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Review Article

The Journey of Platelet Concentrates: An Era of Regeneration in Medicine and Dentistry: A Review

Nimmi Janardhanan[1], Sayana Nazrine[1] and Shivaprasad BM[2]*

[1]Postgraduate Student, Department of Periodontology, Rajarajeswari Dental College and Hospital, Bangalore, India

[2]a. Implantologist, Tooth Priority: The Family Dental Care, Bangalore and b. Professor, Department of Periodontology, Rajarajeswari Dental College and Hospital, Bangalore, India

***Corresponding Author:** Shivaprasad BM, a. Implantologist, Tooth Priority: The Family Dental Care, Bangalore and b. Professor, Department of Periodontology, Rajarajeswari Dental College and Hospital, Bangalore, India.

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Abstract

Platelets are small cells that circulate in blood playing an important role in managing hemostasis and vascular integrity. They are also known to release several growth factors which stimulate tissue regeneration. The ability of platelet concentrates (PC) to achieve the goals of tissue regeneration has been explored in sports medicine, orthopedics and maxillofacial surgeries. The use of PC in the treatment of periodontal or bone defects is a much more natural approach compared to other modalities such as guided tissue and bone regeneration. Currently platelet concentrates are utilized in various regenerative and rehabilitative surgeries such as perio-plastic surgeries, ridge preservation and implant surgeries. Platelet concentrates have the ability to harness body's own growth factors and utilize it for regeneration. It is a trialed and proven fact that they can dramatically increase the treatment results in a beneficial manner.

Keywords: Platelet Concentrates; Regeneration; Dentistry; Medicine

Introduction

Human body consists of about 30 trillion cells and they work in a coordinated manner every single day, every single minute and every single second for maintaining homeostasis. When an injury occurs to living tissues by a cut, blow or other impacts a cascade of steps get initiated.

Wound healing is a complex and intricate process which begins by clot formation, followed by a proliferative stage which consists of epithelialization, angiogenesis, granulation tissue formation, collagen deposition and ultimately collagen maturation and contraction. This involves adherence and aggregation of platelets, which helps in the formation of thrombin and fibrin. The healing of hard and soft tissue is a fascinating process that are moderated by various intra and extracellular events and signalling proteins play a major role in regulating them. Understanding the entire process of wound healing is still unfinished. Yet, it is known that platelets play an important role not only in haemostasis, but also in the wound healing process [1].

Various researches done on periodontal wound healing over the years aided us in understanding the basic mechanisms favouring periodontal tissue regeneration. Diverse studies were conducted at both cellular and molecular levels and the valuable findings from these studies were later used in the engineering of the regenerative biomaterials that have helped periodontal medicine reach new heights.

Platelets are well known for their role in releasing various growth factors which affects tissue regeneration. They usually ex-

ist as inactive or partially active precursors which require a proteolytic activation. Sometimes they may require further binding to matrix molecules for its equilibration.

Numerous techniques for platelet concentrates have been established in surgical field for the avoidance of haemorrhage and spurring of tissue regeneration and they have helped us in treating periodontal diseases in a much more profound manner [2].

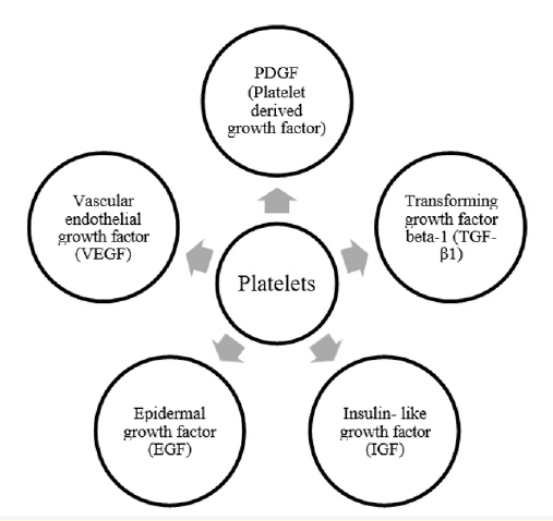


Figure 1: Growth factors released by platelets [3].

