Journal of Current Medical Research and Opinion Received 17-02-2022| Revised 28-03-2022| Accepted 29-03-2022| Published Online 01-04-2022

DOI: https://doi.org/10.52845/CMRO/2022/5-4-1 **ISSN (O) 2589-8779 | (P) 2589-8760**

CMRO 05 (04), 1163−1174 (2022)

ORIGINAL RESEARCH

Never-ending Journey of Platelet Concentrates

Dr. Manisha Rani[1], Dr. Baljeet Singh[2], Dr. Tarun Nanda[3], Dr. Tanvi Ohri[4], Dr. Kanika Aggarwal[5], Dr. Abhinav Bhasker[6], Dr. Arshdeep Kaur[7]

[1]Postgraduate student, Department of Periodontology and Implantology, Bhojia Dental College and Hospital Baddi, Himachal Pradesh, India
[2]MDS, HOD and Professor, Department of Periodontology and Implantology, Bhojia Dental College and Hospital Baddi, Himachal Pradesh, India
[3]MDS, Professor, Department of Periodontology and Implantology, Bhojia Dental College and Hospital Baddi, Himachal Pradesh, India
[4]MDS, Senior Lecturer, Department of Periodontology and Implantology, Bhojia Dental College and Hospital Baddi, Himachal Pradesh, India
[5]MDS, Senior Lecturer, Department of Periodontology and Implantology, Bhojia Dental College and Hospital Baddi, Himachal Pradesh, India
[6]Postgraduate student, Department of Periodontology and Implantology, Bhojia Dental College and Hospital Baddi, Himachal Pradesh, India
[7]Postgraduate student, Department of Periodontology and Implantology, Dasmesh institute of Research and Dental Sciences, Faridkot, Punjab, India

Abstract:

Platelet concentrates have been used in various applications of dentistry for many years. Technological advancement in this field shows promising results. Various studies have been conducted to determine the utilization of platelet concentrates in various procedures i.e periodontology, oral surgery, and implant dentistry and encouraging results have been obtained in both soft and hard tissue regeneration. Presently, it's not wrong to say that the Golden era of platelet concentrates is arriving. This review aims to describe platelet concentrates advancements and various applications that have been made in the several years.

Keywords: Platelets, Platelet-Rich Fibrin, Periodontology, Oral surgery, Dental implant

Introduction:

Blood is an inherent element of the human body. It includes four components: Platelets, White Blood Cells, Red Blood Cells and Plasma. Each component plays its specific and significant role in the human body. Platelets especially, plays a prime role in the release of growth factors at the site of injury to begin wound healing; so this process is mandatory for cellular proliferation, organization and remodelling.(1)

Platelet Concentrate (PC) term is used in hematology to denote a greater than 1 ml/µL concentration of platelets.(2) While the normal range of platelets in the whole blood of healthy individuals is 150,000 to 350,000 platelets/µl of whole blood, the working definition of **Platelet Concentrate** is a concentration of 10,000,00 platelets/µl of platelet preparation and its composition shown in Table 1. (3)

TABLE 1: Composition of Natural Clot and Platelet Rich Clot

COMPOSITION (4)		
Type of Cells	**Natural Blood Clot**	**Platelet Enriched Clot**
Red Blood Cells	95%	4%
White Blood Cells	1%	1%
Platelets	4%	95%

Rationale of platelet concentrate: Platelets are well known for their "core and shell" action at the injury site as in Figure 1. Platelets contain more than 30 bioactive proteins that are actively secreted within 10 minutes after clotting, with more than 95% of the presynthesized growth factors secreted within 1 hour. By virtue of these properties, the concept of using platelet concentrates for therapeutic purposes was introduced in the past. (5)

