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Review Article

Explicit role of platelet derived concentrates PRP and PRF in orthodontics - A detailed review

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ABSTRACT

There has been significant growth and advancement since, the last few decades in the use of platelet and its derivatives in dentistry predominantly in oral surgery and periodontology. Very little is known about the same in orthodontics. There is emerging literature on the use of platelets and its derivatives in orthodontics. Platelets being the reservoir of cytokines and growth factors plays a crucial role in various regenerative processes. This review attempts to summarise the literature concerning to the application and role of platelet derived concentrates in orthodontics. The most commonly used platelet derived concentrates being the platelet-rich plasma (PRP) and Platelet-rich fibrin (PRF), their advancement and various roles and future opportunities of research have been described in this article.

1. Introduction

In Oro-dental and maxillo-facial defects, Regenerative strategies is quite challenging because the oral cavity has distinct cell populations (ectodermal and mesodermal) which make up the tissues, this makes regenerative procedures more complex. Bone and soft tissue regeneration may be indicated for managing defects, such as congenital defects (cleft lip and palate), alveolar bone resorption, periodontal defects (recession coverage and furcation defects), cystic cavities, bone infection (osteomyelitis), and traumatic bone destruction. In the present scenario, the clinical approaches have several limitations, namely limited self-renewal capacity and/or limited donor supply, risk of immune response, operative time, and costs and donor site morbidity. As a consequence, new biomaterials have been developed to modulate inflammation and enhance the healing process.[1,2]

One of the new emerging approaches in orthodontics is tissue regeneration because a huge percentage of patients need both regeneration and orthodontic treatment. Orthodontic treatment can be performed on children, young adults, and adults. All of these patients may need regenerative approaches due to different indications (e.g., children with cleft lip and palate who need closure of alveolar cleft; older patients who need an orthodontic treatment due to bone defect as a result of tooth loss). Moreover, the application of mechanical force on the teeth affects the periodontal ligament and the alveolar bone, which allows orthodontic tooth movement (OTM). Thus, a change in support structures may interfere with orthodontic success. Therefore, the use of platelet derived concentrate i.e PRP/PRF can improve orthodontic treatment results, since it promotes a biological response involving a minimally invasive procedure.

2. Platelet Derived Concentrates

Platelet concentrates are products that have been derived from centrifugation of blood concentrating platelets,

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leukocytes and fibrin to a clinically useful form. The potency of the concentrate depends on the platelet concentrate, number and type of leukocyte in the fibrin membrane and successive release bioactive molecule from the site of clot triggering the regenerative process.

2.1. Types of platelet derived concentrates

According to the classification proposed by Ehrenfest et al. (2009), four main families of preparations can be defined, depending on their cell content and fibrin architecture.[3]

1. Pure Platelet-Rich Plasma (P-PRP) or leucocyte-poor PRP products are preparations without leucocytes and with a low-density fibrin network after activation.
2. Leucocyte- and PRP (L-PRP) products are preparations with leucocytes and with a low-density fibrin network after activation. It is in this family that the largest number of commercial or experimental systems exist. Particularly, many automated protocols have been developed in the last years, requiring the use of specific kits that allow minimum handling of the blood samples and maximum standardization of the preparations.
3. Pure platelet-rich fibrin (P-PRF) or leucocyte-poor platelet-rich fibrin preparations are without leucocytes and with a high-density fibrin network. These products only exist in strong activated gel form and cannot be injected or used like traditional fibrin glues.
4. Leucocyte and platelet-rich fibrin or second generation PRP products are preparations with leucocyte with a high-density fibrin network.[3]

Considering the bioactive properties of platelets in the healing process, they can be used as a valuable therapeutic adjunct in medicine and dentistry.[4] The autologous products derived from platelets are platelet rich plasma (First generation platelet concentrate) and platelet rich fibrin (Second generation platelet concentrate). They are both clinically effective in accelerating the healing process. They can be used in injectable form and fibrin.[5]

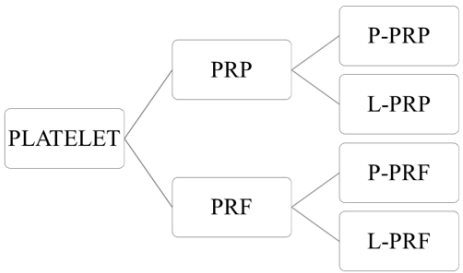

Fig. 1:

3. What is PRP?

PRP was introduced in dental literature, in 1998, by Robert Marx[1], as an adjunct in the mandibular reconstructive procedure, enhancing the radiographic maturation rate of the graft alone. Platelet-rich plasma (PRP) is an autologous concentration of human platelets in a small volume of plasma. It comprises of the concentration of platelets and the several fundamental growth factor which are actively secreted by platelets to initiate wound healing is approximately 1,000,000/μl compared to the normal range of 1,50,000/μl to 3,50,000/μl[2].

