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REVIEW

Fundamental Concepts and New Perspectives for Periodontal Regeneration

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Abstract

Purpose of Review Treatment of intrabony defect directly improves the prognosis of periodontally compromised tooth. Innovation in periodontal regenerative techniques and clinical improvements in execution are highlighted in this review.

Recent Findings Periodontal surgical techniques are effective in pocket closure and improvements in clinical attachment level. To prevent the tooth loss and edentulism in a global scale, regenerative periodontal surgical techniques should be applied when it is indicated. It is critical to underline the importance of flap design and clear shift in biomaterial technologies towards growth factors application.

Summary Evidence based periodontal regeneration provides better prognosis for periodontally compromised teeth. Clinical attachment level gains with minimal post-operative gingival recession can be obtained by using sophisticated flap designs and indicated biomaterial technologies.

Keywords Guided tissue regeneration · periodontal · Periodontitis · Surgical flaps · Wound healing

Introduction

Treatment of periodontitis requires four clinical steps, from diagnosis of the disease to supportive periodontal care [1–3]. Third step of periodontitis treatment has been recommended for surgical intervention or repeated subgingival instrumentation [4]. Surgical approach can be applied as an access flap, resective or regenerative surgery [5–9]. Recently, a systematic review and meta-analysis clearly demonstrated the superiority of regenerative treatment of intrabony periodontal defects compared to access flap alone [10]. The authors concluded that regenerative biomaterial application either with growth factors or barrier membranes in combination with papilla preservation flaps should be considered the treatment of choice for residual pockets with deep intrabony (≥3 mm) defects. Ultimate goal of periodontal regeneration is to obtain pocket closure without any significant gingival recession, to change the prognosis of compromised tooth by improving the clinical attachment level and to provide long-term stability [11–14].

Periodontal defects can be classified as infrabony, suprabony and interradicular or furcation defects [15]. Infrabony or infraosseous defects were divided as intrabony (1-, 2-, 3-wall defects or combination) or craters. Among those defects, treatment of intrabony defects has been studied and very well researched with randomized controlled clinical trials and long-term studies [16–21]. If left untreated, an intrabony lesion tends to progress and risk for tooth loss is higher when compared to healthy periodontium [22].

Fundamental Concepts in Periodontal Regeneration

It is important to underline the success of periodontal regeneration depends on several factors such as biofilm level, residual bleeding on probing, systemic conditions, smoking status, defect morphology, tooth mobility, early and late wound stability, type of biomaterials, choice of flap design

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and surgical skills of the clinician [23–29]. First, it has been recommended to control or modify the patient-related factors, site-related factors and surgical factors for optimal clinical outcomes.

Healing of a periodontal defect has been considered one of the complex wound healing model in a human body [30, 31]. Different tissue characteristics are involved: epithelium, connective tissue, periodontal ligament, alveolar bone and cementum [32]. When compared to reconstructive bone surgery (guided bone regeneration), in a partially edentulous site, periodontal regeneration site has some disadvantages in terms of primary wound healing [33]. First, it is an open wound system with an interface of avascular root surface. A preclinical study demonstrated that the wound tensile strength of a flap adhering to root surface has been found weaker than those to the native bone [34]. This important finding can be considered the one of the first proofs of early improved stability in periodontal wound healing. In case of instability of the periodontal wound (i.e. tooth mobility, occlusal trauma, muscle pull on flap margins, traumatic suture removal), epithelial downgrowth will prevent the cascade of regeneration [35–38]. Second, the incision on the defect-associated interdental papilla for the access will heal on the biomaterials/membrane or a blood clot. In a biological and vascular perspective, there is a lack of wound bed for revascularization, and the flap will heal with its own healing potential. Therefore, it is essential to understand the protection of the regeneration space undisturbed is critical and impairment of the wound healing system will deteriorate desired regeneration outcomes [39, 40].