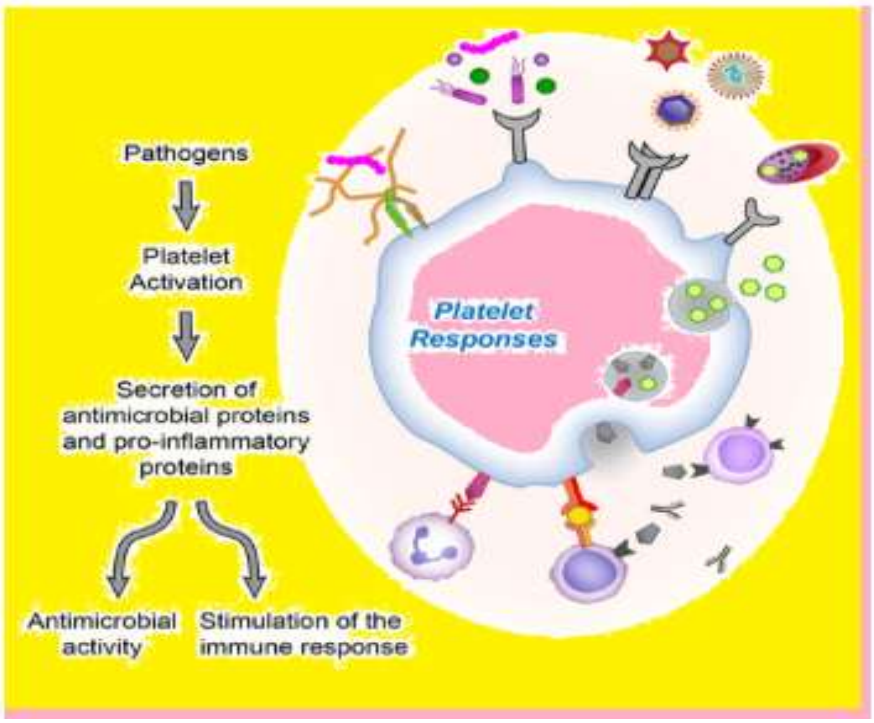


FIGURE 1: Platelet Response to pathogens

Objective of Platelet concentrates:

To segregates myriad of platelets from whole blood, afterward utilizing them to boost up wound healing.

Discussion:

History of Platelet Concentrates: Brief history about Researcher's work and contribution in the Platelet Concentrates (PCs) is presented in the tabulated form in Table 2 & Researcher's work in classification systems of platelet concentrates in Table 3.

TABLE 2: History of platelet concentrates

YEAR	RESEARCHER	CONTRIBUTION
1954	Kingsley(6)	• First used the term "**Platelet Rich Plasma" (Ist generation of PCs)**
1970	Matras(7)	• Introduced Fibrin Glue
1975-1978	Numerous research workers (8,9)	• Promoted concepts of blood extracts by making Platelet-Fibrinogen-Thrombin mixtures. • Termed Gelatin Platelet - Gel foam.
1986	Knighton(10)	• Termed Platelet Derived Wound Healing Factors **(PDWF)**
1988-1990	Kingsley(6)& Knighton(11)	• Changed term **PDWF** to Platelet derived wound Healing Formula.

1997	Whitman(12)	• Proposed term **PRP** (platelet rich plasma). • Platelet Gel alternative to Fibrin Glue. • First to used PRP in dentistry.
1998-1999	Marx(13,14)	Put forward Techniques for Commercially available PRP • **PRGF** (Platelet Rich Growth Factor) in Spain. • **Vivostat PRF** (Alleroed, Denmark) as the name implies it is not a PRF but produces a PRP product.
2000	Choukroun(15)	First used the term and introduced "**Platelet Rich Fibrin" (IInd generation)**
2006	Sacco(16)	Introduced new concept of Concentrated Growth Factors (**CGF**) which was richer in growth factors, CD34+ stem cells, platelets and leucocytes than conventional PRF. **(Advanced IInd generation)**
2008	Evert(17)	Introduced two types of concentrates i.e., • **Nonactivated** that was called "Platelet-Leukocyte Rich Plasma" (**P-LRP**) • **Activated** which was labeled "Platelet-Leukocyte-Gel" (**PLG**).
2010	Sohn(18)	Gave the concept of **Sticky bone** (autologous fibrin glue mixed with bone graft).
2013	Tunali(19)	Introduced **T-PRF** (Titanium prepared PRF) and **MT-PRF** (Modified Titanium prepared PRF) **(IIIrd generation)**
2014	Ghanaati et al.(20)	Proposed Advanced PRF which was called **A-PRF** (more monocytes and porous than the conventional PRF).
2014	Fujoka-kobayashi(21)	Introduced Advanced PRF plus called as **A-PRF^{+}** (improved growth factor release pattern and directly detached from red cell phase than A-PRF).
2015	Mourao et al.(22)	Gave the concept of **I-PRF** (Injectable-PRF). This was used in liquid or polymerized form, used for bone grafting as an alternative to PRP.
2018	Mourao et al.(23)	• Introduced **Alb-PRF** (Albumin Gel-PRF) Mixing denaturized albumin with CGF
2019	Miron et al.(24)	• Proposed **BIO-PRF** (Horizontal Centrifugation Protocol)
2020	Mourao and Javid (25)	• **Laser Pulse-PRF (L-PRF)** high power laser is used to heated up the one side of PRF membrane to increased its stability, while allowing the inverse part to remain with the macrostructure and elasticity similar to the standard PRF membrane.

Table: 3 Classification systems of platelet concentrates

YEAR	RESEARCHERS	CLASSIFICATION SYSTEMS (Only limited to PRP except Dohan et al.2009 Classification).
2009	Dohan et al.(26)	Pure PRP (**P-PRP**) Leucocyte-rich PRP (**L-PRP**) Pure PRF (**P-PRF**) Leucocyte-rich PRF (**L-PRF**).
2012	Mishra et al.(27)	Proposed classification only for **Sports medicine**. Type 1 PRP is a L-PRP solution. Type 2 PRP is a L-PRP gel. Type 3 PRP is P-PRP solution. Type 4 PRP is a P-PRP gel.
2012	Delong et al.(28)	Introduced **PAW** (Platelet, Activation, White cells) classification.
2013	Dohan et al.(29)	Purposed **POSEIDO** (Periodontology, Oral Surgery, Esthetic and Implant Dentistry Organization) classification.
2015	Mautner et al.(30)	Introduced **PLRA** (Platelet count, Leukocyte presence, Red blood cell presence, and use of Activation) classification.
2016	Magalon et al.(31)	Introduced **DEPA** (Dose, Efficiency, Purity, and Activation) classification.

