REVIEW ARTICLE

Critical Issues in Periodontal Regeneration

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ABSTRACT

Once upon a time, repair and damage control were the expected outcomes of periodontal therapy. However, recent advancements have led to the shift in ideology with regeneration and replacement of what is lost as the ultimate goal of the therapy. Although regeneration is possible and predictable, there are many factors which restrain it from being achievable. The following article addresses such critical issues which are a hindrance in accomplishment of the goal long lasting and stable periodontal tissue regeneration.

Key words: Periodontal therapy, regeneration, repair

INTRODUCTION

Major advances in periodontal therapy have resulted in paradigm shifts in the periodontal field, resulting in more patients benefitting from care. One of the biggest advancements in recent years was the realization that periodontal tissues can be regenerated, rather than simply repairing the tissue after periodontal disease has occurred.

Hence, what is regeneration and repair?[1] Regeneration is defined as the reproduction or reconstitution of a lost or injured part of the body in such a way that the architecture and function of the lost or injured tissues are completely restored. Repair implies healing without restoration of the tooth attachment apparatus and is often associated with the formation of a long junctional epithelium.

Although we have tried to achieve epitome of periodontal regeneration by various techniques, still there is a long way to achieve a predictable one. There is not enough evidence in favor of long-term stability. As regeneration has been factually achieved; still, there remain certain critical issues [Table 1] which affect achievement, quality, and stability of new attachment. These can be summarized under the following headings:

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Conceptual Lacunae

The aim of regenerative periodontal therapy is to restore the structure and function of the periodontium.[1] New attachment with periodontal regeneration is the ideal outcome of therapy.

New attachment of junctional epithelium to the tooth surface and of connective tissue fibers to the root surface is very critical components of true periodontal regeneration. After most of periodontal surgical procedures, tissues usually do not heal by the formation of new connective tissue attachment to root surfaces but result in long junctional epithelium, and it has been speculated that this type of dentogingival unit may be weaker and that inflammation may rapidly separate the long junctional epithelium from the tooth. Thus, treated periodontal patients may be predisposed to recurrent pocket formation, thereby leading to failure of regenerative procedure.

Most of the materials aimed at achieving periodontal regeneration by aiming at regeneration of lost bone, periodontal ligament, and cementum with the help of bone fillers, i.e. autografts, allografts, xenografts, and alloplastic materials. Therefore, bone formation has been seen histologically. However, whether new connective tissue attachment occurred or not was still controversial. The main concern regarding histological evaluation is that most of them have been tried on animals. Hence, its implication on human clinical trials is still not much promising.

Table 1: Critical issues in periodontal regeneration

Related to concept	Related to material	Related to technique	Patient-related outcome	Evidence available	Factors affecting regeneration
Whether true regeneration is a fact/ fantasy	Type of material	Type of technique	Tangible versus nontangible benefits	Few systematic reviews and meta-analyses available	Tooth anatomy
Does true regeneration occurs/not	Delivery and resorption time	Surgical issues	Clinical versus statistical significance	Few randomized controlled trials	Effect on pulpal status
Quantity of regeneration	Maneuverability		Systemic conditions such as smoking and diabetes	Studies on different races	Proximity of crown margins
Quality of regeneration	Particle size		Patient compliance	Publication bias	Baseline/pre-operative pocket defect depth
Time of regeneration	Growth factors		Patient dexterity		Defect morphology
					Discrepancies in measurement
					Gingival biotype
					Oral hygiene status
					Exposure of barrier membrane

So far, the regeneration of lost periodontium was limited to bone formation. However, with due time, it was realized that the concept of regeneration was mainly tipping toward cementogenesis as new connective tissue attachment requires the formation of new cementum to a previously diseased root surface that was modified following periodontal therapy.

Then, the use of guided tissue regeneration came into play to prevent the epithelial migration along the cemental wall of the pocket. Next came the use of growth factors and enamel matrix proteins in periodontal regeneration. The biologic rationale for the use of Emdogain as a biomimetic is to recapitulate developmental mechanisms, whereby enamel matrix proteins are proposed to play a crucial role in stimulating cementogenesis.[2] Based on circumstantial evidence, the original idea emerged that there was a causal relationship between enamel matrix proteins and cementogenesis. However, such a cause-effect relationship has never been proven experimentally.

Types of Bone Graft

Human cancellous bone graft treated site was found to be 16 times more effective in achieving 50% vertical defect fill than open flap debridement.[3]

Growth Factors

The regenerative potential can be attributed to the presence of bone morphogenic protein (BMP), mainly BMP 2 and 7.[1]

Delivery and Resorption Time

Delivery time of osteoinductive factors and resorption time of grafts and barrier membranes have to match with body's healing timetable. These factors are uncontrollable, but still, certain modifications have been done in providing reservoirs and controlling release of growth factors as well as resorption.

