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PRF AND REGENERATIVE PERIODONTICS- A BRIEF OVERVIEW OF ITS TYPES AND CLINICAL APPLICATIONS

Periodontology

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ABSTRACT

Regenerative periodontal therapy comprises of techniques which are designed to restore those parts of the tooth-supporting structures which have been lost due to periodontitis or gingival trauma. The tissue engineering triad is essential for regeneration. Platelet concentrates act as bioactive surgical additives that are applied locally to induce wound healing & regeneration. The present review summarizes the different types of PRF used in regenerative periodontics and highlights their clinical applications.

KEYWORDS

PRF; Regenerative Periodontics; Tissue Engineering

INTRODUCTION

Periodontitis is a chronic inflammatory disease affecting the supporting structures of the teeth and results in loss of alveolar bone eventually leading to tooth loss.[1]

Regenerative periodontal therapy consists of techniques which are particularly designed to restore those parts of the tooth-supporting structures which have been lost due to periodontitis or gingival trauma.[2]

Tissue engineering has brought about a drastic improvement in the healing response of tissues.[3] It is based on cells, scaffolds and signalling molecules.[4] (Figure 1)

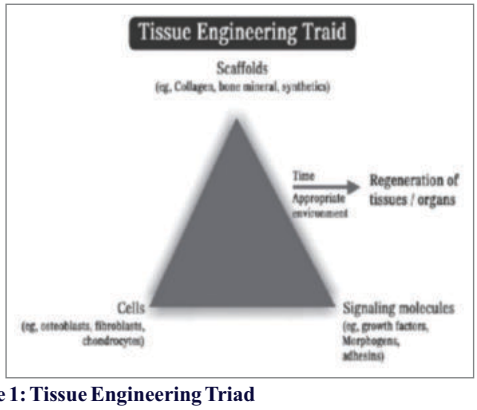

Figure 1: Tissue Engineering Triad

The latest innovation in dentistry is the use of platelet concentrates (signalling molecules) for *in vivo* tissue engineering applications. Platelet concentrates are a concentrated suspension of growth factors found in platelets, which act as bioactive surgical additives that are applied locally to induce wound healing & regeneration.[5]

Platelet Rich Fibrin (PRF) was first used in 2001 by **Choukroun et al**. in France and it is a second generation platelet concentrate.[3] It consists of a matrix of autologous fibrin that is responsible for increased collagen production, cell mitosis, blood vessels growth, recruitment of cells that migrate to the site of injury and cell differentiation.[5] It contains numerous growth factors. (Table 1)

Table 1: Growth factors in PRF and their functions

Growth factor	Functions
Platelet-derived growth factors (PDGFs)	Specific roles include proliferation of cells, cellular migration and collagen production for remodeling of extra-cellular matrix to repair the wound.
Transforming growth factor β1 (TGF-β1)	Tissue repair, extracellular matrix synthesis and immune modulation. Specific roles played by TGF-β1 includes angiogenesis, re-epithelization and regeneration of connective tissue. Due to bone morphogenetic proteins (BMPs) being part of TGF family. They also play role in bone formation.
Vascular endothelial growth factor (VEGF)	Primary function is angiogenesis. Also, plays a role in tissue remodeling.
Endothelial growth factor (EGF)	Proliferation and multiplication of endothelial and mesenchymal cells, which leads to epithelization.
Insulin-like growth factors (IGFs)	Cell-protective in nature and participates in proliferation and differentiation of a variety of cells.

PRF PREPARATION

A blood sample is taken without anticoagulant in a 10-ml glass tube which is immediately centrifuged in a table centrifuge at 3000 rpm for 10 min.[6]

The resultant product consists of the following layers: (Figure 2)

- Topmost layer consisting of acellular Platelet Poor Plasma
- PRF clot in the middle
- RBCs at the bottom [6]

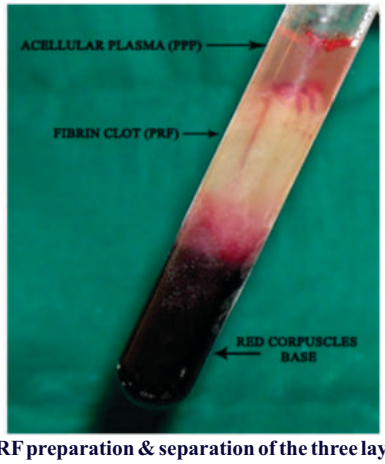

Figure 2: PRF preparation & separation of the three layers

This accumulates platelets and the released cytokines in a fibrin clot. PRF requires only centrifuged blood without any addition of anticoagulant and bovine thrombin.[7]

Thus blood begins to coagulate as soon as it comes in contact with the silica particles on the glass surface. Therefore, for successful preparation of PRF, speedy blood collection and immediate centrifugation, before the clotting cascade is initiated, is absolutely essential. PRF can also be obtained in the form of a membrane by squeezing out the fluids from the fibrin clot in the PRF box.[7]

ADVANTAGES

- Single step centrifugation.
- Obtained from autologous blood sample.
- Eliminates the redundant process of adding anticoagulant as well as the need to neutralize it.
- The addition of bovine-derived thrombin to promote conversion of

fibrinogen to fibrin is also eliminated, thus reducing the overall biochemical handling of blood.
- Can be used solely or in combination with bone grafts, depending on the purpose.
- It is an economical and quick option compared with recombinant growth factors.
- When used as a membrane, it avoids an additional donor site surgical procedure hence resulting in a reduction in patient discomfort.[8]

