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RESEARCH ARTICLE

PLATELET RICH FIBRIN: THE POTENTIAL REGENERATIVE BIOFUEL IN DENTISTRY

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ABSTRACT

Regulation of inflammation and increasing healing are the great challenges faced in clinical research and surgical denstistry. The use of platelet□rich fibrin (PRF) is one of the promising innovations in the field of surgical dentistry. Platelet-rich fibrin (PRF) belongs to a new generation of platelet concentrates having simple process of preparation without biochemical blood handling. It accelerates the healing mechanism of the tissue and reduces the inflammation. Platelet-rich-fibrin (PRF) is one such material that holds on to these growth factors enmeshed in the fibrin network which results in their sustained release over a period of time. This slowly releasing property of platelet can accelerate the wound healing process. It can be used alone or as an additive with other biomaterials. Thus PRF has emerged as one of the promising regenerative biomaterials in the field of dentistry. This article serves as an introduction to the PRF, its preparation and its potential clinical applications with emphasis on regeneration and wound healing.

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INTRODUCTION

Wound healing has been and remains an important topic in dentistry and other medical fields. Healing generally is a complex process involving cellular organization, chemical signals, and the extra-cellular matrix for tissue repair (Maniyar, 2018). Biomaterials proved to be beneficial in the process of wound healing. They are being used to regulate the inflammation and enhance the speed of healing process (Borie, 2015). Various evidences have proved that the presence of growth factors and cytokines in platelets play important roles in inflammation and wound healing process. Some proteins such as fibrin, fibronectin, and vitronectin which are secreted by platelets act as a matrix for the connective tissue and as adhesion molecules and helps in efficient cell migration. These properties of platelets have led to the idea of using platelets as therapeutic tools and to further improve tissue repair particularly in periodontal wound healing (Chandran, 2014). Afterward, different types of platelet concentrates were developed.

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Based on the leukocyte content and fibrin structure, platelet concentrates can be classified into four main categories (Dohan Ehrenfest, 2014)

- Pure platelet-rich plasma (P-PRP) without leukocytes and with a low-density fibrin network after activation
- Leukocyte- and platelet-rich plasma (L-PRP) with leukocytes and with a low-density fibrin network after activation
- Pure platelet-rich fibrin (P-PRF) without leukocytes and with a high-density fibrin network
- Leukocyte- and platelet-rich fibrin (L-PRF) with leukocytes and a high-density fibrin network.

First generation of platelet concentrates

Whitman, Berry, and Green in 1997 (Whitman, 1997) and Marx and colleagues in 1998 (Marx, 1998) first promoted the

use of PRP in oral and maxillofacial surgery. PRP is an increased concentration of autologous platelets in a small amount of plasma. It is obtained after centrifugation. The preparation is quite complex. There was great variability in study designs (e.g., small groups of patients, no control groups) and also in preparation protocols (e.g., without clear classification), which made comparisons difficult. Furthermore, the preparation protocol was expensive, complicated, and very operator dependent and the need for animal thrombin as a coagulant raises legal issues in some countries (Prakash, 2011).

Second generation of platelet concentrates

Furthermore, new techniques were investigated to overcome the disadvantages of PRP. Choukran *et al*. described Platelet rich fibrin (PRF) which allows one to obtain fibrin mesh enriched with platelets and growth factors, from an anti-coagulant free blood harvest. The process was without any artificial biochemical modification (Panda, 2014). The PRF clot forms a strong natural fibrin matrix. The clot concentrates almost all the platelets and growth factors of the blood harvest and shows a complex architecture as a healing matrix, including mechanical properties no other platelet concentrate offers (Chang, 2011). PRF contains dense fibrin network with leukocytes, structural glycoproteins, cytokines and also growth factors such as transforming growth factor b1, platelet-derived growth factor, vascular endothelial growth factor and glycoproteins such as thrombospondin-1 during ≥7 day. PRF scaffold contains concentrated leukocytes which play an important role in growth factor release, anti-infectious activities, immune regulation, and matrix remodeling during wound healing. PRF with slow polymerization mode and cicatricial capacity creates a physiologic architecture favorable for wound healing (Chandran, 2014).

Protocol for preparation of PRF

The classical technique for PRF preparation was invented by Dr. Choukroun in 2000. The PRF protocol is very simple: A blood sample is taken without anticoagulant in 10-mL tubes which are immediately centrifuged at 3000 rpm (approximately 400g according to our calculations) for 10 minutes. The absence of anticoagulant implies the activation in a few minutes of most platelets of the blood sample in contact with the tube walls and the release of the coagulation cascades. Fibrinogen is initially concentrated in the high part of the tube, before the circulating thrombin transforms it into fibrin.