The utilisation of platelet concentrates and their ability to form a natural three-dimensional scaffold has been explored not only in oral and maxillofacial and periodontal surgeries but also in sports medicine and orthopaedics. In fact, platelet concentrates are even utilised for treating androgenetic alopecia. In the future we are sure to see the application of platelet concentrates in different sectors of medicine [3,4].

Evolution of platelet concentrates

1954

Dr.C.S Kingsley first used the term PRP after conducting various experiments on blood coagulation [5].

1970

Surgical additives containing fibrin sealants were commercially introduced in Europe. "Fibrin glue", a product made of polymerizing fibrinogen with thrombin and calcium was introduced by Matras which enhanced healing of skin wounds in rat models [6].

1971-1978

The concept of "platelet-fibrinogen-thrombin mixture" was introduced after conducting numerous researches on blood extracts.

1979

"Gelatin platelet - gel foam" was introduced. This new suggestion came after various studies proved the performance of platelets, and exhibited excellent preliminary results in general surgery, neurosurgery and ophthalmology. These studies mainly focused on its "gluey effect", rather than its effects on growth factors or their healing properties.

1986

Knighton et al successfully demonstrated that PC contains "platelet-derived wound healing factors (PDWHF)": favourable for the treatment of skin ulcers [7].

1997

Whitman et al introduced "platelet gel" which had a similar consistency of fibrin gel [8].

1999

Preparations of PC were marketed commercially in Europe as plasma rich in growth factors (PRGF) also known as preparation rich in growth factors and Vivostat PRF.

2006

Cieslik-Bielecka et al and Bielecki et al [9] proposed that PRP was an inactive substance, while PRG (Platelet Rich Gel) was more active, consisting of a fibrin matrix which is rich in leukocytes, platelets and relative active molecule. Also, the concept of CGF was introduced by Sacco [10].

2008

Everts et al focused on the activated and inactivated leukocyte component of the platelet concentrate. The inactivated substance was called "platelet-leukocyte rich plasma" (P-LRP) on the other hand the activated gel was called "platelet-leukocyte-gel" (PLG) [11].

2009

Dohan Ehrenfest et al proposed the first classification for platelet concentrates [12].

2010

Dong-Seok Sohn introduced the concept of sticky bone (autologous fibrin glue mixed with bone graft) [2].

2012

Mishra et al came up with another classification which was limited to PRP and applicable to sports medicine only. DeLong et al also came up with another classification system called PAW (Platelet's quantity, Activation mode, White cells presence) [13].

2014

Choukroun introduced A-PRF (claimed to contain more monocytes) while Tunalı et al introduced T-PRF (Titanium prepared PRF) [14].

2015

Mourão et al gave a detailed description on preparation and usage of i-PRF [15].

Classification

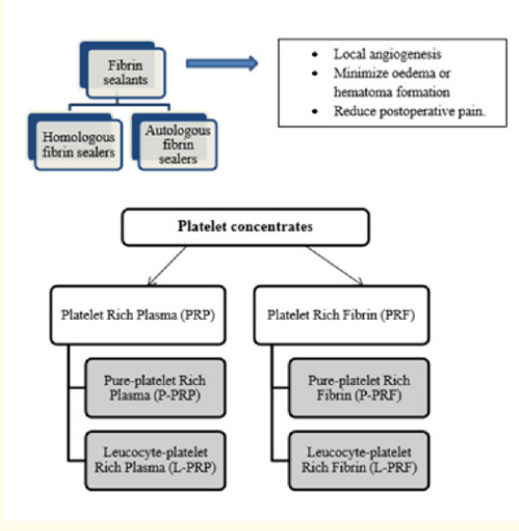


Figure 2: Classification of Platelet Concentrates.