Preparation Techniques for Platelet Concentrates

I. **Platelet Rich Plasma (PRP):** Platelet-rich plasma is a volume of autologous plasma that has a platelet concentration above baseline.

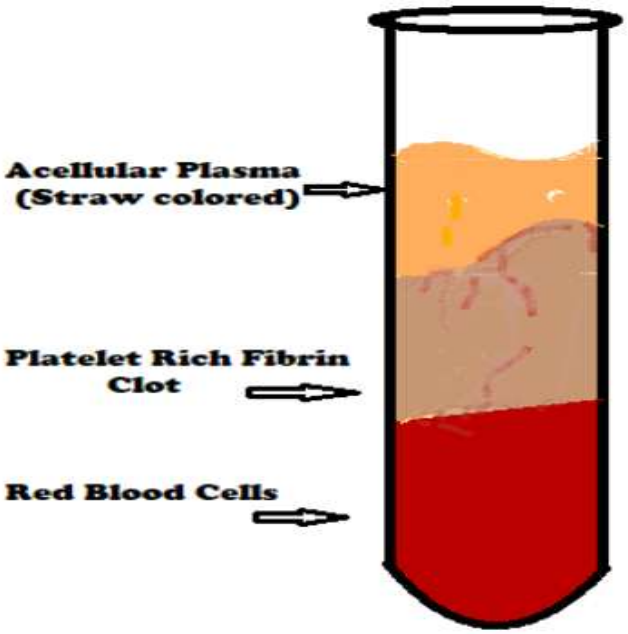
Preparation of PRP:

- 8.5 mL venous blood is collected into a tube having **anticoagulant** (acid citrate dextrose etc.) To avoid platelets activation and degranulation.
- **Soft-spin** centrifugation 110 x g (Relative Centrifugation Force) for 15 min, 22℃ Now, Platelets suspended in the plasma, WBCs & RBCs were sedimented in the tube.
- Using **pipette** to collect upper 25% of PRP into a fresh tube to avoid contaminated by WBCs & RBCs.
- **Hard-spin** centrifugation 1000 x g (Relative Centrifugation Force) for 15 min, 22℃. To sediment platelets in the tube. Carefully remove the plasma supernant and discard it.
- To form gelling material, bovine thrombin is added to **PRP** or can be stored for used within 5 days of collection. For storing process, PRP should be passing through a leukocyte depletion filter to remove leukocyte that is known as **Pre-storage Leukoreduction.**

II. **Platelet Rich Fibrin (PRF):** is a 3D fibrin (i:e fibronectin, vitronectin) scaffold having autologous cells like platelets, macrophages, WBCs, RBCs and wide range of natural growth factors.

Preparation of PRF:

- 9 mL venous blood is drawn into a tube **without** any anticoagulant **Blood is activated when in contact with glass tube.**
- **Single centrifugation** cycle 3000 revolution per min (rpm) for 10 min.
- After centrifugation, blood is separated into **three** layers as shown in Figure 2:



F**IGURE 2: Bottom layer-RBCs, Middle layer-Platelet Rich Fibrin, Superficial layer-Acellular Plasma**

- Acellular plasma is removed, PRF clot is scra pped off from the RBCs layer with preserving a **small RBC layer** at the end of the PRF clot. Because this Small RBCs layer collects huge amount of platelets & leucocytes.
- **PRF** clot is squeezed between two gauge pieces, the fluid squeezed out is known as **Platelet Rich Fibrin Releasate.**
- **Platelet Rich Fibrin Releasate:** The serum exudate rich in vitronectin and fibronectin is expressed from the PRF clot.
- **PRF membrane** is ready to use and **PRF releasate** may be used to hydrate graft materials, rinse the surgical site & store autologous graft.

III. **Advances of PRF:** Evolution of PRF wholly and solely depends on the Low- speed centrifugation concepts for the invention of solid and injectable forms of PRF as followed in Table 4.

