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Critical Issues in Periodontal Regeneration: A Review

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ABSTRACT
Periodontal disease (PD) is one of the most common inflammatory oral diseases, affecting approximately 47% of adults aged 30 years or older in the United States. If not treated properly, PD leads to degradation of periodontal tissues, causing tooth movement, and eventually tooths loss. Periodontal Regeneration can be defined as the complete regeneration of the lost tissue, restoring there complete structure and function by recapitulating the crucial wound healing events associated with their development. The regeneration or restitution of lost supporting tissue has always been considered the ideal objective of periodontal therapy. However, attempts to convert this intention into solid clinical practice can become tremendously complex, the results of which are very different from the original intention. The aim of this article is to offer an up-to-date, general perspective on periodontal regeneration, orienting the clinician within the global strategy for oral treatment. To this end, we revise the healing process of periodontal injury, the different therapeutic approaches, the interpretation of the results, and finally, limiting factors in periodontal regeneration.

Keywords: NIL.

INTRODUCTION

Periodontitis is one of the most common inflammatory diseases of humans and a leading cause of tooth loss in adults. It is characterized by progressive destruction of the tooth-supporting apparatus, including gingiva, alveolar bone, periodontal ligament (PDL), and root cementum; if left untreated, it can lead to the loosening and subsequent loss of teeth(1,2).

The pathogenesis of periodontitis involves a complex interaction between the host immune response to microbial plaque, and modifying host factors, including smoking, genetic influence and systemic disorders such as diabetes, osteoporosis, coronary artery disease(3,4). The ultimate goal of periodontal therapy includes control of infection and final reconstruction of gingival connective tissue, cementum, alveolar bone and PDL. In addition, formation of sharpey's fibres, and oriented PDL embedded in both newly formed cementum and alveolar bone, are essential and challenging for periodontal regeneration. Therefore amidst all speculations, facts and clinical outcomes few questions do arise, Is periodontal regeneration reliable and predictable?? What are the possible horizons of endeavor which require to be peeped upon for long term stability of the regenerated tissues?? The possible difficulties to be encountered when desiring true periodontal regeneration in it's strict sense?? All these grey areas need to be assessed and answered, this review aims to highlight and outline these potential areas.

Why periodontal regeneration is difficult??

Because, of the simple fact that, the periodontium is composed of four embryologically, morphologically and functionally different tissues, viz.cementum, periodontal ligament, alveolar bone and gingival soft tissue, as a matter of fact to regenerate these tissues there is a keen requirement of simulation of exact biological mechanisms supplemented with a suitable conducive environment and rich supply of various bio-mediators incorporated with the proper orchestrated cascade of signaling mechanisms, to fully appreciate what is involved, the cross-talk among the components of the periodontium (cellular and matrix), together with the inherent regenerative capacity of this tissue, needs to be considered[5]. Unfortunately, very little is known about the signals that initiate and regulate these interactions in vivo[5].Therefore, therapeutic failure, in terms of regeneration appears to be more frequent in periodontal surgery than in other pathological states[6,8].Although the general principles of healing and the cellular and molecular events observed in non-oral sites also apply to the healing processes that take place after periodontal surgery, a more difficult and complex situation presents itself when a mucoperiosteal flap is opposed to an instrumented root surface previously deprived of its periodontal attachment[7].

In due, consideration of the present state of art like, open flap debridement, guided tissue regeneration (GTR), bone and non-bone grafts, enamel matrix protein and growth factors etc . it's not possible to say whether strict periodontal regeneration can be achieved or not, so there is a meticulous need of refinement in this field, for which a clear understanding of the basic physiology of the periodontium is of utmost importance.

Historical perspective:

The concept that new attachment was a clinically achievable technique was established by the work of Pritchard who showed that three-wall defects could fill with bone following routine surgical subgingival debridement(8). These results were attributed to the favourable anatomy of the treated intrabony defects (three-wall), and several subsequent histological studies have demonstrated that new attachment is not routinely achieved following subgingival debridement, with the formation of a long junctional epithelium along the root surface being the routine response[9]. However, the work by Pritchard provides ''proof of principle'' evidence that periodontal regeneration is achievable in ''ideal'' clinical situations by surgical debridement without the need for supplementary techniques. Needless to say, these ''ideal'' clinical situations are rarely encountered in day to day practice. Therefore, over the years, a number of different techniques have been attempted in order to achieve periodontal regeneration.

Biological principle:

Periodontal regeneration requires new attachment to the root surface, a process that involves the regeneration of periodontal ligament fibers and the insertion of these fibres into newly formed cementum on a root surface that has been exposed previously to periodontal pathogens. It has been shown that cells derived from the gingival connective tissues and the alveolar bone lack the ability to form such an attachment[10,11]. On the other hand, if preference is given to repopulation of the root surface by periodontal ligament cells, new connective tissue attachment including new cementum with inserting collagen fibres can be formed[12]. Hence, the periodontal ligament is of critical importance in the regenerative process. In order for periodontal regeneration to occur, progenitor periodontal ligament cells must migrate to the denuded root surface, attach to it, proliferate and mature into an organized and functional fibrous attachment apparatus that inserts into newly formed cementum. Likewise, progenitor bone cells must also migrate, proliferate and mature in conjunction with the regenerating periodontal ligament. Therefore, the concept of periodontal regeneration is based on the principle that remaining healthy cells, and or cells attracted to the healing site, have the potential to promote regeneration. However, achieving conditions that allow selective repopulation by periodontal ligament cells is difficult to obtain clinically. The very next question which arises, why it is difficult to have such conditions / environment which will form a conduit for cells of PDL to repopulate in that area?? The answer is the difference in the state of development of periodontal tissues as per embryological rules due the complex interaction between undifferentiated mesenchymal cells and the developing connective tissue within the germ layers, which herein gets compromised due to previous

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disease process, gets contaminated with plaque and calculus, saliva and to add on rapid epithelial proliferation by default.