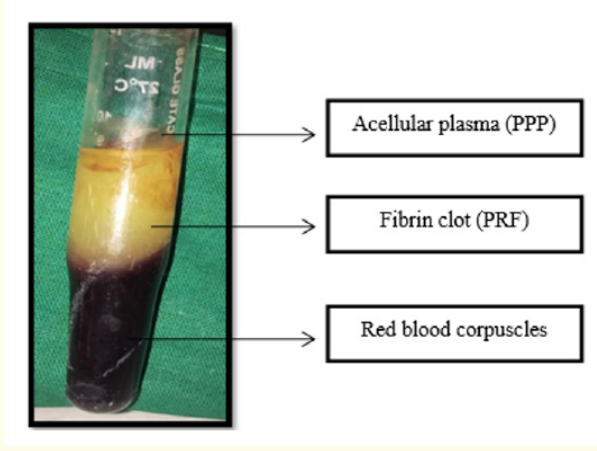
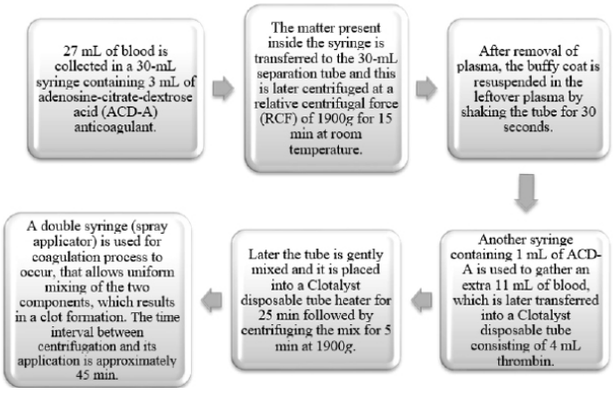


Figure 3: Layers formed after centrifugation.

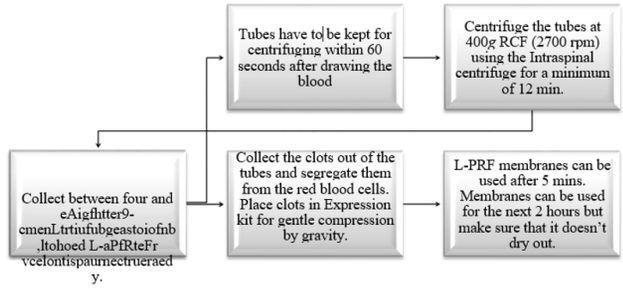
Platelet concentrate	PRP	PRGF	L-PRF	A-PRF
Generation	1	1	2	2
Anticoagulants use	CPDA	Sodium citrate	No	No
Protocol (rpm/min) (Centrifuge tube)	900/5 +1500/15 (Plastic tubes)	1850/8 (Plastic tubes)	2700/12 (Glass tubes)	1500/14 (Glass tubes)
Fibrin membrane	-	Yes	Yes	Yes
Leukocytes	Non determined	0%	50-65%	50-65% (increase in neutrophils)
Growth factors	Small amount	Medium amount	Very good amount	Excellent amount
Bone regeneration	Small	Medium	Good	Good
Presentation form	Gel	Liquid Clot Supernatant Fibrin membrane	Plugs (for alveolar filling) Exudate Fibrin membrane	Plugs (for alveolar filling) Exudate Fibrin membrane

Table 1: Properties of different Platelet Concentrates [16].