Tangible Versus Intangible Benefits

The clinical significance of a treatment depends on whether the benefits identified are tangible or intangible. Tangible benefits are those treatment outcomes that reflect how a patient feels, functions, or survives, for example, decrease in bleeding after brushing, prevention of tooth loss, or elimination of a painful periodontal abscess. Intangible benefits cannot be realized by the patient's mind, for example, changes in probing attachment level, changes in size of periapical radiolucency, and changes in enamel mineralization level.

A treatment that provides extensive periodontal bone regeneration (an intangible benefit) can lead to tooth loss (a tangible harm).[4]

Clinical Versus Statistical Significance

In various studies, even though statistical significance has been observed, clinically only 1 mm or less of bone or attachment gain has been

achieved. This discrepancy creates lacunae in evidence and translation of this benefit clinically seems non-convincing.

Smoking

Cigarette smoking is considered a behavioral and environmental factor related to the treatment outcome of subjects with furcation, intrabony, and recession defects. Some studies have shown negative correlation with regenerative outcomes[5] and no correlation.[3]

These effects can be due to decreased vascular supply, nicotine toxicity, cytotoxic effects on cementoblast, osteoblasts, and fibroblasts, and alteration in inflammatory and immune response.

Patient Compliance

The more often patients present for recommended supportive periodontal treatment (SPT), the less likely they are to lose teeth. Patients with inadequate SPT after successful regenerative therapy have a 50-fold increase in risk of probing attachment loss compared with those who have regular recall visits.[6]

Tooth Anatomy

Differences in tooth morphology, furcation anatomy (cervical enamel projection), and access might affect the regenerative outcomes. Limited access reduces efficiency in debridement of root surfaces and influence treatment outcomes.

Effect on Pulpal Status

There has been some controversy between the pulpal status of teeth and their regenerative potential. Some have suggested that endodontically treated teeth may be less than ideal candidates for regenerative therapy.[3]

Proximity of Crown Margins

The proximity of crown margins to furcation may inhibit the epithelial and/or connective tissue attachment to form coronally.[3]

Baseline/Pre-operative Pocket Defect Depth

Pre-surgery pocket depth and defect depth have been found to be directly correlated to the amount of clinical attachment level gain and bone formation following regenerative procedures. Pre-operative bone level was found to be highly representative of the distance between the gingival margin and the bottom of the defect at probing. This might suggest that deeper the defect, the more undisturbed the regeneration away from environmental factors.

Defect Morphology

Defect morphology plays an important role. Regeneration is most predictable in three walled defects with even bone grafts alone. Combination therapy (barrier membranes and bone grafts) is desirable where defects are non-contained i.e. one walled defects.

This may be partly due to the wound stability effect of the membrane, space making effects related to the membrane positioning coronally to the alveolar crest might overcome differences in regenerative potential inherent in the intrabony defects.

A significant relationship between the bone margins and the root surface and extent of bone formation has been shown for supra-alveolar defects, where space provision related to defect morphology is minimal.

Discrepancies (Limitations) in Measurement

Limitations in diagnostic accuracy inherent to conventional linear and radiographic measurements in assessing the three-dimensional pattern of bone regrowth following guided tissue regeneration and other regenerative outcomes might also be a reason of discrepancy and lead to difficulty in estimation.

Gingival Biotype

Tissue biotype is a significant factor that influences the esthetic treatment outcomes. In root coverage procedures, a thicker flap was associated with a more predictable prognosis. A flap thickness of 0.8–1.2 mm was associated with a more predictable prognosis.[7] Patients with thin-scalloped biotypes are considered at risk as they have been associated with a compromised soft tissue response following surgical and/or restorative treatment. The gingival thickness affects the treatment outcome possibly due to the difference in the amount of blood supply to the underlying bone and susceptibility to resorption.[8]

Oral Hygiene Status

High oral hygiene standards allow for minimizing the influence of supragingival plaque accumulation in levels of repair.[6]

Exposure of Barrier Membranes

Exposure has been related to compromised clinical outcome with the major impact relating to the possibility of the patient requiring additional post-operative appointments or the use of systemic antibiotics.[9]

CONCLUSION

At 1 time, regeneration was a dream, a miracle accomplished only by God. However, constant tries and efforts of periodontists have made regeneration now achievable. The maintenance of the achieved is still a matter of concern as many controllable and uncontrollable factors determine it. Literature is lacking in evidence to evaluate the long-term predictability and stability of the results achieved using various modalities of regeneration. Studies are required with strict stringent inclusion and exclusion criteria assessing one variable and one outcome at a time with long-term follow-up. Regeneration is affected by plethora of factors; many factors acting in unison. Maximum regeneration can be achieved by addressing as many factors as possible.

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