3.1. Composition of PRP[2]

PRP comprises of platelets which release the various growth factors as follows:

The following growth factors are released by high concentration of platelet:

1. Three isomers of platelet-derived GF (PDGFAaa, PDGFbb and PDGFab).
2. Transforming GFs-b (TGFb1 and TGFb2).
3. Vascular endothelial GF (VEGF).
4. Epidermal GF(EGF).

Fig. 2:

Small volume of plasma containing[6]

1. Cytokines, interleukins and tumour necrotic factor.
2. Cell adhesion factor-fibrin, fibronectin and vitronectin.
3. Proteases and anti-proteases.

3.2. How PRP works

Platelets are one of the initiators both in the soft and hard tissue wound healing processes.[7,8] Platelets contain growth factors such as the platelet-derived growth factor, transforming growth factor, endothelium growth factor, and

the others. These growth factors are critical in the regulation and stimulation of the wound healing process, and they play an important role in regulating cellular processes such as mitogenesis, chemotaxis, differentiation, and metabolism.[7] Peripheral blood contains 94% of red blood cells (RBCs), 6% of platelets, and < 1% of white blood cells (WBCs), while PRP contains 5% of RBCs, 1% of WBC, and 94% of platelets.[9]

3.3. The preparation of platelet rich plasma for orthodontic purpose[10]

Should be prepared under aseptic processing procedures

A volume of 60 ml of whole blood is drawn from the medial cubital vein of a patient using three 30 ml syringes that each contained 3 ml of 10% sodium citrate solution as an anticoagulant. Heparin is not recommended for using as the anticoagulant due to its systemic effects and inducing alveolar bone resorption. 1ml of the blood is used for checking the platelet counts.

The remaining 59 ml of whole blood is first centrifuged under 1000 rpm for 1-2 min at room temperature. The blood is then separated into its 3 basic components as the RBCs at the bottom, the buffy coat (platelets) in the middle, and the platelet poor plasma (PPP) at the top.

The RBCs is discarded, and the remaining buffy coat and PPP are collected and centrifuged again under 3000 rpm for 8 min. After the second centrifugation, the PPP is removed until 4 ml remained and then the remaining PPP is mixed with the buffy coat to become PRP. One ml of the PRP is analysed for its platelet count.

Under such a preparation, the PRP contains anticoagulant, high concentration of platelets, and a few of RBC's and WBC's and it has to be injected shortly after injection

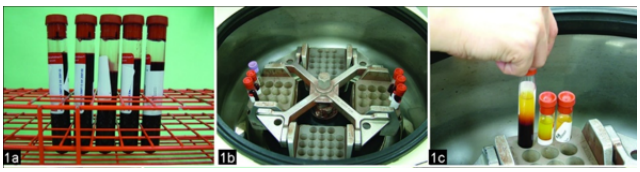

Fig. 3: The preparation of platelet rich plasma. (a-c): The blood sample is first centrifuged under 1000 rpm for 12 min and separated into the red blood cells at the bottom, the buffy coat (platelets) in the middle, and the platelet poor plasma at the top.

3.4. The submucosal injection of platelet rich plasma for orthodontic purpose

The PRP containing anticoagulants is injected submucosally. Due to the presence of anticoagulant, it was concluded that after injection of PRP, only part of the platelets adhere and aggregate little by little on the surfaces of collagen fibres, the intrinsic and extrinsic pathways of

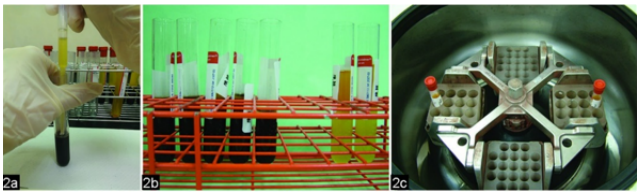

Fig. 4: The preparation of platelet rich plasma. (a-c): The buffy coat and platelet poor plasma are pipetted and collected with care, and centrifuged again under 3000 rpm for 8 min.

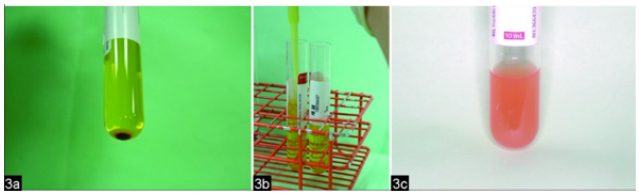

Fig. 5: The preparation of platelet rich plasma. (a-c): After the second centrifugation, the platelet poor plasma is removed until 4 ml remained and then the remaining platelet poor plasma is mixed with the buffy coat to become platelet rich plasma.

hemostasis initiate to generate thrombin gradually, platelet clots lay down little by little above the periosteum, and then the growth factors release and infiltrate little by little into the periosteum and alveolar bone.