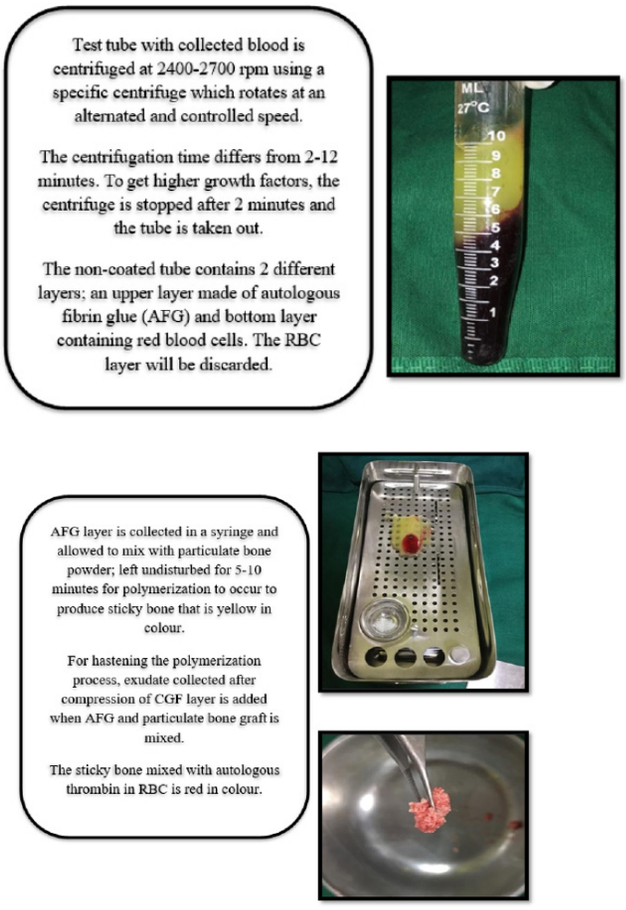
Box 1: Preparation of PRP [4].



Box 2: Preparation of PRF [4]



Box 3: Preparation of sticky bone [2].



Concentrated Growth Factor (CGF): The Newest Platelet Concentrate

In 2006, Sacco described the newest platelet concentrate-CGF, which is produced in a manner similar to PRF, but different centrifuge speed. CGF contains a richer and denser GF-fibrin matrix with 3D fibrin network where growth factors are closely bound to one another, as compared to PRF. This promotes the slow release of growth factors, which aids in wound healing. As described by Bozkurt et al., IV blood collected in two 10 mL glass-coated plastic tubes without anticoagulant. The tubes are immediately centrifuged: 30" acceleration, 2' 2700 rpm, 4' 2400 rpm, 4' 2700 rpm, 3' 3000 rpm and 36" deceleration until end. Four layers are obtained from bottom to top: RBC layer, GF and stem cell layer (CGF), Buffy coat, serum layer (PPP). CGF layer can be separated using sterile surgical scissors; the clot is then squeezed at a thickness of 1 mm and used for the procedure [17,18].

Current applications of PRF in dentistry [19]

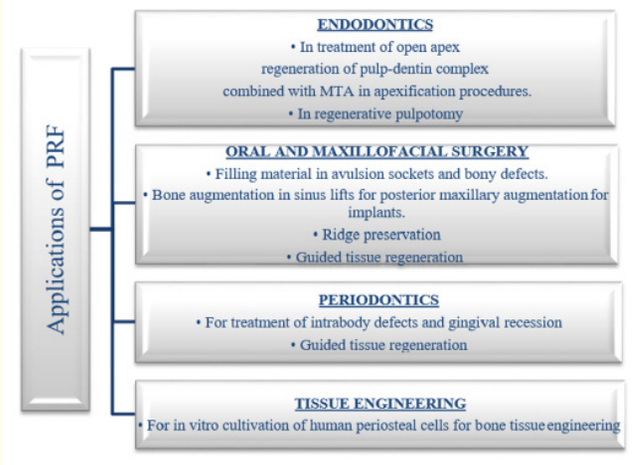


Figure 4: Applications of platelet concentrates.

Clinical implications and periodontal considerations

PRF in periodontal intrabony defects

The use of PRF in the treatment of periodontal or bone defects is a much more natural approach compared to guided tissue and bone regeneration. The defect is filled with PRF (along with a biomaterial to avoid collapse) and later it is sealed with PRF membranes. These membranes provide protection and acts as a competitive barrier [2]. The cells from the periodontal ligament and periosteum are given time to regenerate into cementum, bone and ligament by warding off epithelial and connective tissue cells from the crater site. This also results in much faster neo-angiogenesis.

Pradeep AR conducted a study to comprehend the clinical and radiographic changes after using autologous PRF versus PRF + Hy-

droxyapatite in treatment of intrabony defects (IDB) in patients with chronic periodontitis. He found out that treatment of IBD with PRF results in significant improvements of clinical parameters compared to baseline [20].