Table 4: Advances of PRF and their preparations

PRF ADVANCEMENTS	VOLUME OF BLOOD SAMPLE	REVOLUTION PER MINUTE (rpm)	TIME	TUBES
Concentrated Growth Factor (CGF)	9 mL		30 sec acceleration	Vacuette tubes
		2700 rpm 2400 rpm 2700 rpm 3000 rpm	2 mins 4 mins 4 mins 3 mins 36 sec deceleration	

Titanium- Platelet Rich fibrin (T-PRF)	9 mL	2800 rpm	12 mins	Grade IV Titanium Tubes
Advanced Platelet Rich Fibrin (A-PRF)	9 mL	1500 rpm	14 mins	Plain sterile glass tubes
Advanced Platelet Rich Fibrin + (A-PRF+)	9 mL	1300 rpm	8 mins	Plain sterile glass tubes
Injectable Platelet Rich Fibrin (I-PRF)	9 mL	700 rpm	3 mins	Plastic tubes

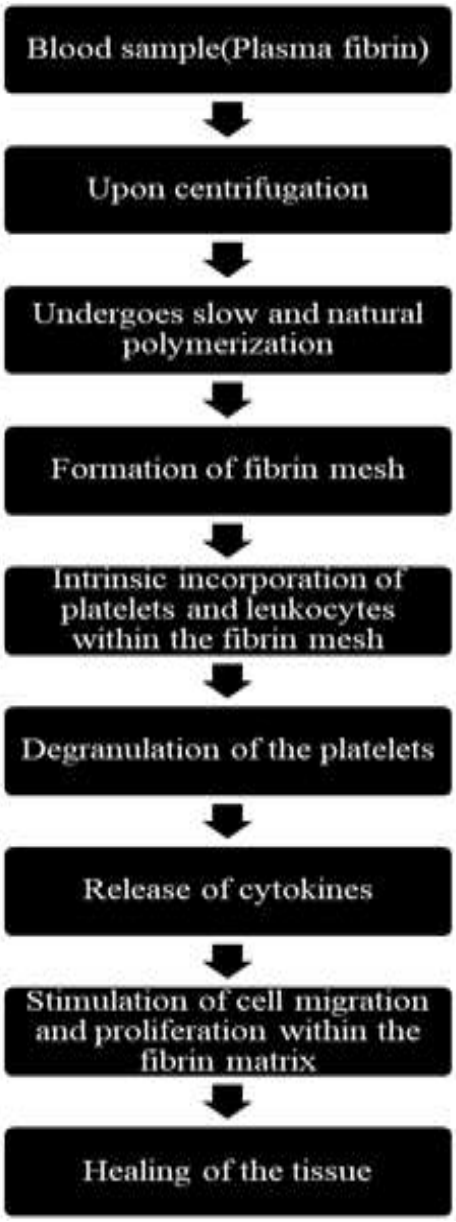


FIGURE 3: Platelet concentrates accelerates wound healing

Application of Platelet Concentrates

1. **Physiological Wound Healing and Growth Factors released by Platelet Concentrates (36)** Platelet concentrates secretes abundant growth factors (Growth factors) like Transforming growth factor-β (TGF-β), Platelet derived growth factor (PDGF), Epidermal growth factor (EGF), Insulin like growth factor (IGF), Vascular endothelial growth factor (VEGF) etc that act similarly as normal platelets in physiological wound healing (Figure 3).

   Kobayashi et al. 2016 (37) reported three findings related to Growth factors released from all PCs.

   Firstly, PDGF-αα was found released from all PCs at 6-10 folds higher concentration than PDGF-αβ & PDGF-ββ.

   Secondly, A-PRF^{+} showed 3 times higher release of growth factors than L-PRF.

   Thirdly, For fast delivery (within 8hrs) of Growth factors PRP can be used and for long- term delivery (upto 10 days) of Growth factors A-PRF can be used.

   Chatterjee A et al. 2019 (38) did in-vivo study, evaluation and comparison of various Growth factors released from PRFM (platelet rich fibrin matrix) & PRF. They concluded that for rapid and early healing and regeneration, both the PCs can be utilized in periodontal therapy.

   Gummaluri et al. 2020 (39) stated that T-PRF and L-PRF both ameliorates the clinical variables, thus convenient for soft tissue healing.

   Thus, it can be said that PCs can be used as an alternative to commercially available Growth factors as they are very expensive.

2. **Guided Tissue Regeneration/Guided Bone Regeneration Procedures:**

   Work of preceding years and current understanding of growth factors on bone and tissue regeneration approves PCs as barrier membranes and additional healing scaffold, with a resorption time of 10-14 days. PRP with Growth factors in a sustained manner is important for periodontal tissue engineering.(40) Various studies report that the affinity of PRF membrane appears to be superior than PRP.

   Chang et al. 2009 (41) reported that PRF stimulates proliferation of osteoblasts, periodontal ligament cells and Growth factors during 3-day culture period. Specific cell-type actions may be beneficial for periodontal regeneration.

   PRF membrane can be cut into small fragments, mixed with bone grafting materials. It improves handling and regenerative properties of PCs.

   Marx et al. 1998 (13) put forward a "Bone Graft Regeneration Model" for bone regeneration in cancellous cellular marrow defects. This model explained that PDGF, TGF-β and PRP induces exacerbated portion of growth factors that enchances the rate and quantity of bone formation.

   Lei et al. 2018 (42) used I-PRF & A-PRF mixed with Bio-Oss to make a steak graft membrane in chronic periodontitis patient. They concluded that PRF has mild potential to boost new bone formation and must be used in combination with bone grafting materials. GBR alone with PRF is not sufficient.

