Review Article

Role of platelet-rich fibrin in dentistry

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ABSTRACT

Platelet-rich fibrin (PRF) is an autogenous biomaterial which is consist of growth factors and cytokines entrapped in a fibrin matrix. It combines the fibrin sealant properties along with growth factors thereby providing an ideal environment for wound healing and regeneration of tissues. Moreover, PRF has been used in various disciplines in dentistry in a wide range of treatment modalities. The wound healing and sealing capacity, bone growth and maturation, graft stabilization and hemostasis ability of PRF are useful in various fields of dentistry. Thus, this article gives a review of the roles of the PRF in dentistry.

KEY WORDS: Dentistry, Fibrin, Platelet concentrate, Platelet-rich fibrin

INTRODUCTION

In dentistry, vigorous research is galvanized with respect to wound healing and osseous defects, as they are of major concern in surgical practice. Biomaterials such as hydroxyapatite, freeze-dried bone graft, tricalcium phosphate (TCP), and bioactive glass have been constantly tested for its role in repair and regeneration of hard and soft tissue. Apart from these materials, current studies have been more focusing on the usage of an autogenous material called platelet-rich fibrin (PRF), which provides an osteoconductive scaffold along with growth factors to stimulate regenerative response of patient's own cell.[1]

PRF is an autologous dense fibrin matrix that has a large concentration of platelets, leukocyte cytokines, and wide range of key healing proteins. Its enhances hard and soft tissue healing while protecting surgical and grafted site as it has strong fibrin architecture and slow release of growth factors which forms a resorbable natural bioactive membrane. Growth factors have very high proliferative and rate of new blood vessel formation which makes it important in wound healing.[2]

Blood-derived products have been used for wound healing since 1970 where fibrin glues or fibrin sealants that were formed by polymerizing fibrinogen with thrombin and calcium have been used. However, the stability and quality of the fibrin glue were low as the fibrinogen content were low in plasma. Researchers identified platelet-derived growth factor as a potent serum growth factor for fibroblasts, smooth muscle cells and glial cells (Kohler and Lipton, 1974; Ross *et al*., 1974; Westermark and Wasteson, 1976). Platelets provide a rich pool of varied growth factors such as fibroblast growth factor, platelet-derived growth factors (PDGF)-AB vascular endothelial growth factors (VEGF), epidermal growth factor, connective tissue growth factor, insulin-like growth factor. Better understanding of advantages and physiologic properties of platelets in wound healing in past decades has increased its therapeutic application.[3]

Platelet concentrates were initially used in transfusion medicine by prevention of hemorrhage due to extreme thrombocytopenia, acute leukemia, or marked blood loss during prolonged surgical procedures. Other than that, platelet concentrates have been constantly used in plastic surgery, nerve injuries, tendinitis, osteoarthritis, etc.

In recent times, a variety of platelet concentrates has been developed and has shown promising results. Platelet concentrates have been developed with an idea of providing an ideal base for wound healing and regeneration of tissues. Platelet-rich plasma (PRP), the first generation platelet concentrates showed

Access this article online

Website: jprsolutions.info | ISSN: 0974-6943

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Received on: 27-10-2017; Revised on: 24-11-2017; Accepted on: 17-12-2017

positive results. However, the complexity of PRP preparation protocol and the risk of cross-infection led to development a newer generation of completely autologous platelet concentrates - PRF also called as Choukroun's PRF named after its inventor.[4]

PRF has more simpler and effective method of preparation and eliminates the usage of bovine thrombin, thus eliminating cross infection. It has been discovered that the use of bovine thrombin may be associated with the development of antibodies to the factors V, XI, and thrombin, which results in risk of life-threatening coagulopathies.[5] Rate of natural polymerization in both the media makes PRF more superior. PRF has slow natural polymerization which results in physiologic thrombin concentration. On the other hand, PRP has sudden fibrin polymerization depending on the amount of surgical additives such as thrombin and calcium chloride. PRF also has fine and flexible three-dimensional structure which is more favorable to cytokine enmeshment and cellular migration. In addition, PRF has supportive effect on immune system and aids in hemostasis.[6]