Transformation from Conventional Ample Flap Reflection To Minimal Flaps

From the first human histological proof of new connective tissue attachment formation, the way of performing periodontal regenerative surgery has been changed many times [41]. In time, two major contributors have paved the way for minimal flaps. First, improvements in the biomaterial technology helped clinicians to shift from applying a barrier membrane under a flap to use of biologics (i.e. recombinant growth factors, amelogenins, hyaluronic acid) [42–47]. This shift definitely improved the rate of primary wound closure rate, in other words, decreased the incidence of wound failure. Second, innovations in microsurgery, use of microscope or surgical loupes with illumination and use of mini instruments instead of large ones improved the flap revascularization and primary wound closure rate [48–55].

The journey of minimal invasive procedures in periodontal surgery actually started with George T. Raust in 1969 who published in January 1969, Journal of Periodontology "the mini flaps" where he treated over 300 patients with mini flaps with successful outcomes. In the 70's, Yukna et al. published the excisional new attachment procedure (ENAP), another minimal invasive surgical procedure with good clinical outcomes but without providing any histological evidence of regeneration, that was mandatory in those days. In the same period, Ramfjord and Nissle introduced the modified Widman flap with the aim of preserving the soft and hard tissues at maximum level. The aim was the remove the calculus, biofilm and granulation tissue. This approach provided good clinical outcomes. Also, it is important to mention that modified Widman flap was often misunderstood in some clinical studies, mostly performed with the principles of Kirkland flap by excessively removing all the interdental tissues, with an idea of curettage. However, modified Widman flap recommends to preserve the residual fibers, indiscriminate curettage of residual fiber attachment should be avoided since such action may disturb the tissue healing.

In 1985, Takei introduced the papilla preservation technique that allow to access the defect and seal the interdental soft tissues after cleaning and grafting [56]. The incision performed generally from palatal side and if defect reaches to palatal side, incision location should be shifted to buccal side. In 1995, Cortellini et al. proposed the incision located only in the buccal aspect, so it allows to release the periosteum [57]. In this way, the tension-free buccal flap can be prepared and minimized the risk of membrane exposure and subsequent infection. In those days, the only technique with evidence to achieve periodontal regeneration was the use of membranes (GTR). In 1997, a new concept of regeneration was introduced with Enamel Matrix Derivative (EMD) in gel form [42, 43, 58–64]. Using EMD, Rasperini et al. described a surgical technique that allows a smaller flap elevation, the Laurell-Gottlow suturing technique performed before placing the gel and left untied [65]. EDTA 24% was applied for 2 min. on the root surface, rinsed with sterile saline, then EMD was applied onto the clean and dry root surface and the suture was than tightened and secured the knot. This biomaterial allowed to start the era of minimal invasiveness, also providing periodontal regeneration with human histological studies [66–70].

Minimally Invasive Regenerative Periodontal Surgery

In 1990, the definition of a minimal invasive procedure has been discussed in medicine [71]. First appearance of "minimally invasive procedures" in periodontal surgical literature was published in 1995 by Harrel and Rees [72]. This approach performed through smaller access flaps with enhanced visualisation and aimed to reduce patient

morbidity. Cortellini and Tonetti has demonstrated the benefits of using microsurgical principles in GTR procedures, with an increased rate of primary closure (92.3%) [49]. However, the use of membrane despite its bio-absorbable characteristics, still required the elevation of flaps in full-thickness beyond the mucogingival line and detaching the muscular attachments. To eliminate this, same authors proposed "Minimally invasive surgical technique" (MIST) to limit the mesio-distal extension of the flap, and corono-apical flap reflection to increase flap stability [73]. Amelogenins were used as a regenerative biomaterial. Primary closure rate was 95%, and 1-year clinical attachment gain was 4.9 ± 1.7 mm. MIST consists of reflection of buccal and oral papillae. To improve the blood clot stability, the elevation of single buccal flap was recommended [74, 75]. Namely" Single flap approach" (SFA) and "Modified minimally invasive surgical technique" (m-MIST) aimed at preserving the intact attachment of oral papilla (Fig. 1). The difference between these two approaches is the application of regenerative biomaterials and corono-apical flap reflection. SFA allows placement of a barrier membrane due to access for deep intrabony defects, m-MIST can be applied