   Alb-PRF membrane may provide autologous flexible and stable biomaterials for soft tissue barrier. But, there is lack of research on its use as a GTR membrane.(23)

3. **Furcation Defects**: Grade I and II furcation defects seem to have benefical therapeutic outcomes from use of PC's.

   Sharma A et al. 2011 (43) in randomized controlled clinical trials, literature review stated that significant probing depth reduction (PDR), radiographic bone fill and clinical attachment (CAL) gain was reported in grade I and II furcation defects (66.7%) treated with L-PRF.

   Qiao et al. 2017 (44) in their comparative study with CGF in grade II furcation defects reported positive outcomes.

4. **Infrabony Defects (IDs):** Intrabony defects are a common and challenging sequel of periodontal disease. Platelets are not osteoinductive as it does not contain Bone morphogenic proteins (BMP).(45) However, when used with bone substitutes, PC's indirectly stimulates the adult mesenchymal stem cells lineage, leading to osteoblasts, that enchances bone formation as shown in figure 4.(46,47)

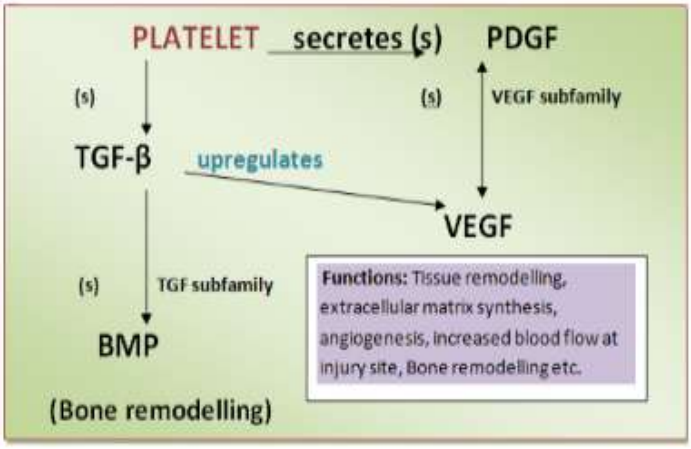


FIGURE 4: Growth factors of Platelets and their Functions.

PRP vivifies osteogenesis in such a manner that bone activation and formation is greater than resorption by releasing Growth factors. Use of PRP with bone grafts turns up bone formation by 1.62-2.18 times, also boost up 15-30% trabecular bone density.(48)

Liu K et al. 2012 (49) used bovine porous bone mineral (BPBM) with PRF in intrabony defects, showed significant clinical improvement in periodontal intrabony defects, which used combination threapy (BPBM+PRF) than using BPBM alone.

Thanasrisuebwong et al. 2019 (50) investigated biochemical properties of fractioned I-PRF Red and Yellow. They concluded that Red I-PRF had better biological properties and Yellow I-PRF had greater viscoelastic properties. Hence, suitable I-PRF fraction can be used for different types of periodontal regenerative therapies.

T-PRF could promote periodontal osseous defect healing via upregulated phosphorylated extracellular signal-regulated protein kinase expression and suppress osteoclastogenesis by promoting the secretion of osteoprotegerin in osteoblast cultures. (51)

5. **Recession Coverage:** Miller's class I and II recession defects have shown better clinical outcomes when treated with PCs.

Padma et al. 2017 reported that addition of PRF to coronally advanced flap (CAF) improved the clinical parameters after six months with 100% root coverage achieved than controls (64.88%).

Fibrin Assisted Soft Tissue Promotion (FASTP) follows the concept of "biotensegrity and back packing". A minimum of 3-4 PRF membranes per pair of teeth are recommended for recession coverage.

Turer et al. 2020 stated that gingival recession decreased when I-PRF was used with CAF.

PCs can be used as **palatal bandage** when graft is procured from the palate.

6. **Use of PCs in Periodontally Accelerated Osteogenic Orthodontics (PAOO):**

PAOO is a part of surgical orthodontics introduced by Wilcko in 2008. Most studies on PAOO are related to PRF only, as benefits of PRF over PRP were well known that time.

Munoz et al. 2016 in modified Wilcko's PAOO method, in which L-PRF was used. They concluded that combining L-PRF stimulates the wound healing, decreases postoperative pain & infection, increases patient acceptability.

7. **Gingival Thickness:** Thin biotype of the gingiva causes gingival and periodontal problems. PCs stimulates blood supply of the periosteum and improves blood supply to keratinized soft tissue favoring its thickness.

Miron et al. 2017 noticed that I-PRF showed higher cell migration, whereas PRP had cell proliferation.

Ozsagir et al. 2020 found that I-PRF and I-PRF + microneedling can boost up gingival thickness without any surgical intervention**.**

8. **Dressing Material for Oral Mucosal Lesions:** Potential of PCs to overhaul hard and soft tissues is illimitable. PCs can be used as membrane dressing material, when exicisonal or incisional biopsies are done in oral mucosal lesions like oral lichen planus, leukoplakia etc.

