Review Article

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CRITICAL ISSUES IN PERIODONTAL REGENERATIVE THERAPY

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ABSTRACT:

Development of periodontal regenerative medicine in the past 25 years has followed two distinctive but interlaced paths. The interest of researchers focused on regenerative materials and products on the one side and on novel surgical approaches on the other side. The availability of advanced diagnostic methods, the use of three-dimensional imaging modalities, the increasing access to optimized scaffold fabrication technology, and new surgical protocols and tools that minimize trauma and enhance wound healing are paving the road to a more predictable future in periodontal regenerative sciences. But, complete regeneration is still not achieved. Here we are going to discuss about various issues that critically influence periodontal regeneration.

Keywords: Periodontal regeneration, smoking, defect morphology, furcation defects, surgical technique.

INTRODUCTION:

Regeneration is the natural renewal of a structure, produced by growth and differentiation of new cells and intercellular substances to form new tissues or parts. Regeneration occurs through growth from the same type of tissue that has been destroyed or from its precursor.[1]

The availability of advanced diagnostic methods, the use of three-dimensional imaging modalities, the increasing access to optimized scaffold fabrication technology, and new surgical protocols and tools that minimize trauma and enhance wound healing are paving the road to a more predictable future in periodontal regenerative sciences.[2] Here we are going to discuss about the various issues that critically affect periodontal tissue regeneration in various therapeutic modalities.

CRITICAL ISSUES IN REGENERATIVE THERAPY:

SMOKING:

Ah et al. (1994) reported that, smokers of more than 10 cigarettes a day respond less favourably to both conservative and surgical periodontal therapy than do non-smokers.[3] According to Tonetti et al. (1995) and Machtei et al. (2003), cigarette smoking has been associated with a reduced healing response during tissue maturation phase following Guided Tissue Regeneration (GTR) treatment. Machtei in 2003 stated that when GTR is

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performed for class II furcation defects in smokers, anti-infective therapy should be incorporated into the treatment protocol to enhance the regenerative outcome.[4,5]

Souza et al. (2008) conducted a study to evaluate root coverage in areas of gingival recession and to compare graft vascularisation in 15 smokers and 15 non-smokers who had Miller Class I or II recession in non-molar teeth. The recessions were treated surgically with a coronally positioned flap associated with a subepithelial connective tissue graft. A small portion of this graft was prepared for immunohistochemistry. Blood vessels were identified and counted by expression of factor VIII–related antigen–stained endothelial cells. The patients were evaluated at 3 and 6 months. The results showed that smokers had less root coverage than non-smokers. Furthermore, the smokers had more gingival recession than the nonsmokers. Histomorphometry of the donor tissue revealed a higher blood vessel density for non-smokers than smokers.[6] Galindo R et al. (2015) showed that smokers who attended less than 75% of their scheduled maintenance appointments within 1 year showed a 100% recurrence rate.[7]

PERSISTENT INFECTION:

Nowzari & Slots in 1994 suggested that infection could be a major obstacle for periodontal regeneration.[8]Nowzari et al. (1995) conducted a study to determine the microbial composition of apical parts of membrane surfaces facing the gingiva and the tooth. He also determined microbial and clinical features of 2-to-3 wall periodontal bony defects treated with membranes, with or without concomitant use of systemic antibiotic therapy. The results of the study showed that, at the time of removal, membranes in the antibiotic group showed significantly fewer organisms than membranes in the control group. Sites free of pathogens on the membrane surface toward the tooth gained the maximum clinical attachment, despite the presence of various pathogens on the gingiva-facing membrane surface.[9]

MORPHOLOGY OF THE DEFECTS:

Clinical efficacy of GTR procedures in intra-bony defects depend on defect morphology. Tonetti (1996) showed that intrabony defects deeper than 3 mm show greater probing attachment gain and bone fill than shallow defects.[10] According to Klein et al. (2001) and Eickholz (2004) intra alveolar defects of defects that are less than 3 to 4 mm deep tend to lose rather than gain bone substance when subjected to regenerative measures.[11,12]Cortellini et al. (1998) stated that intra-bony defects with narrow radiographic angle (< 25 degrees) consistently gained more attachment than wide defects (> 37 degrees). Outcome of regenerative therapy in one and two walled defects is not as predictable as in 3-walled defects.[13]

TOOTH MOBILITY:

Conflicting data exists regarding the effect of tooth mobility on regeneration. Trejo and Weltman (2004) reported that intraosseous defects of teeth with Miller's grade 1 and 2 mobility responded favourably to regenerative therapy.[14] However according to Cortellini et al. (2001), presurgical tooth mobility has a negative effect on the clinical outcome of GTR and should be controlled through splinting and/or occlusal adjustments.[15]

LOCAL ANATOMIC FACTORS AFFECTING PERIODONTAL REGENERATION:

The predictability of periodontal regeneration is strongly influenced by local anatomy and morphology of the defect. Cervical enamel projections (CEPs) and enamel pearls interfering in periodontal regeneration should be removed during regenerative procedures. Lim HC et al. (2015) evaluated the prevalence of cervical enamel projections in mandibular molars, and analyzed the correlation between CEPs and furcation involvement based on cone-beam computed tomography (CBCT) data in a Korean population. The results of the study showed that there was statistically significant, but negligible correlation between the CEP grade and the degree of furcation involvement on the buccal and lingual surfaces.[16]Anderegg et al. (1991) showed that gingival thickness of ≤ 1mm is associated with increased prevalence and severity of flap dehiscence over GTR membranes.[17] Hwang D and Wang HL (2006) conducted a systemic review to appraise any association between gingival thickness and root coverage outcomes. Fifteen investigations were included and all of these reported at least 0.7 mm of flap thickness, although measurement locations varied. Treatment modalities included coronally advanced flap, connective tissue graft and guided tissue regeneration with and without bone replacement graft. The results showed that, a critical threshold gingival thickness of > 1.1 mm should exist for complete root coverage. The type of treatment rendered also influenced root coverage. High correlation existed between thickness and mean root coverage in connective tissue grafting and guided tissue regeneration but not coronally advanced flap therapy.[18]

