmission [18]. Freeze-dried bone can be used in two forms, demineralized freeze-dried bone allograft (DFDBA) or mineralized freeze-dried bone allograft (FDBA). Since FDBA is mineralized, it elicits slower resoprtion than DFDBA and provides an osteoconductive scaffold when implanted in mesenchymal tissues. For DFDBA, the demineralization process removes the mineral phase of the graft which can expose the underlying bone collagen and possibly bone growth factors like BMPs, because of this, DFDBA may have a higher osteoinductivity than FDBA[19]. However, this osteogenic potential depends on the quality and quantity of the bone matrix in the graft material.

Xenogenic Bone Grafts

Xenografts are tissue grafts obtained from a species other than the host species. The representative xenograft materials are natural hydroxyapatite (HA) and deorganified bovine bone (anorganic bone matrix or ABM). These graft materials are inert osteoconductive filler material, which serves as a scaffold for new bone formation. Natural hydroxyapatite is extracted from animal bones. It has the three-dimensional microstructure of natural bone and is highly biocompatible to adjacent hard and soft tissues. ABM is an inorganic bone of bovine origin. It is a carbonate containing apatite with crystalline architecture and a calcium/phosphate ratio similar to that of natural bone mineral in humans. With time, ABM graft material becomes integrated into the human bone and is slowly replaced by newly formed bone.

Synthetic / Alloplastic Bone Grafts

Alloplasts are an inert synthetic graft material. The most commonly used alloplast materials are calcium carbonate, calcium sulfate, bioactive glass polymers and ceramic materials, including synthetic hydroxyapatite and tricalcium phosphate (TCP). The mechanism of action of these materials is strictly osteoconduction. They provide a scaffold for enhanced bone tissue repair and growth. The use of autografts, allografts, xenografts, or alloplasts, alone or in combination, should be based on the individual's systemic healing capacity, the osteogenic potential of the recipient site, and the time available for graft maturation. Due to the absence of definitive conclusions as to the relative efficacy of xenografts and alloplasts in the management of periodontal defects, they are recommended to be combined with allografts for small defects in healthy patients. Autogenous bone should be added for progressively larger defects, especially for defects and/or patients with lower osteogenic potential. Additionally a barrier membrane should be utilized for better results [20].

Guided Tissue Regeneration

Guided tissue regeneration is a barrier technique used for the treatment of periodontal bone defects. Guided bone regeneration is used to enhance bone growth of the alveolus for implant placement and around peri-implant defects. The principles of selective cell repopulation, ultimately termed GTR were developed by Nyman by using selective approximation of periodontal instead of gingival tissue, new connective tissue attachment can form on previously diseased roots. The use of membrane filter also fulfilled the principles of tissues exclusion. Earlier studies had suggested exclusion of the oral epithelium could lead to improvements in periodontal healing

after surgery[21]. This concept lead to the development of epithelial exclusion methods, which apparently lead to turn to more predictable filling of intra-osseous defects around periodontally diseased teeth. In addition to bone grafting material in case of severe bone loss the use of barrier membrane in regenerative procedures may enhance clinical success by offering better protection and containment of bone substitute inside the defect. The development of various barrier-based treatment modalities and techniques and a wide range of non resorbable and resorbable membrane gave rise to the acceptance of tissue regenerative approach focused solely on bone regeneration, guided bone regeneration. Histologic studies of bioabsorbable membranes indicate that regeneration can occur after healing, although repair was seen in certain cases. Bioabsorbable membranes have been found to achieve better regenerative outcomes in infrabony defects as compared with furcation.

Growth Factors / Cytokines / Host Modulating Agents

The application of local growth factors has been studied to enhance the healing and regeneration potential of periodontal surgery. PRP, growth factors including BMPs, PDGF, and EMD are the most commonly used agents. Other promising therapeutics include collagen fragments bound to bone grafts, PTH, and transforming growth factor beta 3 (TGF-b3). PRP is a highly concentrated suspension of autologous platelets, which secrete bioactive growth factors on activation. Because these growth factors are present at increased concentrations in PRP, they help to enhance key stages of wound healing and regenerative processes including chemotaxis, proliferation, differentiation, and angiogenesis. Similarly, autologous platelet concentrate (APC) contains PDGFs that promote regeneration. Studies comparing APC with a bioabsorbable membrane in infrabony defects found similar results between the 2groups, suggesting that APC could be used instead of a G T R membrane. BMPs have an anabolic effect on periodontal tissues through stimulation of osteoblastic differentiation in human periodontal ligament cell. Animal studies have shown new bone formation and connective tissue attachment with cementum regeneration occurred around circumferential periodontal defects in dogs treated with rhBMP-2compared with controls. However the use of BMPs in humans have not become widespread due to the finding of ankylosis in animal studies.. To date, sufficient human studies with BMPs in periodontal defects are lacking. PDGF is a growth factor involved in wound healing

that stimulates the regenerative potential of periodontal tissues including bone, cementum, and periodontal ligament. PDGF-BB is one form of PDGF, and it has shown the most promise as a regenerative agent. PDGF has also been studied to enhance implant site development[22].

EMD are deposited onto the dentin root surface and provide the initial step in the formation of acellular cementum. Auto radiographic and scanning electron microscopy studies have provided additional evidence that EMD are responsible for both initiation and modulation of cementogenesis. Consequently, they have been incorporated into GTR and attempts have been made to promote cementogenesis and, thus, periodontal regeneration. Several studies have suggested that EMD and growth factors are promising in terms of their ability to promote tissue/bone regeneration, but that long-term data and sufficient evidence are still lacking. A15 amino acid sequence from collagen has been incorporated into an inorganic bovine matrix and marketed as ABM/P-15 to rely on collagen to promote the binding of fibroblasts and osteoblasts in the tissue matrix. Here are only very few studies evaluating the ability of ABM/P-15 to promote periodontal regeneration[23].

PTH is an endogenous hormone with anabolic actions at low intermittent doses. Preliminary animal studies have shown that this might be a promising technique for regenerating bone in the periodontium.

Recently a arginine-glycine-aspartic acid (RGD) modified polyethylene glycol–based matrix (PEG) containing covalently boundpeptides of the parathyroid hormone (PTH(1-34)) to promote bone regeneration around dental implants was introduced . Studies found this technique enhanced bone regeneration in a similar magnitude as autogenous bone grafting in animals.

CONCLUSION

It is important to understand the various limitations in the assessment of periodontal regeneration, such as confirming the formation of bone rather than ectopically mineralized fibrous tissues, as well as the reformation of the attachment apparatus after therapy. The predictability of regeneration is affected by anatomic factors, as outline at the outset of this presentation and by the host systemic factors (eg. Smoking and chronic diseases) moreover as stated above, even with the best regenerative treatments available. As per our understanding of stem cells, matrix and morphogens increases, there is hope that their contribution to regeneration will eventually lead to combined therapy based on sound principles.

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