Mohanty et al. 2014 & Pathak et al. 2015 revealed that PCs adds up to oral mucosal lesion's improved healing, haemostasis and strength of the defect.

Tunali et al. 2018 found that I-PRF injection worked similar to corticosteroid injection in the treatment of erosive oral lichen planus.

9. **Antimicrobial Material:** Various studies have revealed the antimicrobial efficacy of PCs. PRP has shown antibacterial property for periodontal pathogens. Newer generations of PRF like CGF has CD34+ stem cells, A-PRF has monocytes, I-PRF has highest

concentration of leukocytes and platelets that adds to the antimicrobial aspects of PCs.

Kaur et al. 2018 reported that PRP and I-PRF are more active against P.gingivalis and A.actinomycetemcomitans strains than PRF.

10. **Adjunctive role of Platelet Concentrates in Oral Implantology:** Implants coated with PRP before placement into the alveolus had better osseointegration with earlier implant loading in normal and compromised bone.

a. PRF has been used at osteotomy site and beneath the mucoperiosteal flap raised for implant insertion to improve soft tissue healing and peri-implant defects.

b. PRF has been used in sinus lift augmentation grafting, alveolar ridge preservation, horizontal and vertical ridge augmentation**.**

c. GLAM (Guided Bone Regeneration with L-PRF in the Atrophic Maxilla) technique (2017) is used to place implant simultaneously with regeneration procedure. (52)

d. **DV-PIMS** (Deepak Vikhe-Pravara Institute of Medical Sciences) technique (2019) in this newer implant design is aimed to disperse an I-PRF solution from inside out in the osteotomy site after implant placement. (53)

Merits of PRF: (54)

1. Easy to prepare and use.
2. No biochemical modification.
3. Cost effective process.
4. Long term effect.
5. Supports cytokines enmeshment and cellular migration.
6. Amplified incorporation of the circulating intrinsic cytokines in the fibrin meshes.
7. An immune organizing node.
8. Due to slow polymerization, supports and accelerates the healing process.
9. Helps in hemostasis.
10. Elasticity and flexibility due to three dimensional structure of PRF membrane.

Demerits of PRF:

1. Less amount of PRF is obtained, because of autologous blood.
2. The clinical advantage of PRF depends on time gap in speed of handling between blood collection and centrifugation as PRF is prepared without addition of any anticoagulant.(55)
3. The fibrin matrix contains all the highly antigenic plasmatic molecules and the circulating immune cells that is why PRF is totally specific to the donor.
4. 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.(56)
5. Risk of bacterial contamination when stored in refrigerator.

Conclusion:

The world of PCs for surgical use is actually a jungle of commercial proposals and their unclear products, but till date no accurate classifying system has developed. Limited evidence and heterogeneity among different centrifugation speeds, angulations, duration and hematocrit count, limits the quality and quantity of PCs. However, since knowledge on this topic is still in its infancy, the effectiveness of these platelet concentrates in regenerative procedures should be evaluated in large samples.

References:

1. Goel A, Windor LJ and Blanchard S. Platelet-Rich Fibrin: Utilization in the Treatment of Periodontitis. In: Manakil J, editor. Periodontology and Dental Implantology. London: Intech Open; 2019.p.1-14.
2. Lozada JL, Caplanis N, Proussaefs P, Willardsen J, Kammeyer G. Platelet-rich plasma application in sinus graft surgery: Part-I background and processing techniques. J Oral Implantol 2001;27(1):38-42.
3. Pourmokhtar M, Salek ME, Abbasi F, Zarei N. Comparative study of four platelet-rich plasma methods for preparing platelet concentrates. Iran J Blood Cancer 2014;6(3):103-7.