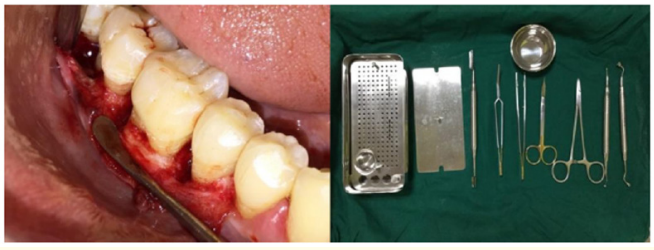


Figure 5: a) Intrabony Defect after flap reflection.

Figure 5: b) PRF after Centrifugation and c) PRF membrane.

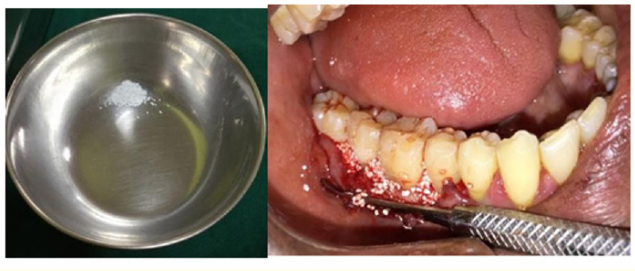


Figure 5: d) Bone graft placed in the intrabony defect.

Figure 5: e) PRF membrane placed and sutured.

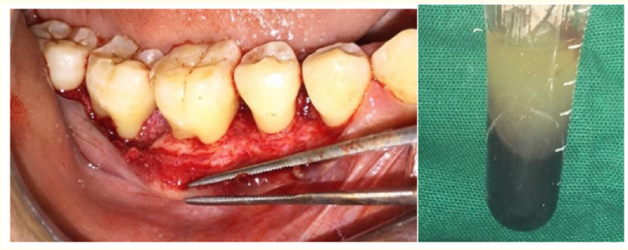


Figure 6: a) Intrabony defect after flap reflection and debridement b) PRF obtained after centrifugation.

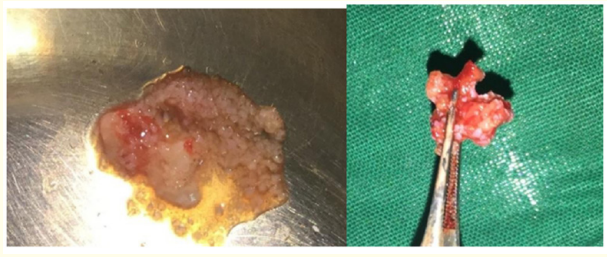


Figure 6: c) Sticky bone prepared using bone graft and PRF.

Figure 6: d) Sticky bone placed and sutured e) Preoperative and post-operative radiograph.

PRF for Ridge Preservation

Studies have shown that bone loss can occur very quickly after extraction, often in as little time as 6 weeks. So, it is important to preserve these socket sites for further replacement therapies. The use of L-PRF is an affordable, simple and much more efficient treatment method [4] A study conducted by Hauser et al found out that L-PRF application resulted in better preservation of the width of the alveolar ridge as well as maintaining better bone quality [21].

A systematic review by Jiayu Pan et al assessed the potential of PRF to preserve the alveolar ridge. They evaluated postoperative

pain, soft-tissue healing, bone density, horizontal and vertical ridge dimension changes, and histologic analysis. Promising results were found in reducing postoperative pain and ridge dimension changes after tooth extraction. This proposes that consideration should be given to PRF treatment after extraction in a mainstream manner.

PRF for Periodontal Mucogingival Surgery

Due to its ability to form a strong three-dimensional fibrin network, PRF is helpful in mucogingival surgeries. The possibility of using it not only as a membrane but also a soft tissue graft is a promising leap when it comes to periodontal medicine.