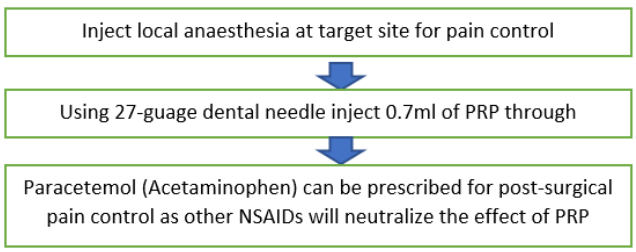

Fig. 6: The procedure

3.5. The dosage and effects of Submucosal injection of platelet rich plasma

A single injection of PRP lasts for 5-6 months clinically. Clinically the fastest rate in the acceleration of tooth movement was observed during second to fourth month post injection.

The applied regimen for different purposes is summarized:[10]

1. For the purpose of alignment and levelling single injection in the beginning and then followed by a booster injection of PRP 6 months post the first injection.
2. Similar protocol as the one for the purpose of alignment and levelling is followed in the case of

anterior retraction and/or protraction of posterior segment of teeth.

3. Clinical data by liou et al[10] revealed that the submucosal injection of PRP accelerated orthodontic tooth alignment and decreased the alveolar bone loss on the pressure side of orthodontic tooth movement. It was concluded that the optimal PRP fold for a higher than 2-fold acceleration of orthodontic tooth movement and no pressure side alveolar bone loss is 11.0–12.5.

3.6. The clinical applications for platelet rich plasma

The PRP injection could be applied for

3.6.1. Accelerating orthodontic tooth alignment and leveling in anterior crowding

The target sites of injection are the labial and lingual/ palatal sides of the anterior teeth when the purpose of injection is to accelerate the alignment and leveling.

A study done by El-Timamy A et al[11] concluded that PRP showed positive potential to accelerate tooth movement when injected. Rashid, et al[12] and gluec et al.[13] found similar significant results of PRP accelerating tooth movements in their animal studies. However, there is a lot of scope for research in this regard

3.6.2. Molar protraction

The target sites could be the buccal, lingual/palatal, and mesial sides of the posterior teeth when the purpose is to accelerate the protraction of posterior teeth or preserve the alveolar bone.

3.6.3. Preserving the pressure side alveolar bone of en-masse anterior retraction

The target site is the lingual/palatal side of anterior teeth when the purpose is to accelerate anterior retraction or to preserve the pressure side alveolar bone. Eric liou et al from his study on rats concluded that PRP resulted in preservation of the pressure side alveolar bone in cases of en-masse retraction.[10]

3.6.4. Alveolar bone grafting in cleft patients

In a study by Gupta et al,[14] secondary alveolar bone grafting with PRP showed higher bone density up to 6-month post-surgery.

3.7. Platelet rich fibrin (PRF)

Platelet-rich fibrin (PRF) was first described by choukroun., et al[15] is mainly a platelet concentrate containing platelet and growth factors on the form of fibrin membranes is prepared from autologous blood and free of any anti-coagulant and other artificial biochemical modifications.

3.8. Advantages of platelet rich fibrin over platelet rich plasma

1. Easier, Simplified, and Cost effective.[16]
2. No biochemical handling of blood is needed.[15]
3. Flexible matrix is formed by the clot, favouring entrapment of cells.[17]
4. Due to slow polymerization, favourable healing occurs.[18]
5. Compared to recombinant growth factors, PRF is an economical and quick option

3.9. Composition of PRF

Analysis of PRF reveals that it consists of fibrin clot-enriched with platelet, immune cytokines, leukocytes and circulating stem cells. Even though for the biological activity platelets and leukocytes are main cells, fibrin matrix has the important role for therapeutic effect of this platelet concentrate.[16]

Table 1: Certain growth factors and cytokines present in PRF[19]

S.No.	Growth Factor/Cytokines	Biological Action
1	Transforming growth factor-β (TGF- β)	Stimulates angiogenesis induces fibroblast and immune cells chemotaxis collagen production
2	Platelet-derived growth factor (PDGF)	Promotes angiogenesis, macrophages chemotaxis and its activation
3	Insulin growth factor-1 (IGF-1)	Stimulates chemotaxis and activates the osteoblasts and there by promotes bone formation
4	Vascular endothelial growth factor (VEGF)	Initiates angiogenesis enhances permeability of the vessels
5	Epidermal growth factor (EGF)	Promotes angiogenesis stimulates epithelial cell proliferation and differentiation
6	Interleukin-1 β (IL-1β)	Activates osteoblasts stimulates helper T cell, chemotaxis of lymphocytes
7	Tumor necrosis factor-α (TNF-α)	Increase the remodelling capacities of fibroblasts, stimulates cell survival and proliferation.

