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Platelet rich fibrin and its applications in dentistry: An update

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Abstract
Platelet rich fibrin (PRF) is an autogenous biomaterial consisting of growth factors and cytokines entrapped in a fibrin matrix. It combines the fibrant sealant properties along with growth factors thereby providing an ideal environment for wound healing and regeneration of tissues. PRF is a second-generation platelet concentrate which is prepared from the patient's own blood free of any anticoagulant. Present review of literature aims to provide details of PRF preparation and its application in dentistry.

Keywords: platelet rich fibrin (PRF), platelet rich plasma (PRP), growth factors, wound healing, dentistry

Introduction

In the last few decades a variety of biomaterials have been introduced in dentistry that can be used to treat osseous defects and promote wound healing. Materials like bioactive glass, freeze dried bone graft, hydroxyapatite, tricalcium phosphate, etc. have been widely used to promote healing and regeneration of soft and hard tissues [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 period and that can serve as a scaffold of resorbable membrane [2]. It can be obtained from patient's own 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 [3]. PRF is superior to other blood products like PRP due to its ease and inexpensive method of preparation and also it does not need any addition of exogenous compounds like bovine thrombin and calcium chloride. Thus PRF has emerged as one of the promising regenerative materials in the field of dentistry [4]. Present review of literature aims to provide details of PRF preparation and its application in dentistry.

Method for formation of platelet-rich fibrin

It was first described by Dr. Joseph Choukroun in France to promote wound healing in implants [5]. 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. The top most 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 [6]. 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. 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 exudates. PRF exudates 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; therefore can be used for biomaterial impregnation, rinsing surgical sites, hydration of graft materials and for storage of autologous grafts [7].

Difference between PRP and PRF [8]

Table 1: Difference between PRP and PRF

	PRP	PRF
Generation	First generation	Second generation
Based on processing technique	Use of bovine thrombin and calcium chloride (anticoagulants)	No anticoagulant used
Based on architecture	Sudden fibrin polymerization depending on the amount of surgical additives (thrombin and calcium chloride)	Slow natural polymerization on contact with glass particles of the test tube results in physiologic thrombin concentration
Based on biological property	There is immediate release of growth factors	Growth factors are released slowly over a period of 7 or more days
Based on therapeutic concern	Concern over the use of bovine thrombin, bovine factor Va may be a contaminant in certain bovine thrombin commercial preparations, antibodies to bovine factor Va may cross react with human factor Va and may produce coagulopathies and rare bleeding episodes	No coagulopathies and no bleeding episodes An *in vitro* study showed that PRF is superior to PRP, considering the expression of alkaline phosphatase and induction of mineralization, caused markedly by release of TGF-β, and PDGF-AB

Application of PRF in dentistry

Table 2: Application of PRF in dentistry

Endodontics	Oral and maxillofacial surgery	Periodontics	Pedodontics	Tissue engineering	Implant
In treatment of open apex For regeneration of pulp-dentin complex In combination with MTA to create root end barriers in apexification procedures to prevent extrusion of material In regenerative pulpotomy To fill in bony defect after	Filling material in avulsion sockets, bony defects etc. Bone augmentation in sinus lifts for posterior maxilla augmentation for implants, bony defects etc. Ridge preservation guided bone regenetration	For treatment of intrabony defects For treatment of gingival recession Guided tissue regeneration Periapical lesions	Pulpotomy agent in primary teeth	For *in vitro* cultivation of human periosteal cells for bo	To enhance osseointegration of implant

Use 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 intra bony defect [9].

Use of PRF in Endodontics

PRF can be used as a scaffolding material in an infected necrotic immature tooth for pulpal regeneration and tooth revitalization. Also, some case reports show that the combination of PRF membrane as a matrix and MTA in apexification procedures prove to be an effective alternative for creating artificial root-end barriers and to induce faster periapical healing in cases with large periapical lesions [10].

Use of PRF in Pediatric dentistry

Patidar S *et al*. (2017) evaluated effectiveness of platelet-rich fibrin and mineral trioxide aggregate as pulpotomy agent in primary molars. In radiographic and clinical evaluation PRF group found to be an acceptable alternative in pulpotomy of primary teeth. PRF holds a promising future in the area of primary tooth vital pulp therapy [11].

Use of PRF Oral and Maxillofacial surgery

PRF can be used as filling material in extraction sockets specially during filling material in extraction sockets; PRF will act as a stable blood clot for neovascularization and accelerated the tissue regeneration. This can be used to improve wound healing in immunocompromised patients [12].

Use of PRF in Tissue engineering

The use of PRF as a tissue engineering scaffold was investigated by many researchers for the past few years. PRF appears to be superior to collagen as a scaffold for human periosteal cell proliferation and PRF membranes can be used for *in vitro* cultivation of periosteal cells for bone tissue engineering. Thus PRF is a potential tool in tissue engineering but clinical aspects of PRF in this field requires further investigation [3].

Advantages of PRF [13]

1. Simple and cost effective method of preparation of PRF.
2. No need of addition of anticoagulant thereby no biochemical handling of blood.
3. Slow natural polymerization leading to favourable healing.
4. PRF helps in hemostasis.
5. PRF has supportive effect on immune system.
6. Standard preparation protocol.
7. 3-D structure gives elasticity and flexibility to the PRF membrane.

Disadvantages of PRF [13]

1. Only limited volume of PRF can be used as it is obtained from autologous blood sample, the quantity of PRF produced is low and this limits its use for general surgery.
2. Its storage for longer duration is also not possible because of the shrinkage and altering the structural integrity of PRF.
3. Quick handling is required immediately after collection. The technique entirely depends on the speed of blood collection and transfer to the centrifuge.

Conclusion

Platelet rich fibrin (PRF) is an autogenous biomaterial consisting of growth factors and cytokines entrapped in a fibrin matrix. It combines the fibrant sealant properties along with growth factors thereby providing an ideal

environment for wound healing and regeneration of tissues. PRF contains cytokines, glycanic chains, and structural glycoproteins which are enmeshed within the slowly polymerizing fibrin network. These biochemical components have well known synergetic effects on healing processes. The ease of PRF formation and its application has various beneficial outcomes, which also includes reduction in bleeding, graft stabilization and bone growth. More long term studies are required to evaluate deeper knowledge about the efficacy of this biomaterial and to optimize its use in routine clinical dentistry.

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