4. Mehta S and Watson JT. Platelet rich concentrate: Basic science and current clinical applications. J Orthop Trauma 2008;22:433-38.
5. Harrison P, Cramer EM. Platelet alpha-granules. Blood Rev 1993;7:52-62.
6. Kingsley CS. Blood coagulation: Evidence of an antagonist to factor VI in platelet-rich human plasma. Nature 1954;173(4407):723-24.
7. Matras H. Effect of various fibrin preparations on reimplantations in the rat skin. Osterr Z Stomatol 1970;67(9):338-59.
8. Rosenthal AR, Egbert PR, Harbury C, Hopkins JL, Rubenstein E. Use of platelet-fibrinogen-thrombin mixture to seal experimental penetrating corneal wounds. Albrecht Von Graefes Arch Klin Exp Ophthalmol 1978;207(2):111-5.
9. Agrawal AA. Evolution, current status and advances in application of platelet concentrate in periodontics and implantology. World J Clin Cases 2017;5(5):159-71.
10. Knighton DR, Ciresi KF, Fiegel VD, Austin LL, Butler EL. Classification and treatment of chronic nonhealing wounds. Successful treatment with autologous platelet-derived wound healing factors (PDWHF). Ann Surg 1986;204(3):322-30.
11. Knighton DR, Doucette M, Fiegel VD, Ciresi K, Butler E, Austin L. The use of platelet derived wound healing formula in human clinical trials. Prog Clin Biol Res 1988;266: 319-29.
12. Whitman DH, Berry LR, Green DM. Platelet Gel: An autologous alternative to fibrin glue with applications in oral and maxillofacial surgery. J Oral Maxillofac Surg 1997;55(11):1294-9.
13. Marx RE, Carlson ER, Eichstaedt RM, Schimonele SR, Strauss JE, Georgeff KR et al. Platelet-rich plasma: Growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;85(6):638-46.
14. Ehrenfest DMD, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). Trends Biotechnol 2009;27(3):158-67.
15. Choukroun J, Adda F, Schoeffler C, Vervelle A. PRF: An opportunity in perio Implantology. Implantodontie 2000;42:55-62.
16. Sacco L. Lecture, International academy of implant prosthesis and osteoconnection. Lecture 2006;12:4.
17. Everts PA, Van ZA, Schönberger JP, Devilee RJ, Knape JT. What do we use: platelet rich plasma or platelet-leukocyte gel?. J Biomed Mater Res A 2008;85(4):35-1135-6.
18. Sohn DS. Lecture titled with sinus and ridge augmentation with CGF and AFG. Symposium on CGF and AFG Tokyo 2010.
19. Tunali M, Ozdemir H, Kucukodaci Z, Akman S, Firatli E. In vivo evaluation of titanium-prepared platelet-rich fibrin (T-PRF): A new platelet concentrate. Br J Oral Maxillofac Surg 2013;51(5):438-43.
20. Ghanaati S, Booms P, Orlowska A, Kubesch J, Lorenz J, Rutkowski J et al. Advance platelet-rich fibrin: A new concept for cell-based tissue engineering by means of inflammatory cells. J Oral Implantol 2014;40(6):679-89.
21. Kobayashi E, Fluckiger L, Fujioka-Kobayashi M, Sawada K, Sculean A, Schaller B et al. Comparative release of growth factors from PRP, PRF and advanced-PRF. Clin Oral Investig 2016;20(9):2353-60.
22. Mourao CF, Valiense H, Melo ER, Mourao NB, Maia MD. Obtention of injectable platelets rich-fibrin (I-PRF) and its polymerization with bone graft: technical note. Rev Col Bras Cir 2015;42(6):421-3.
23. Mourao CF, Gheno E, Lourenco ES, Barbosa RD, Kurtzman GM, Javid K et al. Characterization of a new membrane from concentrated growth factors associated with denaturized albumin (Alb-CGF) for clinical applications: A preliminary study. Int J Growth Factors Stem Cells Dent 2018;1:64-9.
24. Miron RJ, Chai J, Zheng S, Feng M, Sculean A, Zhang Y. A novel method for evaluating and quantifying cell types in platelet rich fibrin and an introduction to horizontal centrifugation. J Biomed Mater Res Part A. 2019;107(10):2257-71.