Fig. 1 **a**) Baseline probing. **b**) Modified minimally invasive surgical technique using amelogenins and anorganic bovine bone mineral. **c**) Primary wound closure. **d**) Optimal wound healing conditions at 1-week. **e**) Probing depth of 2 mm at 1-year control appointment. **f**) Baseline radiograph. **g**) 1-year radiograph

with amelogenins, combination of amelogenins-bone grafts and blood clot alone [76, 77]. Interestingly, in a three-arm randomized-controlled clinical trial, m-MIST with or without regenerative biomaterials resulted in similar clinical and radiographic outcomes [77]. Following this trial, the choice of flap design according to defect morphology and improving the wound stability seem to be primary key in periodontal regeneration.

New Perspectives for Periodontal Regeneration

Innovations in the biomaterial technology and adoption of microsurgery lead to an era of minimal flap design. Paradigm shift from GTR concept to biologics application decreased the complication rate and improved the patient reported outcome measures [78, 79]. Adjunctive use of amelogenins in non-surgical periodontal therapy eliminated the flap reflection (flapless approach), promoted an improved wound healing and resulted in significant pocket closure [80–83].

Recently, a novel surgical approach, the entire papilla preservation technique (EPPT) has been recommended in the regenerative treatment of isolated deep and wide intrabony defects (Fig. 2) [84–87]. The idea behind the concept of EPPT is the preservation of interdental soft tissues and flap integrity by eliminating the incision on the defect-associated papilla and the initial incision has been altered to a relatively safer site. EPPT only requires a single buccal vertical incision on the defect-associated tooth, extending only 1–2 mm apical to the mucogingival junction and positioned contralateral to the bone defect. In a recent randomized clinical trial, test (with biomaterials) and control (without biomaterials) groups showed 100% primary closure during the early and late wound healing phases [88]. Control group (EPPT without biomaterials) resulted in an amount of CAL gain (5.83 ± 1.12 mm) and PD reduction (6.2 ± 1.33 mm) which demonstrated a significant clinical improvement.

In case of an associated buccal gingival recession, coronally advanced entire papilla preservation (CA-EPP) technique has been proposed in the treatment of intrabony defects and adding connective tissue graft under the buccal flap may promote the gingival profile and stability [89]. The combination of entire papilla preservation and coronally advanced flap technique provides an opportunity for simultaneous hard and soft tissue reconstruction.

Fig. 2 **a**) Soft tissue crater formation and uneven papillary levels with 9 mm pre-operative probing depth. **b**) Inter-dental tunnel preparation and surgical access to the defect for debridement. **c**) Severity of intrabony defect. Note the elasticity of alveolar mucosa. **d**) Application of 24% EDTA gel for 2 min to remove the smear layer. **e**) EMD application. **f**) Placement of deproteinized bovine bone mineral into the intrabony defect. **g**) Primary closure of the single vertical incision. **h**) Excellent wound healing at 14 days after surgery. **i**) Immediately after suture removal. Note the integrity of gingival margin and interdental papilla. **j**) One-year after surgery. Improved papilla height on the distal side of second bicuspid and no scar formation along the vertical incision. **k**) Four mm of residual probing depth with no bleeding on probing. CAL gain of 5 mm without any gingival recession. **l**) Baseline radiograph. **m**) One-year radiograph

Conclusions

Treatment of osseous periodontal defect using regenerative periodontal surgical techniques is an effective treatment modality. Microsurgical tissue handling with improved flap designs may improve the clinical outcomes and the rate of pocket closure.

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  A new perspective in papilla preservation surgical approach, showing predictable 100% primary closure rate.

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  After the new periodontal classification, this paper highlighted the new perspectives to interproximal attachment gain.


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Author Contributions S.A. wrote the main manuscript text and S.A. and G.R. have revised the text. S.A. prepared Figure 1. All authors reviewed the manuscript.

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Declarations

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