Anil Kumar K in his case report used PRF membrane on the labial surfaces of the mandibular anterior teeth for root coverage; achieved using a laterally displaced flap technique along with platelet rich fibrin (PRF) membrane. The patients did not complain of any post-operative complications. Also, complete coverage was achieved six months later, with good tissue contour and colour.

PRF and Implant Surgery

Clearly dental implants are the present and future of restorative dentistry. Researches are conducted worldwide for increasing the stability and efficiency of implants and utilisation of platelet concentrates along with implantology is a tried and proven technique to improve its productivity. A study by Öncu and Alaaddinoglu concluded that implants coated with L-PRF placed in osteotomies treated with L-PRF showed a statistically higher Implant Stability Quotient value compared with the control group, especially up to 4 weeks of healing. Also, while L-PRF is used during one-stage implant placement, the amount of initial bone remodeling seems to reduce significantly.

Choi et al in 2006 conducted an animal study to compare the sinus lining perforation repair using either the (AFG) autologous fibrin glue or the collagen membrane. This study found that in sites where AFG was used, newly regenerated continuous epithelium was discovered across the original perforation site as compared to collagen membrane treated site and inflammatory infiltration along with extensive fibrosis was seen even after 2-week of healing.

Extraoral application of platelet concentrates

Diabetic Foot Ulcers

Numerous clinical studies have been published showing promising results after topical application PRP gel for the treatment of chronic or non-healing wounds. Various studies focused on diabetic patients since they often face challenges in terms of healing. The results have been encouraging and could be used in general mass.

Tendon Remodeling

Platelet concentrates are used in various orthopaedic surgeries with favourable results. A prospective cohort study carried on human athletes having sutured Achilles tendons treated with and without PRP were compared. The group treated with PRP showed general improvement in different parameters like greater range of motion, earlier recovery, improved functional recovery, earlier time to gentle exercise and earlier time to training Also, ultrasound exams conducted between 32 and 50 months showed that the treatment group gained adequate tendon remodeling compared to smaller increase in cross- sectional area in the non-treatment group.

Alopecia

Androgenetic alopecia is a condition that causes hair follicles to shrink and more than one million cases are reported every year in India alone. PRP injections has become a new method for the treatment of alopecia. A case reported by Ritika Arora et al, utilised injectable-PRF (i-PRF) which is an advanced version of liquid, injectable PRF. It contains stem cells with high regenerative potential in alopecia. Hair regeneration was seen even in Type VI and Type VII which are difficult to treat which proves that hair growth with i-PRF has good regenerative potential.

Osteoarthritis

The use of PRP in the treatment of degenerative knee OA is a recent advancement in medical science. It is popular due to ease of synthesis, administration and high margin of safety. Studies have reported the enhanced effectiveness of PRP for treatment of pain and knee joint function when compared to HA or placebo and provided positive outcomes in all stages of knee OA (early, middle and late). In addition, the effects of PRP seemingly last longer and are superior in comparison with intramuscular injection therapies.

Limitations

- Amount of platelet concentrates obtained will be low since they are autologous blood.
- Difficulty in collection and handling of blood samples and transference to centrifuge.
- Requirement of a glass coated tube to achieve clot polymerisation.
- PRF tissue banks are unfeasible.
- Fibrin matrix contains circulating immune cells and highly antigenic plasmatic molecules demonstrating why PRF membranes are specific to donor and cannot be used as an allogenic graft tissue.

Conclusion

The benefits of using the first-generation platelet concentrates were very controversial; however, the second-generation platelet concentrate (L-PRF) seems to show more consistent and predictable results. The merits of using L-PRF are its autologous nature, simple collection, ease of chair-side preparation and clinical application without the risks associated with allogenic products. Therefore, it seems suitable to be used in either a specialized or general practice.

Platelet concentrates have the ability to harness body's own growth factors and utilise it for regeneration of periodontal tissues. It is a trialed and proven fact that they can dramatically increase the clinical outcomes in surgical periodontal therapy. As people of science, we must educate the patient about the perks of this method and employ it in our clinical practice.

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