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Review Article

The platelet concentrates' the hallmark in regeneration

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ABSTRACT

Numerous studies have been done on the use of biocompatible materials in regenerative medicine. Platelet concentrates, also known as concentrated growth factor, platelet-rich fibrin, and platelet-rich plasma, are the result of centrifuging blood to separate out the platelets. Platelet concentrations have generated a great deal of discussion in both soft and hard tissue engineering. In fact, growth factors, fibrin matrix, and platelets are among the components of autologous platelet concentrate that are essential for the healing of wounds. Modern techniques for tissue restoration by increasing the properties of autologous platelet concentrates are the subject of current research. The usage of platelet concentrates and their role in tissue regeneration are addressed in the current study, along with a number of new advances and its biological effects.

1. Introduction

The attachment apparatus or periodontium is continuously replenished by physiological processes.[1] Wear and tear repair is the process of continuously producing new cells and tissues to replace those that typically age and die. The main causes of periodontal illnesses, which are chronic inflammatory diseases, are periodontal microorganisms and the toxins that they release, which cause the periodontium to degenerate.

Periodontal therapy promotes regeneration and repair by getting rid of bacterial plaque. Re-establishing a healthy gingival sulcus at the root in the precise location of the bottom of the previous periodontal pocket is the process of scar healing.[1] Despite having no effect on gingival attachment or bone height, this stops bone degeneration. However, the periodontium entirely regenerates using a variety of materials, including guided tissue regeneration, platelet concentrates, and bone grafts.[1]

2. Different Types of Platelet Generation

ists the various forms of platelet concentrates, and Table 2 details how they are prepared according to time and revolutions per minute (RPM).

Table 1: Various platelet concentrate generations.[2]

First generation	Second generation
Plasma rich in growth factors[2]	Platelet-rich fibrin (PRF)[2]
Platelet-rich plasma (PRP)[2]	Leucocyte platelet-rich fibrin (L-PRF)[2]
	Advanced platelet-rich fibrin (A-PRF)[2]
	Injectable platelet-rich fibrin (I-PRF)[2]
	Titanium -platelet rich fibrin(T-PRF)[2]

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Table 2: Preparation of different types of PRF according to revolutions per minute (RPM) and time.[2]

S.No.	Types	Rpm	Time
1.	PRP	2000	10 min
2.	PRF	2700	12 min
3.	S-PRF	2700	12 min
4.	A-PRF	1500	14 min
5.	I-PRF	700	3 min
6.	L-PRF	2700	12 min
7.	T-PRF	3500	15 min

2.1. Platelet-rich plasma

Whitman et al.[3] employed platelet-rich plasma (PRP) for the first time ever in oral and maxillofacial surgery. PRP has the power to accelerate wound healing and tissue regeneration, including the development of new blood vessels.[4] PRP is a biological treatment that is created using the patient's whole blood supply and contains more platelets with anti-inflammatory and pro-regenerative properties that speed up the body's ability to heal tissue lesions.

PRP boosts stem cells' angiogenesis, chemotaxis, paracrine activity, and cell proliferation in the immediate environment.[5] The two main PRP activators, calcium hydrochloride and thrombin, cause growth factor release within an hour.[6] After PRP injection, the growth factors can be released gradually for up to 7 days with the help of the second activator. But there is evidence that PRP contains an anticoagulant that prevents the body from mending wounds normally.[7,8]

For PRP preparation, thrombin, calcium, or other physiologically acceptable anticoagulants are usually required.[9–13] These compounds may affect blood coagulation and result in an immune response. It is not necessarily required to add because platelet-rich fibrin (PRF) contains fibrinogen, which is converted to fibrin by the action of physiologically available thrombin. This significantly lowers the likelihood of complications following surgery.[12,14]

2.2. Platelet-rich fibrin

Choukroun et al. Discovered PRF in 2001. Due to its widespread application in dentistry and medicine,[15–18] PRF has received a lot of attention recently. Hard and soft tissue healing have both benefited greatly from the use of this PRF.[19]

2.3. PRF preparation

One blood sample is needed to create PRF, an autologous healing biomaterial that is mostly made up of leukocytes, platelets, and growth factors in an autologous fibrin matrix.[20,21] The PRF approach is currently the most straightforward and economical way to make platelet concentrates. During surgery, a blood sample is collected from the patient, and it is centrifuged just once with a unique centrifugation and collecting kit—there is no blood manipulation involved. Neither calcium chloride nor bovine thrombin could polymerize the blood's fibrin without the application of an anticoagulant.[22]

Following centrifugation, three different fractions are obtained.[23]

1. The test tube's bottom contains concentrated red blood cells, which can be thrown away.
2. A platelet-depleted plasma liquid serum makes up the upper layer.
3. A membrane can be created from the substantial PRF clot that makes up the intermediate fraction.

2.4. Making and advanced PRF

The blood is divided into the three layers indicated below by spinning 10 ml of venous blood at 1500 rpm for 14 minutes without the use of an anticoagulant.