After centrifugation, the resultant product consists of three layers:

- The topmost layer consisting of acellular PPP (platelet poor plasma),
- PRF clot in the middle and
- RBCs at the bottom ofthe test tube

The fibrin clot obtained after centrifugation is removed from the tube. The attached red blood cells scraped off from it. Discarded PRF can also be prepared in the form of a membrane by squeezing out the fluids present in the fibrin clot. The success of this technique entirely depends on the speed of blood collection and transfer to the centrifuge. Indeed, the blood samples start to coagulate almost immediately upon contact with the tube glass without anticoagulant, and it takes a minimum of a few minutes of centrifugation to concentrate fibrinogen in the middle and upper part of the tube. To obtain a clinically usable PRF clot, quick handling is the only way. Failure will occur if the duration required collecting blood and launch centrifugation is overly long. The fibrin will polymerize in a diffuse way in the tube therefore only a small blood clot without consistency will be obtained (Dohan, 2006).

Clinical applications

PRF is a powerful healing biomaterial with inherent regenerative capacity and can be used in various dental procedures.

Periodontics

- For treatment of intrabony defects
- For treatment of gingival recession
- Guided tissue regeneration
- Periapical lesions

Endodontics

- 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 periapical surgeries like root resection
- Oral and Maxillofacial Surgery:
- 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

Tissue Engineering

- For in vitro cultivation of human periosteal cells for bone tissue engineering (Agrawal, 2014).

Advantages of PRF

Ease of preparation/application (Kumar, 2013), Lack of biochemical modification (Kumar, 2013), Simplified and cost effective process (Dohan, 2006), Long-term effect (Kumar, 2013), Able to support cytokines enmeshment and cellular migration (Kumar, 2013), Increased incorporation of the circulating cytokines in the fibrin meshes (intrinsic cytokines) (Kumar, 2013), It is an immune organizing node (Kumar, 2013), It supports and accelerates the healing process (Mourão, 2015), due to slow polymerization (Dohan, 2006), Helps in hemostasis (2015), Three-dimensional structure gives elasticity and flexibility to PRF membrane (Mourão , 2015).

Drawbacks of PRF

Low quantity of PRF is obtained (Khiste, 2013), because of autologous blood so application in general surgery is limited (Bansal, 2017). The clinical benefit of PRF depends on time interval between speed of handling between blood collection and centrifugation as PRF is prepared without any addition

anticoagulants (Chandran, 2014). The fibrin matrix contains the circulating immune cells and all the highly antigenic plasmatic molecules that is why PRF is totally specific to the donor (Agrawal, 2014). PRF membrane should be used immediately after preparation as it will shrink resulting in dehydration altering the structural integrity of PRF and leukocyte viability will be adversely affected altering its biologic properties (Dohan, 2018). PRF when stored in refrigerator can result in risk of bacterial contamination (Chandran, 2014).

Recent Advances

Mourao *et al* (2015), described a technique to obtain an injectable form of PRF called i-PRF. In this technique a short centrifuge for 2 min at 3300 rpm gave an orange color fluid which can be injected or mixed with bone graft to give a well agglutinated "steak" for bone grafting. Tunali *et al* in 2014 introduced a new product called T-PRF (Titanium prepared PRF) (Agrawal, 2017). The hypothesis for T-PRF method is that titanium may be more effective in activating platelets than the silica activators used with glass tubes in Chouckroun's leukocyte- and platelet-rich fibrin (L-PRF) method. The T-PRF samples seemed to have a highly organized network with continuous integrity compared to the other L-PRF samples. On Histomorphometric analysis, it was showed that T-PRF fibrin network covers larger area than L-PRF fibrin network; also fibrin seemed thicker in the T-PRF samples. This is the first human study to define T-PRF as an autogenous leukocyte- and platelet-rich fibrin product. The platelet activation by titanium seems to offer some high characteristics to T-PRF (Agrawal, 2017).

Conclusion

Fibrin glues were blood-derived products and first used to seal wounds and stimulate healing. They were first described 40 years ago and constituted of concentrated fibrinogen (polymerization induced by thrombin and calcium) (Dohan Ehrenfest, 2009). Platelet-rich fibrin (PRF), described by Choukroun *et al*. It was firstly introduced into clinical application in oral maxillofacial and implants surgery in Southern Europe[19]. It is in the form of a platelet gel and can be used in conjunction with bone grafts (Sunitha Raja, 2008). Although PRF belongs to new generation of platelet concentrate and is an autologous preparation from patient own blood, it is less time consuming and also decreases the cost of the regeneration therapy both for surgeon and patient[23]. Nevertheless, its ease of use, combined with its low cost and autologous source, makes it an ideal biomaterial worth further investigation across a variety of surgical procedures in dentistry. Therefore, further understanding of components and significance of PRF is necessary.

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