ORIGINAL RESEARCH PAPER

Periodontology

PLATELET RICH FIBRIN IN PERIODONTICS – A REVIEW.

KEY WORDS: Platelet rich fibrin, platelet rich plasma, autologous growth factors

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ABSTRACT

Platelet-rich fibrin (PRF), is a second generation platelet concentrate widely used to accelerate soft and hard tissue healing. Its advantages over the better known platelet-rich plasma (PRP) include ease of preparation/application, minimal expense, and lack of biochemical modification (no bovine thrombin or anticoagulant is required). PRF is a strictly autologous fibrin matrix containing a large quantity of platelet and leukocyte cytokines. This article serves as an introduction to the PRF "concept" and its potential clinical applications.

Introduction:

It was first described by Dr. Joseph Choukroun in France to promote wound healing in implants. Currently, the studies have been focussed on the use of an autogenous material called Platelet Rich Fibrin that provides an osteoconductive scaffold along with growth factors to stimulate patient's own cells towards a regenerative response [1].

Platelet rich fibrin (PRF) is a fibrin matrix in which platelet cytokines, growth factors and cells are trapped and may be released after a certain time and that can serve as a resorbable membrane [2]. It can be obtained from blood with the help of a simple process. PRF is basically a concentrate of growth factors that promote wound healing and regeneration which is used in various disciplines of dentistry to repair various lesions and regenerate dental and oral tissues.

Healing of any wound is initiated by clot formation and inflammation, followed by a proliferative stage which comprises of epithelialization, angiogenesis, granulation tissue formation and collagen deposition and finally collagen maturation and contraction. Growth factors are mitogenic (proliferative), chemotactic (stimulate directed migration of cells) and angiogenic (stimulate new blood vessel formation). Therefore, they appear to be critical to the wound-healing process.

Platelet rich plasma (PRP), the first generation platelet concentrates showed positive results, however, the complexity of PRP preparation protocol and the risk of cross-infectiondue to the use of bovine thrombin led to development a newer generation of completely autologous platelet concentrates- platelet rich fibrin also called as Choukroun's platelet rich fibrin named after its inventor.

PRF was developed in France by Joseph Choukroun et al. in 2001. They used PRF to improve bone healing in cases of implants. It is a fibrin matrix in which platelet cytokines, growth factors and cells are trapped and may be released after a certain time and that can serve as a resorbable membrane. Growth factors are released after activation from the platelets trapped within fibrin matrix, and have been shown to stimulate the mitogenic response in the periosteum for bone repair during normal wound healing .

A variety of materials are available for bone regeneration, which are highly osteoconductive or osteoinductive like, freeze dried bone graft, bioactive glass, emdogain, PTR polymer, MTA, tricalcium phosphate, and octacalcium phosphate. PRF is an autogenous osteoinductive material that enhances osteogenesis in the extraction tooth socket in comparison to the physiological healing process. It is an optimized blood clot. It also provides a significant postoperative protection of the surgical site and seems to accelerate the integration and remodeling of the grafted biomaterial [3].

Preparation of PRF:

For preparation of PRF, blood sample is collected from the patient without anticoagulant using a butterfly needle and 10 ml blood collection tubes. After collection of blood, it is immediately centrifuged on a table-top centrifuge at a rate of 3000 rpm for 10 minutes. After centrifugation, 3 layers are obtained in the test tube (Figure 1). The topmost layer consisting of acellular PPP (platelet poor plasma), PRF clot in the middle and RBCs at the bottom of the test tube. The middle layer of PRF clot is then removed with sterile tweezers and separated from the underlying RBC layer using scissors and then transferred on a sterile dish and stored in a refrigerator. It is supposed that the junction of PRF to the RBC layer is rich in growth factors and therefore this region is preserved [4].

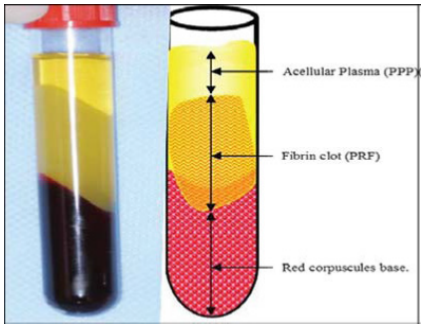

figure 1 – Layers of PRF

PRF results from a natural and progressive polymerization which occurs during centrifugation . Because of the absence of an anticoagulant, blood begins to coagulate as soon as it comes in contact with the glass surface. Therefore, for successful preparation of PRF, speedy blood collection and immediate centrifugation, before the clotting cascade is initiated, and is absolutely essential . The slow handling of blood to centrifugation process will result in diffuse polymerization of fibrin leading to the formation of a small blood clot with irregular consistency.