According to Nieri (2009), the distance between the gingival margin and the cemento-enamel junction immediately after coronally advanced flap procedure was affected by the baseline recession depth. Deeper recessions were associated with a more apical location of the gingival margin after surgery with a lesser probability of complete root coverage.[19]

Mandibular first and second molars frequently exhibit differences in root morphology and furcation access, which may affect surgical management. Lindhe (1995) observed the largest clinical improvement in class II furcations of mandibular molars followed by buccal

class II furcations of maxillary molars with interproximal furcation lesions exhibiting the least or no improvement. He emphasised that the reason for different outcomes of GTR in maxillary and mandibular furcation defects was most likely related to the anatomy of the defects, the presence of deep grooves in the root surface of the maxillary furcations, limited access for root surface debridement and the amount of remaining periodontium facing the defect.[20]

In a prospective study by Bowers et al. (2003), multiple factors predictive of positive clinical outcome in the treatment of facial class II furcations in mandibular molars were identified which included increase in probing pocket depth, decrease in horizontal probing attachment level, decreased distance from roof of the furcation to the base of the defect and to the crest of the bone, interproximal bone height at the same level as the roof of the furcation or above, increased distance from bone crest to base of defect, decrease in root divergence, decreased root trunk length, increased root cone length.[21] Reddy MS et al. (2015) in their consensus report from AAP regeneration workshop had stated that the Class II furcation defects represent a highly predictable scenario. Hence, regenerative periodontal therapy should be considered before resective therapy or extraction.[22]

SURGICAL TECHNIQUE:

Pini Prato et al. (1992) reported that the irritating effect of the membrane and the handling of the tissues may account for 1 mm recession observed at follow-up. Inadvertent thinning of flap margins during sulcular incisions increase the risk of recession post surgically.[23]Combination technique using GTR with bone grafts show better regeneration in Class II mandibular furcation defects according to study by Simonpietri et al. (2000).[24] According to systematic review by Murphy and Gunsolley (2003), use of augmentation materials in addition to physical barrier enhances the regenerative outcome. Care should be taken to avoid collapse of the membrane by providing adequate space maintenance. Overzealous filling with bone grafts should also be avoided.[25]Reddy MS et al. (2015) in their consensus report from AAP regeneration workshop had stated that the application of a combined therapeutic approach (i.e., barrier, bone replacement graft with or without biologics) appears to offer an advantage over monotherapeutic algorithms.[22]

Oates (2003) conducted a systematic review including 32 randomized controlled clinical trials to evaluate the efficacy of various surgical procedures for gingival augmentation and concluded that sub-epithelial connective tissue graft showed better root coverage when compared to free gingival graft, GTR procedure and allogenic soft tissue augmentation. Stability is important for success of grafting procedure and should be

achieved with firm but minimal number of sutures.[25]

ISSUES REGARDING TYPE OF REGENERATIVE MATERIALS USED:

According to a systematic review by Murphy and Gunsolley (2003), nonabsorbable expanded polytetrafluoroethylene (ePTFE) membranes are considered "gold standard" in guided tissue regeneration. Early exposure occurred in patients who underwent GTR using ePTFE when compared to bio-absorbable membrane. If exposure occurs in bio-degradable membrane, early degeneration can occurs leading to compromised regeneration. Thus regeneration using ePTFE shows a more predictable outcome when compared to bio-degradable membranes.[26] Schwartz et al. (1998) examined the effects of donor age and gender on the bone induction capability of demineralised freeze dried bone graft and found that the age of the donor plays a role in induction capability.[27]

ISSUES DURING POST OPERATIVE PERIOD:

Optimal plaque control is a crucial factor. Nowzari et al. (1996) demonstrated that poor oral hygiene and persistent infection with *Actinobacillus actinomycetemcomitans* had a detrimental effect on healing of class II furcation defects.[28]Karring and Gotlow (1992) found that newly generated periodontal tissues are stable and similar to the healthy periodontium, when accompanied by a good regimen of supportive periodontal therapy regimen.[29]Cortellini (2006) suggested that full mouth plaque scores and bleeding scores should be less than 15% to achieve optimal regenerative outcomes after GTR procedures.[30]Galindo R et al. (2015) showed that, the need for retreatment due to the recurrence of periodontal disease was higher than 70% in patients who attended less than 75% of their scheduled maintenance appointments within 1 year.[7] Reddy MS et al. (2015) in their consensus report from AAP regeneration workshop had stated that stringent postoperative care and subsequent supportive periodontal therapy are essential to achieve sustainable long-term regenerative outcomes.[22]

CONCLUSION:

The ultimate goal of periodontal therapy is the regeneration of lost periodontal tissues. With recent development in material sciences, providing new regenerative materials and delivery systems it is possible to establish a scientifically sound evidence-based rationale which is critical to the success of regenerative therapy. At present continuing efforts are being made to improve the understanding of periodontal regeneration biology and to resolve various issues that critically impact periodontal regeneration.

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