DISADVANTAGES
- Possible refusal of treatment by the patient due to the puncture required for blood collection.
- Only an experienced clinician can manipulate PRF.
- The fibrin matrix contains all the circulating immune cells and the highly antigenic plasmatic molecules. That is why PRF membranes are totally specific to the donor and cannot constitute an allogenic graft tissue.[9]

TYPES OF PRF
L-PRF/ Leukocyte and Platelet Rich Fibrin (L-PRF)
(Choukroun's PRF protocol, Process protocol, Nice, France).[10]

The PRF clot forms a strong fibrin matrix with a complex three-dimensional architecture, in which most of the platelets and leucocytes from the harvested blood are concentrated.[10]

A-PRF
It utilizes "low-speed concept". Advanced PRF can provide an increase in platelets and neutrophilic granulocytes within the PRF clot and prolong the release of certain growth factors.[11]

Ghanaati et al conducted a study to compare the clinical efficacy of A-PRF versus L-PRF. A-PRF was prepared by centrifuging 10 ml of blood at 1500rpm for 14 minutes. It was concluded that A-PRF might influence bone and soft tissue regeneration, especially through the presence of monocytes/macrophages and their growth factors.[12]

i-PRF
PRF variants are mostly solid or dense gels and cannot be injected. The recently developed **injectable PRF (i-PRF)** is formulated utilizing lower centrifugation forces for shorter time periods.[13]

R J Miron et al in his study used i-PRF and compared it with PRP and observed significantly higher levels of growth factor release in i-PRF which was formulated by taking 10ml of blood centrifuged at 700rpm for 3 minutes.[14]

T-PRF
Titanium-PRF (**T-PRF**) was developed by **Mustafa et al in 2014**. This is based on the hypothesis that titanium may be more effective in activating platelets than the silica activators used with glass tubes in L-PRF.[15]

PERIODONTAL APPLICATIONS
A true regenerative procedure in periodontology includes regeneration of both soft tissues (periodontal ligament) and mineralized tissues (cementum and alveolar bone).[1]

Management of extraction sockets
Following tooth extraction, alveolar bone dimensions are reduced both in vertical and horizontal dimensions as part of the normal healing process. Considering the beneficial properties of the PRF, it has been used as an adjunct in socket grafting procedures with or without bone graft materials to improve healing and maintenance of the alveolar ridge dimensions.[1]

Guided bone regeneration (GBR)
Although GBR procedures for horizontal bone augmentation have shown predictable results, there are multiple complications associated with it which can lead to poor or failed treatment outcomes, the most common complication being membrane exposure. PRF can be used as an adjunct in such procedures to enhance healing and regeneration.[1]

Intrabony defect regeneration
Various studies report that additional use of PRF increased Pocket Probing Depth reductions and Clinical Attachment Level gains when compared to Open Flap Debridement alone for regeneration of intrabony defects.[16]

Some studies comparing intrabony defect healing with PRF versus a bone grafting material (DFDBA) found no significant differences between treatment groups.[17] Other studies found that the use of PRF in combination with a bone-grafting material was superior to either PRF alone, or bone-grafting material alone. Also, the supplemental use of PRF in combination with a barrier membrane was superior to barrier membrane alone.[18]

In another study, the additional use of PRF with Emdogain showed no differences between the test and control (EMD alone) groups.[19]

Furcation defect regeneration
PRF has shown to be statistically superior to controls (OFD alone) in regeneration of furcation defects. While these studies reveal the potential of PRF to improve clinical parameters, no data exists to date confirming periodontal regeneration via histological evaluation.[20]

Sinus augmentation procedures
Sinus augmentation is used to restore posterior maxilla with deficient bone height. Due to the healing and regenerative properties of PRF, it has been incorporated into sinus procedures: as a sole grafting material, in combination with allograft and xenograft material, as a membrane to cover the graft material, and to repair intra-operative Schneiderian membrane perforations. PRF has shown positive and promising results with respect to faster healing and maturation of bone.[1]

Root coverage
Predictable results have been observed when PRF was used for root coverage procedures for Miller's Class I and II defects. Clinical studies have shown comparable results to subepithelial connective tissue grafting when PRF is used for such procedures.[1]

PRF Membrane as a Periodontal Dressing
PRF has proven its role in improving angiogenesis and epithelization in the wound healing process. The coverage of exposed connective tissue after depigmentation procedure during the initial postsurgical phase minimizes the likelihood of postoperative bleeding and facilitates unperturbed healing by preventing surface trauma.[21]

Conventional periodontal dressings can lead to a feeling of foreignness in the mouth and abundant plaque accumulation along the undersurface during the healing phase.[22]

R Dahiya et al reported that PRF membrane provided satisfactory patient comfort and enhanced the wound healing cascade.[22]

The various applications of PRF in regenerative periodontics have been summarized in Table 2.

Table 2: Summary of applications of PRF in Regenerative Periodontics

1	Socket preservation after tooth extraction
2	Protection and stabilization of grafts during guided bone regeneration
3	Regenerative procedures in the treatment of intra-bony defects
4	Treatment of furcation defects
5	Used as membrane in combination with bone grafts during direct sinus augmentation procedure
6	Root Coverage
7	As a periodontal dressing after depigmentation and free gingival grafting
8	Combined perio-endo lesions

CONCLUSION

PRF is a simple and inexpensive biomaterial utilized for the successful regeneration of periodontal tissues.

The current research focuses on the clinical applications of the PRF in periodontology and implant dentistry and has shown promising results with better healing outcomes and less patient discomfort. However, there is still a need to evaluate the properties of PRF which includes quantification of growth factors and the number of growth factors released from PRF over time. In the future more studies and clinical trials are needed to investigate potential applications of PRF in the field of periodontal regeneration and tissue engineering to extend its clinical applications.

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