25. Mourao CF, Javid K. New and improved platelet-rich fibrin membranes. Int J Growth Factors Stem Cells Dent 2020;3:1-2.
26. Ehrenfest DMD, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). Trends Biotechnol 2009;27(3):158-67.
27. Mishra A, Harmon K, Woodall J, Vieira A. Sports medicine applications of platelet rich plasma. Curr Pharm Biotechnol 2012;13(7):1185-95.
28. Delong JM, Russell RP, Mazzocca AD. Platelet-rich plasma: The PAW classification system. Arthroscopy 2012;28(7):998-1009.
29. Ehrenfest DMD, Sammartino G, Shibli JA, Wang HL, Zou DR, Bernard JP. Guidelines for the publication of articles related to platelet concentrates (Platelet-Rich Plasma - PRP, or Platelet-Rich Fibrin - PRF): The international classification of the POSEIDO. POSEIDO 2013;1(1):17-27.
30. Mautner K, Malanga GA, Smith J, Shiple B, Ibrahim V, Sampson S et al. A call for a standard classification system for future biologic research: The rationale for new PRP nomenclature. AAPMR 2015;7(1):53-9.
31. Magalon J, Chateau AL, Bertrand B, Louis ML, Silvestre A, Giraudo L et al. DEPA classification: A proposal for standardizing PRP use and a retrospective application of available devices. BMJ Open Sport Exerc Med 2016;2(1):1-5.
32. Marx RE. Platelet-rich plasma (PRP): What is PRP and what is not PRP?. Implant Dent 2001;10(4):225-8.
33. Mathai J. Problem of bacterial contamination in platelet concentrates. Transfus Apher Sci 2009;41(2):139–44.
34. Blajchman MA. The clinical benefits of the leukoreduction of blood products. J Trauma 2006;60(6):83–90.
35. Ehrenfest DMD, Choukroun JI, Diss A, Dohan SL, Dohan AJJ, Mouhyi J et al. Platelet-rich fibrin (PRF): A second generation platelet concentrate. Part I: Technological concepts and evolution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101(7):37–44.
36. Prakash S and Thakur A. Platelet concentrates: past, present and future. J Maxillofac Oral Surg 2011;10(1):45-9.
37. Fujioka KM, Miron RJ, Hernandez M, Kandalam U, Zhang Y, Choukroun J. Optimized platelet rich fibrin with the low speed concept: Growth factor release, biocompatibility and cellular response. J Periodontol 2017;88(1):112–21.
38. Chatterjee A, Debnath K. Comparative evaluation of growth factors from platelet concentrates: An in vitro study. J Indian Soc Periodontol 2019;23(4):322-8.
39. Gummaluri SS, Bhattacharya HS, Astekar M, Cheruvu S. Evaluation of titanium-prepared platelet-rich fibrin and leucocyte platelet-rich fibrin in the treatment of intra-bony defects: A randomized clinical trial. J Dent Res Dent Clin Dent Prospects 2020;14(2):1-9.
40. Greenwell H. Committee on research, science and therapy, American Acad of Periodontol. Position paper: Guidelines for periodontal therapy. J Periodontol 2001; 72(11):1624–8.
41. Chang IC, Tsai CH, Chang YC. Platelet-rich fibrin modulates the expression of extracellular signal-regulated protein kinase and osteoprotegerin in human osteoblasts. J Biomed Mater Res A 2010;95(1):327–32.
42. Lei L, Yu Y, Ke T, Sun W, Chen L. The application of three-dimensional printing model and platelet-rich fibrin (PRF) technology in guided tissue regeneration surgery for severe bone defects. J Oral Implant 2018;45(1):1-27.
43. Sharma A and Pradeep AR. Autologous platelet-rich fibrin in the treatment of mandibular degree II furcation defects: A randomized clinical trial. J Periodontol 2011;82(10):1396-03.
44. Qiao J, Duan J, Zhang Y, Chu Y, Sun C. The effect of concentrated growth factors in the treatment of periodontal intrabony defects. Futur Sci OA 2016; 2(4):136-38.
45. Lang NP. Focus on intrabony defects-conservative therapy. Periodontol 2000 2000;22(4):51-8.
46. Nurden AT. Platelets, inflammation and tissue regeneration. J Thromb Haemost 2011;105(Suppl1):13–33.

47. Fujioka KM, Miron RJ, Hernandez M, Kandalam U, Zhang Y, Choukroun J. Optimized platelet rich fibrin with the low speed concept: Growth factor release, biocompatibility and cellular response. J Periodontol 2017;88(1):112–21.
48. Anila S and Nandakumar K. Applications of platelet rich plasma for regenerative therapy in periodontics. Trends Biomater Artif Organs 2006;20(1): 78-83.
49. Liu K, Huang Z, Chen Z, Han B, Ouyang X. Treatment of periodontal intrabony defects using bovine porous bone mineral and guided tissue regeneration with/without PRF (Platelet Rich Fibrin) in intrabony defects. J Periodontol 2021;92(11):1546-53.
50. Thanasrisuebwong P, Surarit R, Bencharit S, Ruangsawasdi N. Influence of fractionation methods on physical and biological properties of injectable platelet-rich fibrin: An exploratory study. Int J Mol Sci 2019;20(7):1657.
51. Reddy S, Bhowmik N, Valerian V, Cutinha D, Yadav N, Pandit HR et al. Treatment of intrabony defects using T-PRF: A case report. Int J Appl Dent Sci 2018;41(1):77-83.
52. Carames J, Marques D, Lopes M, Gouveia R, Carames G. Guided bone regeneration with L-PRF in the Atrophic Maxilla – The GLAM technique – A prospective case series study-Preliminary results. Clin Oral Implant Res 2017;28 (Suppl.14):10-15.
53. Vikhe DM, Shah SV, Carrion JB, Palekar UG. Innovative method "DV-PIMS" technique and dental implant design for grafting injectable platelet-rich fibrin around the dental implant – Goat jaw cadaver study. Indian J Dent Res 2019;30(3):450-4.
54. Vinaya R, Shubhashini N. Platelet rich fibrin: A new paradigm in periodontal regeneration. Cell Tissue Bank 2013;14(3):453-63.
55. Patel J, Deshpande N, Shah M, Dave D, Shah C, Shah S. PRF-from self to self. Res Rev J Dent Sci 2013;2(2):30-4.
56. Marx RE. Platelet-rich plasma: Evidence to support its use. Oral Maxillofac Surg 2004;62:489-96.

How to cite this article: Rani, M., Singh, B., Nanda, T., Ohri, T., Aggarwal, K., Bhasker, A., & Kaur, A. (2022). Never-ending Journey of Platelet Concentrates. Journal of Current Medical Research and Opinion, 5(04), 1163-1174. https://doi.org/10.52845/CMRO/2022/5-4-1