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Review Article

Platelet Concentrates: A Brand Biomaterial in Regenerative Era

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Abstract

Platelet rich concentrates, an attractive and potent material for regenerations as it has ability to form hydrogel which is suitable for cellular migration and proliferation. The ideal goal of any periodontal surgical therapy is regeneration. Being a completely autologous, relatively simple to prepare, inexpensive and efficient in terms of trapping platelets, platelet concentrates are efficient additive product for regeneration in periodontal therapy.

Keywords: Blood Platelet; Fibrin; Platelet-Rich Fibrin; Bone Regeneration; Periodontal Surgery

Introduction

"PHYSICIAN TREATS BUT NATURE HEALS". The primary goal of current researches is to develop regenerative biomaterials which optimize healing and regulate inflammation. Platelet-rich concentrates including platelet-rich plasma and platelet-rich fibrin, have been widely utilized in the field of dentistry and medicine as a scaffold capable of facilitating tissue regeneration [1]. Platelet rich plasma contains an array of naturally derived autologus growth factors including platelet derived growth factor (PDGF), transforming growth factors beta (TGF-beta) and vascular endothelial growth factor (VEGF) [2].

This set of growth factors is responsible for facilitating new blood vessel formation as well as inducing the cell migration and proliferation of various cell types [3].

Wound healing

Complex process mediated by interacting molecular signals involving mediators and cellular events. (Figure1)

Its followed by

Figure 1

- Mesenchymal cell recruitment,
- Proliferation and extracellular matrix generation which allows for scar formation. (Good epithelial healing and properly sealed noninfective wound) [4].

3 keys to soft tissue maturation and healing [5].

- Angiogenesis

- Immunity
- proliferation of epithelium.

Preparation methods for various blood derived biomaterials

- Anticoagulated
  - Cryoprecipitate → addition of thrombin → fibrin glue
  - Platelet rich plasma → addition of thrombin and calcium → platelet gel
- No anticoagulant and direct centrifugation → PRF
- Anticoagulated Platelet concentrates + Cryoprecipitate + calcium = PRF GLUE

History

1970	Fibrin glue (MATRAS)
1975-1979	Platelet gel
1998	PRP (MARX., *et al.*)
2000	PRF (Choukran., *et al.*)
2006	CGF (SACCO)
2009	First classification of platelet concentrate (Dohan., *et al.*)
2014	A-PRF by CHOUKRAN
2015	T-PRF by TUNALI., *et al.*
2015	I-PRF (MOURAO., *et al.*)
2018	Alb-PRF

Table a

Classification of platelet concentrates

Depending upon their leukocyte content and fibrin architecture (Dohan Ehrenfest., *et al.* in 2009)

- Pure platelet -rich plasma: without lecukocytes and with a low-density fibrin network.
- Leukocyte and platelet rich plasma: with leukocytes and with a low-density fibrin network.
- Pure platelet-rich fibrin: without leukocytes and with a high-density fibrin network.
- Leukocyte and platelet rich fibrin: with leukocytes and with high density fibrin network.

Why PRP replaced with PRF?

- Preparation protocol of PRP lacks standardization.
- Although never reported, the addition of bovine thrombin to the platelet concentrate could cause adverse reactions such as urticarial rash, bruising, temporary skin discoloration.

These disadvantages have reduced the usage of PRP and lead to evolution of "second generation PRP" coined as Platelet rich fibrin which is purely an autologous human thrombin introduced by choukroun., *et al.* in 2001 [6-8]

- PRF is an autologous fibrin-based (membrane, matrix or scaffold) living biomaterial, derived from human blood.
- This concentrate is usually termed as leukocyte and platelet-rich fibrin (L-PRF) using a protocol of "700*g* for 12-min".
- Since anticoagulants are removed, blood is subject to clotting over time within the blood collection tube, and it becomes critical to begin centrifugation shortly following blood collection to separate blood layers.
- Also called it as an optimized blood clot.

Key elements of Platelet rich fibrin: (Figure 2)

Figure 2

- Fibrin -supporting matrix
- Platelets -rich in growth factors
- Leukocyte stem cells which helps in neovascularisation and regeneration.

Types of PRF (Figure 3)

Each of these concentrates differs in the quantity of the platelets, leukocytes and fibrin because of variation in Time of the speed Spin during preparation.

Figure 3

Figure a

Preparation, protocols and use blood drawing: (Figure 4)

Figure 4

Blood is drawn from the patient (2-12 tubes) using a sterile 10ml vacutainer just before or during surgery.

The tubes with collected samples should immediately put inside the centrifuge (within 2 min.) cause blood will start to coagulate after 1-2 min.

Centrifugation

The tubes should always be BALANCED by opposing two tubes - To equilibrate the centrifugation forces and to prevent vibrations. Both tubes should contain blood only not water because of difference in density.

- The blood sample with clot is allowed to rest for approximately 4-8 minutes before extracting the clot from the tube to allow the maturation of it.
- The centrifugation process activates the coagulation process and separates the blood sample into THREE DIFFERENT LAYERS:

Centrifugation protocols

- Original choukran's PRF protocol: 3000RPM/10 min.
- Dohan ehrenfest's group - leukocyte and platelet rich fibrin (L-PRF): 2700 RPM/12 min.
- Choukrans advanced PRF - 1500 RPM/14 min
- Choukran's I-PRF: 700 RPM/8 min.
- Titanium PRF(T-PRF): 2800 RPM/12 min

Liquid or injectable -blood concentrates

I-PRF: 700 RPM for 3 MIN.