Periodontal regenerative procedures can result in four varied different outcomes, as follows, based upon Melcher's concepts of "compartmentalization":

1. Healing in the form of long junctional epithelium	Healing of periodontal defect by a new epithelial attachment along the instrumented root surface, which is formed by keratinocytes that migrate into the pocket from the crevicular epithelium.
2. Connective tissue repair	Healing of periodontal defect by collagen fibers oriented parallel or perpendicular to a instrumented root surface previously exposed to periodontal disease or otherwise deprived of its periodontal attachment.
3. Bone and or bone-like tissue repair	Healing of periodontal defect by bone or bone-like tissue formation without specific PDL and or acellular extrinsic fiber cementum regeneration.
4. Periodontal tissue regeneration	Healing of the periodontal defect by regeneration of tooth cementum, a functionally oriented PDL, alveolar bone, and gingiva in periodontal defect, it can be partial or complete.

One of the most interesting approaches for clinical practice are factors determining the outcome of periodontal osseous surgery, the idea is to transmit to the reader the complexity involved in trying to include all the different circumstances related with the results when making decisions on treatment, the governing factors are as follows : plaque control, smoking, diabetes, genetic, age, operator skill, surgical approach, root surface preparation, tooth anatomy, root morphology, defect morphology, pulpal status, occlusion, use of antibacterials, plaque control(13).

Future perpectives :

1. Tissue engineering

In light of the clinical unpredictability of currently available surgical techniques to treat all types of periodontal defects, it would appear that these approaches are too simplistic to facilitate the coordinated wound healing events required for the regeneration of a complex organ such as the periodontium. Consequently, a tissue engineering approach has been proposed, whereby periodontal tissues would be constructed in the laboratory under controlled conditions and then surgically implanted into defects. Evidence for the viability of this approach has been demonstrated in animal studies showing that autologous cultured periodontal cells can support regeneration in vivo(14). This approach is further supported by evidence that periodontal ligament cells have stem cell propertie(15,16). A new and promising paradigm to periodontal tissue engineering involves using periodontal cell sheets prepared in vitro and subsequently transplanted into periodontal defects. It has been reported that periodontal ligament cells cultured using this cell sheet technique can regenerate periodontal ligament tissues after transplantation in animal models(17,18).

2. Gene therapy:

One of the major drawbacks related to the use of biologically active agents, such as growth factors, is

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their short biological half-life which results in their rapid degradation following application. Gene therapy can be used to facilitate extended local delivery of growth factors by transferring the growth factor genes into the local cell population. Gene delivery of PDGF (platelet-derived growth factor) has been accomplished by the successful transfer of the platelet-derived growth factor gene into cementoblast and other periodontal cell types[19]. Animal studies have demonstrated that gene delivery of PDGF stimulated more cementoblast activity and improved regeneration compared with a single application of recombinant platelet derived growth factor[20]. Although our understanding of gene regulation of PDGF has improved with experimental gene therapy studies, the safety and efficacy of using gene therapy for regeneration are yet to be fully evaluated.

CONCLUSION:

Over the past 25 years, periodontal regeneration has been the focus of considerable laboratory and clinical research. Indeed, numerous randomized controlled clinical trials have been carried out in order to assess the clinical effectiveness of several surgical techniques aimed at achieving periodontal regeneration.

From the evidence available in the literature, the following conclusions can be drawn, (1) Currently, there are two well-documented clinical techniques, GTR (Guided tissue regeneration) and EMD (enamel matrix protein/derivative), which can be utilized for the regeneration of intrabony and Class II mandibular furcation periodontal defects. [2] In cases where additional support and space making requirements are necessary, both of these procedures can be combined with a bone replacement graft. [3] There is no evidence that the combined use of GTR and EMD results in superior clinical results compared to the use of each material in isolation. [4] Great variability in clinical outcomes has been reported in relation to the use of both EMD and GTR, and these procedures can be generally considered to be unpredictable. Careful case selection and treatment planning, including consideration of patient, tooth, site and surgical factors, is required in order to optimize the outcomes of treatment. [5] There is limited data available for the clinical effectiveness of the commercially manufactured products PDGF ⁄ β-TCP (tri-calcium phosphate) and P-15 (PEPGEN) ⁄ABM (bovine derived hydroxyapatite matrix), and further studies are required to test the clinical performance of these two products. [6] The use of PRP for periodontal regeneration has yielded contradictory results and further studies are required to determine the optimal conditions and methods of preparation. [7] Terms like ligament supported implants (Ligaplants) and bone repair cells (Ixmyelocel-t) are thronging up in the the literature, but there is lack of long term clinical evidence in regarding their success, so caution is warranted if being implemented.

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