Also, PRF membrane can be obtained by squeezing out the liquids present in the fibrin clot. Liquid removal from the PRF fraction can be done through mechanical pressure between gauze layers resulting in a fairly solid, gel-like material that can be used in various clinical applications as a filling material or as a suturing membrane [5]. PRF membrane can also be prepared by compressing PRF clot in special tools like "PRF Box" resulting in standardized membranes of constant thickness and size along with PRF exudate. PRF exudate contains good amount of growth factors (TGF-b1, PDGF-AB, VEGF etc.), matrix glycoproteins (fibronectin, vitronectin etc.) and proteins specialized in increasing cell attachment to biomaterials and titanium and therefore can be used for biomaterial impregnation, rinsing surgical sites, hydration of graft materials and for storage of autologous grafts

Advantages of using PRF :

1. Its preparation is a simplified and efficient technique, with centrifugation in a single step, free and openly accessible for all clinicians.
2. It is obtained by autologous blood sample.
3. Minimized blood manipulation.
4. It does not require the addition of external thrombin because

polymerization is a completely natural process, without any risk of suffering from an immunological reaction.
5. It has a natural fibrin framework with growth factors within that may keep their activity for a relatively longer period and stimulate tissue regeneration effectively.
6. It can be used solely or in combination with bone grafts, depending on the purpose.
7. Increases the healing rate of the grafted bone.
8. It is an economical and quick option compared with recombinant growth factors when used in conjunction with bone grafts.
9. Used as a membrane, it avoids a donor site surgical procedure and results in a reduction in patient discomfort during the early wound-healing period.
10. The studies of PRF present it to be more efficient and with less controversies on its final clinical results when compared to PRP.

Disadvantages of using PRF
1. The final amount available is low because it is autologous blood.
2. The success of the PRF protocol depends directly on the handling, mainly, related to blood collection time and its transference for the centrifuge.
3. Need of using a glass-coated tube to achieve clot polymerization.

Other clinical applications
1. The literature reports some other possible applications of PRF such as:
2. In periodontal bone defects: achieving a probing depth reduction and a radiographic defect fills.
3. In localized osteitis, 90% of osteitis reduction was found in surgical sites of the third molars.
4. As an adjunct to palatal wound healing after harvesting a free gingival graft.
5. As a potential scaffold in pulp revascularization procedures of necrotic immature permanent tooth: as it is rich in growth factors, it seems to enhance cellular proliferation and differentiation, augmenting angiogenesis, acting as a matrix for tissue growth, and regulating the inflammatory reaction.
6. In multiple extractions to preserve the alveolar ridge height.
7. Bone regeneration around immediate implants, inside the alveolar defect.
8. Reconstruction of large bone defects after cancer surgery.
9. In plastic surgery, PRF clots are often directly used to fill cavities or mixed with an adipocyte graft in a lipostructure.
10. In the membrane form, it could be useful for small otologic surgery.

Role of PRF in wound healing:
1. Prolonged release of growth factors at the wound site
2. Proliferation of fibroblasts and osteoblasts.
3. Promotes angiogenesis
4. Induces collagen synthesis
5. Guides in wound coverage
6. Mechanical adhesion by fibrin
7. Trapping of circulating stem cells
8. Regulation of immunity

Role of PRF In Periodontics:
In periodontics, PRF has been used to treat gingival recession, intra-bony defects and periapical lesions. Some case reports show the use of a combination of PRF gel, hydroxyapatite graft and guided tissue regeneration (GTR) membrane to treat intrabony defect. Some studies show the use of PRF gel and PRF membrane in combination with a bone graft for treating a tooth with a combined periodontic- endodontic lesion [6]. Some studies show use of two layers of PRF membrane with to cover the defect. The membranes are very thin and inhomogeneous and leucocytes and platelet aggregates are believed to be concentrated in end of the membrane. Therefore, two layers of membrane in opposite sense can be used to prevent the resorption of the thin membrane and to allow the entire surgical area to be exposed to same components (leucocytes and platelet aggregates). Platelet rich fibrin as a potential novel root coverage approach has been reported by Anil kumar et al. for covering localised gingival recession in mandibular anterior teeth using combined laterally positioned flap technique and PRF membrane.

PRF can promote the healing of osseous defects by the following mechanisms. According to Chang et al. PRF promotes the expression of phosphorylated extracellular signal-regulated protein kinase (p-ERK) and stimulates the production of osteoprotegerin (OPG) which in turn causes proliferation of osteoblasts. Another study by Huang et al. reported that PRF stimulates the osteogenic differentiation of the human dental pulp cells by up regulating osteoprotegerin and alkaline phosphatise expression. PRF also releases growth factors such as platelet-derived growth factor and transforming growth factor which promote periodontal regeneration

Conclusion:
The use of PRF as an adjunct in wound healing and periodontal regeneration has shown promising results. It has been successfully used for correction of osseous defects in periodontics, oral and maxillofacial surgery and implant dentistry. In addition to these, PRF has shown good results in regeneration of pulp-dentin complex for endodontic procedures. However, most studies with PRF have shown short term results only. More controlled clinical trials with long term results are needed to acquire deeper knowledge about the efficacy and credibility of this biomaterial on a long term basis and to optimize its use in daily procedures. In addition to clinical trials, histopathological studies are also required to learn about the nature of the newly formed tissue in the defect and to understand the biology, efficacy and its mode of action of PRF more effectively.

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