Preparation of leukocyte platelet-rich fibrin

3.10. The clinical applications for platelet rich plasma

The PRF injection could be applied for

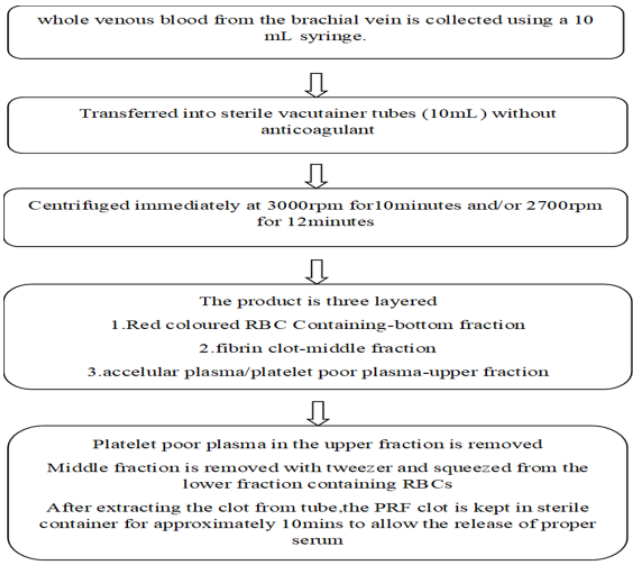

Fig. 7: The preparation of platelet rich fibrin for orthodontic purpose [10,17,18]

3.11. Periodontally accelerated osteogenic orthodontics (PAOO)

It is a procedure that is thought to accelerate movement of teeth by orthodontic forces combined with corticotomies and alveolar bone grafting.

Munoz F et al[20] used L-PRF in PAOO to study the effect of L-PRF on the post operative pain, infection, inflammation and stability post-orthodontically.

Eleven subjects who were involved in the study showed accelerated wound healing with absence of any infection or adverse reaction with mild-moderate surgical pain. In the 2-year follow up the treatment results were stable.

3.12. Alveolar ridge augmentation

Che y et al.[21] proposed the use of PRF to minimize resorption of hard tissues immediately post extraction. The author hypothesized that by preserving alveolar ridge at the time in orthodontic cases, The problems of root resorption and gingival invagination could be minimized. This would also ensure that there is adequate alveolar bone during space closure.

Also, in the pre-prosthetic orthodontics, use of PRF may contribute to the preservation of hard tissue morphology. Thereby, improving the condition of implant sites and resulting in more aesthetic restoration

A Study was done by hakam et Al, on rabbits to assess whether i-PRF may affect orthodontic relapse and it was concluded that i-PRF has the potential to enhance the stability of teeth after orthodontic tooth movements.[20]

As these advances are fairly new, no conclusive long term or controlled trials have been carried out to prove their efficacy over conventional PRP and PRF in orthodontics. There is a scope for research with the same

Table 2: Advancement in PRF technology

Advancement in PRF	Procedure
Advanced platelet rich fibrin(A-PRF) by Ghanaati in 2014[22]	1500 RPM for 14minutes in sterile plain glass based vaccum tubes
Advanced platelet rich fibrin+(A-PRF+) by fujoka-kobayashi in 2016[23]	1300 RPM for 8 minutes in sterile plain glass based vaccum tubes
Injectable platelet rich fibrin(I-PRF) by mourao 2015[24]	700RPM for 3minutes in plastic tubes
Titanium-platelet rich fibrin (T-PRF) Tunali and co-worker 2014[25]	2800RPM for 12minutes in medical grade titanium tubes

Table 3: Comparsion between PRP versus PRF[18,19]

Consideration	PRP	PRF
Generation	1^{ST}	2^{ND}
Components of blood	Platelets	Platelets, white blood cells, stem cells
Concentration of platelet	2 to 5 times higher	Up to 10 times higher
Amount of blood needed	More than PRF	Less than PRP
Coagulation products added	Citrate phosphate dextrose, adenine followed by thrombin and calcium chloride	None
Fibrin formation	None	•
Duration of Growth factors release	A few hours	A Few weeks
Form	Liquid/gel	Plugs Firbrin membranes

4. Conclusion

Various studies have been done in the past which have evaluated the efficacy of platelet concentrates and it has been concluded that these platelet concentrates are safe for their use in humans. These platelet concentrates in the form of PRP and PRF has wide variety of application in medicine and dentistry too. The mechanism of how these growth factors work is not clearly understood yet, these platelet concentrate have beneficial outcome and satisfactory clinical results.

However, in the field of orthodontics there is still a scope for research of the role of these products for accelerating tooth movement and bone regeneration as there are not many human studies done for the same.

5. Conflict of Interest

None.

6. Source of Funding

None.

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