PREPARATION OF PRF

The classical technique for PRF preparation was invented by Dr. Joseph Choukroun in 2000. It is the current PRF technique authorized by the French Health Ministry in which PRF is prepared without using an anticoagulant during blood harvesting or bovine thrombin during gelling.[7]

For the 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 tabletop centrifuge at a rate of 3000 rpm for 10 min. After centrifugation, three layers are obtained in the test tube [Figure 1]. The topmost layer consisting of acellular platelet poor plasma, PRF clots in the middle and red blood cells (RBCs) at the bottom of the test tube. The intermediate layer of PRF clot is then removed with sterile instruments and is separated from the underlying RBC layer using scissors and then transferred subsequently to a sterile dish and stored in a freezer.[8]

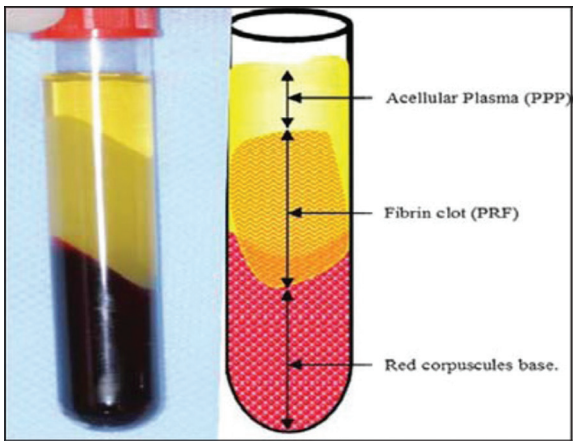

Figure 1: Centrifugation of blood

Besides that, PRF forms by an progressive polymerization during centrifugation process. Since anticoagulant is absent, blood begins to coagulate when it comes in contact with the glass surface. Furthermore, for an accurate preparation of PRF, speedy blood collection and immediate centrifugation, before the clotting cascade is initiated, and is absolutely essential[9]. The slower handling of blood tissue to centrifugation process can result in diffuse polymerization of fibrin particles leading to the formation of a small blood coagulates with irregular consistency.[10,11]

Moreover, 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.[12] PRF membrane can be processed by compressing PRF clot in certain specialized tools like "PRF Box" resulting in standardized membranes of uniform thickness and size along with PRF exudate. PRF exudate contains significant amount of growth factors such as transforming growth factor (TGF)-b1, PDGF-AB, and VEGF and so along with matrix glycoproteins such as fibronectin and vitronectin and proteins specialized in increasing cellular attachment to biomaterials, and therefore, can be used for biomaterial impregnation procedures, rinsing of the surgical sites, hydration of the graft materials and also for storage of autologous grafts.[13]

ROLE OF PRF IN DENTISTRY

In recent times a lot of research has been done on PRF, and numerous cases have been reported regarding the use of PRF clot and PRF membranes. Majority of the research has been concentrated on the use of PRF in oral surgery for bone augmentation, sinus lifts, avulsion sockets and in periodontics to correct intrabony defects, gingival recession, guided bone regeneration, periapical lesions, etc. It has also been used for regenerative pulpotomies, periapical surgeries, open apex regeneration, etc.[14]

In Oral and Maxillofacial Surgery

Studies show that PRF can be used as filling material in extraction sockets especially during filling material in extraction sockets; PRF will act as a stable blood clot for neovascularization and accelerated tissue

regeneration. This can be used to improve wound healing in immunocompromised and diabetic patients. Besides that, PRF can be used as an adjuvant in patients on anticoagulant therapy as it stimulates coagulation and wound closure.[13]

PRF has been commonly used in sinus lift procedures. Besides that, the use of PRF as the sole filling material during sinus lift and implantation. Besides that, studies have proven the use of PRF in combination with other bone graft materials in various direct and indirect sinus lift techniques such as bone-added sinus floor elevation, osteotome-mediated sinus floor elevation, and minimally invasive antral membrane balloon elevation. Some studies also show the use of PRF in combination with beta TCP without bone graft in sinus lift procedures and chronic periodontal lesions.