MPM: 1300 RPM for 3 MIN

AFG: RPM for 13 min, 30 sec acceleration, 2700rpm for 2 minutes, 2400 rpm for 4 minutes, 2700 rpm for 4 minutes, 3000 rpm for 3 minutes, final deceleration for 36 seconds.

Membranous blood concentrates

PRF (choukran., *et al.*)- 3000 RPM for 10 min

L-PRF - 2700 RPM for 12 min

A-PRF - 1300 RPM 15 min

CGF (Sacco., *et al.*)- 30 sec acceleration, 2700rpm for 2 minutes, 2400 rpm for 4 minutes, 2700 rpm for 4 minutes, 3000 rpm for 3 minutes, final deceleration for 36 seconds.

Effect of centrifugation protocols

Depending upon the centrifugal force there is differential distribution of RBC, PLATELETS, LEUKOCYTES in the PRF clot (Figure 5).

Figure 5: Molecular structure -Dohan., et al. 2006 Bilateral junctions in PRP B) Eqilateral junctions in PRF

- Longer the centrifugation = denser the fibrin clot
- Shorter the centrifugation protocol = less dense fibrin clot (loose inter- fibrous structure containing more cells.
- Very recently, it was reported that the horizontal centrifugation of PRF was superior at accumulating platelets and leukocytes when compared to the results from standard fixed-angle centrifuges utilized to produce solid-PRF. Both solid-based and liquid-based PRF matrices were obtained with up to 3.5-fold increase in platelet/leukocyte concentrations. Fibrin matrix formed in PRF, which favors the slow and gradual release of growth factors over time when compared to that in PRP [9].

- Furthermore, by reducing centrifugation speeds and time, a liquid-PRF (injectable-PRF or i-PRF) was developed with an increased concentration of platelets and leukocytes [10].

Newer concepts

Albumin gel platelet rich fibrin mixture (Alb-PRF)

- Kawase., *et al.* 2015
- 700 g for 8 min.
- It is made using Liquid PRF tubes spun using the Bio-PRF horizontal centrifuge for 8 min. and after words undergoing a bio - heating process using the BIO-Heat technology.
- Release 7 key Growth factors PDGF-AA, PDGF-AB, PDGF-BB, TGF-Beta1, VEGF, EGF, IGF1.
- Collect upper most layer of (PPP) and heat at 75 degrees Celsius for 10 min. and form denatured albumin and mix it with the remaining liquid PRF and residual cells inside of buffy coat to form Alb-PRF [11].

BIO-PRF (HORIZONTAL CENTRIFUGATION PROTOCOL)

- Miron., *et al.* (2019) found about horizontal centrifugation concept. Horizontal centrifugation increase both quantity and concentration of platelets and leukocytes [9].
- Protocols utilized using horizontal centrifugation with the Bio-PRF system are able to accumulate up to 4 times more platelets and leukocytes concentrate, compared to standard fixed-angle centrifuges [9]. (Figure 6).

Figure 6

Clinical implication advantages, limitation of platelet concentrates

Platelet rich plasma

Clinical implications	Advantages	Limitations
Intrabony defects (Figure 7) Sinus lift procedures (Figure 9) Augmentation techniques (Figure 8) Peri-implant defects Ridge preservation Root coverage (Figure 10)	Nontoxic Easily available Increased endothelial, epithelial regeneration. Stimulates angiogenesis and enhance collagen synthesis	Presence of bovine thrombin which cause allergic reaction Lack of uniformity in PRP preparation

Table b

Figure 7: Regenerative treatment of intrabony defects with L-PRF carranza 13th edition.

Figure 8: Ridge augmentation with L-PRF carranza 13th edition

Figure 9: Sinus Floor Augmentation carranza 13th edition.

Figure 10: Root coverage procedure carranza 13th edition

Platelet Rich Fibrin

Clinical implications	Advantages	Limitations
Intrabony defects (Figure 7) Sinus lift procedures (Figure 9) Augmentation techniques (Figure 8) Peri-implant defects Ridge preservation Root coverage (Figure 10) Furcation defects Endo perio lesions	Nontoxic Easily available Increased endothelial, epithelial and epidermal regeneration. Stimulates angiogenesis and enhance collagen synthesis Standard concept for preparation.	As it is produced in limited quantities, which limits the usage in general surgery PRF membranes are totally specific to the donor and cannot Containing an allogenic graft tissue.

Table c

Figure 11: Ridge augmentation with L-PRF.

Conclusion

Platelet concentrates being an autologus regenerative material could be a novel step in regenerative periodontal dentistry. Platelet concentrates are easy to use in clinical practice and offer potential benefits including rapid wound healing and bone regeneration and can therefore be considered to be new therapeutic adjuvants. In dental implant surgery they are used in bone reconstruction prior or along with the implant procedures. These new advancements will improve the status of treatment.

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