Its proven that in condition with bony walls are intact shows favorable results during filling of avulsion sockets with PRF. A combination of PRF with bone substitutes and other adjuncts may be necessary in residual defects where one or several walls are missing or damaged to provide an adequate reconstruction of bone volume. Cohesion between the graft materials is increased by PRF as fibrin act as physiological glue between the wound tissues.

In case of complicated conditions such as wide sockets and lesions where primary closure is difficult, PRF membrane can be used as a covering and protective membrane that promotes re-epithelialization of the site and accelerates the merging of the wound margins. The elasticity and strength of PRF fibrin membrane make it easy to suture.

In Periodontics

In periodontics, PRF has been used to treat gingival recession, intrabony defects and periapical lesions. Some case reports show the use of a combination of PRF gel, hydroxyapatite graft and guided tissue regeneration 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 periodontal-endodontic lesion. Some studies show the use of two layers of PRF membrane with to cover the defect. The membranes are very thin and inhomogeneous, and leukocytes 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 (leukocytes and platelet aggregates).[15] PRF as a potential novel root coverage approach has been reported by Anil Kumar *et al*. For covering localized gingival recession in mandibular anterior teeth using combined laterally positioned flap technique and PRF membrane.[16]

PRF can promote the healing of osseous defects by the following mechanisms. According to Chang *et al.* the expression of phosphorylated extracellular signal-regulated protein kinase are promoted by PRF. Moreover, it 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 OPG and alkaline phosphatize expression. Growth factors such as platelet-derived growth factor and TGF which promote periodontal regeneration are released by PRF.[17]

In Endodontics

PRF can be used as a scaffolding material in an infected necrotic immature tooth for pulpal regeneration and tooth revitalization. Other than that, it also can be used in a combined form with mineral trioxide aggregate (MTA) as an alternative for creating artificial root-end barriers and to induce faster periapical healing in cases with large periapical lesions. Usage of PRF in the form of a membrane can prevent the extrusion of material. PRF also can be used in regenerative pulpotomy procedures where the coronal pulp is removed, and the pulp wound is covered by PRF followed by sealing it with MTA and glass ionomer cement. PRF has also been used to fill in the bony defects after periapical surgeries like root-end resection.[18]

PRF also act as a scaffold in revascularization of immature permanent teeth with necrotic pulps as it is rich in growth factors which enhances cellular proliferation and differentiation, and acts as a matrix for tissue growth. In a study by Huang *et al.*, they concluded that PRF causes proliferation of human dental pulp cells and amplifies the protein expression of these dental pulp cells which differentiate into odontoblast-like cells. This has validated the success of PRF usage in open apex treatment.[19,20]

In Tissue Engineering

PRF usage as tissue engineering scaffold has been in a constant investigation by the researchers. Gassling *et al*. reported PRF appear to be superior to collagen as a scaffold for human periosteal cellular proliferation, and PRF membranes can be used effectively for *in vitro* cultivation of periosteal cells for the purpose of bone tissue engineering. Thus, PRF is a beneficial in tissue engineering, but clinical aspects of PRF in this field requires further investigation.

CONCLUSION

Various studies and publications have proven the role of PRF for early wound closure, maturation of bone

graft, postsurgical healing of implant and periodontal soft tissue. This biomaterial is easy to use and inexpensive to be prepared, thus use of PRF in dental surgeries must be taken into consideration for better prognosis of the treatment. The beneficial effects this biomaterial should be spread universally to enhance better care for the patients.

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