At the base of the tube are red blood cells, followed by PRF in the middle layer and acellular plasma at the tube's surface. The PRF was gathered 2 mm below the bottom dividing line after the top straw-colored layer had been removed.[23]

2.5. Standard platelet rich fibrin

The suggested centrifugation method (2700 rpm, 12 minutes) was used to create the S-PRF[25] clot, and it resulted in a solid fibrin clot with a tiny interfibrous gap.[23] Using traditional histochemical staining methods, cells could be seen throughout the clot, although they were more elusive in the PRF clot's more distributed regions.[23]

2.6. Titanium-platelet-rich fibrin

Choukroun's method[19] is inferior to T-PRF,[23] or titanium-prepared platelet-rich fibrin, since titanium tubes have a significantly better capacity to activate clotting factors than glass tubes. The aforementioned substance would be used to eliminate silicon-related issues, as well as parched glass or crystal plastic tubes and their adverse effects over the short or long term. According to study, the co-aggregation produced by titanium was discovered to be similar to that, and the clots that formed in titanium pipes were the same as those that formed in glass vials. T-PRF offers special qualities including higher biocompatibility since titanium particles, not silica particles, are employed to activate platelets.[23]

*2.7. Leukocyte **p**latelet-rich **f**ibrin*

Leukocyte platelet-rich fibrin (L-PRF),[24] a freshly developed technique, is implanted right away after tooth

extraction. This autologous biomaterial has been shown in prior research to help decrease postoperative problems after third molar extractions.[24] L-PRF is a biomaterial made of autologous fibrin and packed with platelets, leukocytes, and cytokines. Biological processes like chemotaxis, angiogenesis, cell proliferation, and cell differentiation have all been shown to be enhanced by L-PRF; as a result, they may all help with wound healing. L-PRF, in contrast to PRP, is a biomaterial without additives that doesn't call for chemical platelet activation. L-PRF[24] is a strong solid biomaterial that does not disperse right away, like PRP.

2.8. Injectable PRF

By modifying spin centrifugation pressures, injectable PRF (I-PRF)[25] was developed in 2014. Blood was centrifuged in non-glass centrifuge tubes at low speeds, resulting in the formation of I-PRF,[25] a flowable PRF. I-PRF is a newly created platelet concentrate that also includes leukocytes and has the ability to promote both soft and hard tissue regeneration.[26] Thanks to I-PRF, which is a liquid for roughly 15 minutes, dental practitioners will have access to another useful form of PRF.[27] The PRF clot in I-PRF that is abundant in growth factors after application eventually transforms into human liquid fibrinogen, which releases growth factors continuously for 10 to 14 days.[28]

2.9. Concentrated PRF

Traditional I-PRF techniques only marginally raises platelet and leukocyte concentrations.[28] With the advent of concentrated PRF (C-PRF)[28] harvesting techniques, more platelets and leukocytes may now be extracted from the buffy coat layer. It was demonstrated that C-PRF produced directly from the buffy coat layer utilizing more rigorous centrifugation procedures exhibited up to a twofold increase in growth factor release when compared to regular I-PRF.[28]

2.10. Biological actions of PRF

Only a few of PRF's biological activities include angiogenesis, immunomodulatory effects, mitogenesis, osteogenic effects, stem cell entrapment, and wound recolonization.[28]

2.11. Angiogenesis

The mediators of angiogenesis are vascular endothelial growth factor (VEGF),[28] platelet derived growth factor (PDGF),[28] angiopoietin, and basic fibroblast growth factor. It increases the production of 53 integrins in endothelial cells, which in turn encourages those cells' adherence to fibrin, fibronectin, and vitronectin.[28]

2.12. Mitogenesis

The action of PRF on mitogenesis is mediated by transforming growth factor(TGF- β)[28] (fine & flexible trimolecular/ equilateral junctions). PRF has the following impacts on mitogenesis:

1. Speedier cellular migration is encouraged by improved cytokine trapping.
2. Reduction of osteoclast activity.[28]

2.13. Immunomodulatory effects

Fibrin and its degradation products, interleukin (IL-4), leukocytes, and fibronectin mediate the action of PRF[28] in terms of immunomodulatory effects by promoting neutrophil phagocytosis, migration, and enzymatic destruction. The effects include some of the following:

Increased expression of the CD11C/CD18 receptor on neutrophils,[28] which encourages fibrinogen and endothelium adherence, and the release of certain chemotactic proteins that regulate macrophage wound colonization.[27,28]

1. Increased degranulation led to the release of many cytokines, including IL-1, IL-4, IL-6, and TNFβ[30];
2. Coherent repair without excessive inflammatory response.

2.14. Wound recolonization

Fibrinogen, fibronectin, vitronectin, tenascin, and fibrin influence the activity of PRF in terms of wound recolonization by impairing and stimulating epithelial cell motility near wound margins. The procedure that leads to wound recolonization is as follows:

1. PRF binds to several substances, including fibronectin, PDGF, and TGF-β, via the V3 integrin.[28,29]
2. Fibroblast migration is encouraged[28,29]

2.15. Osteogenic effects

Some of the osteogenic outcomes of PRF include the following:

Increased expression of osteoprotegerin and alkaline phosphatase; increased osteoprotegerin activity; and increased phosphorylation of extracellular signal-regulated protein kinase.[29]

2.16. Entrapment of stem cells

Although stem cells have a lower intrinsic composition than other cell types, it has been proposed that the fibrin clot acts as a trap for circulating stem cells, allowing them to aggregate to a secretory phenotype and aid in vascular and tissue regeneration.[29]

3. Role of Platelet Concentrates in Tissue Regeneration in Periodontology

In 1974, it was discovered for the first time that platelets could regenerate.[29] Platelets, which are tiny blood cells, carry out numerous physiological processes. They are crucial to preserving adequate blood volume in persons with vascular injury due to their clotting activity and stimulation of the coagulation factors.[29]

The alpha granules are immediately released after platelet activation and contain large sticky proteins like VWF,[9] TSP1, vitronectin,[9] and fibronectin,[9] mitogenic factors like PDGF, VEGF, and TGF, coagulation factors like factors V, VII, XI, and XIII, and protease inhibitors like protein C, PAI-1, and TFPI. Platelets are produced by megakaryocytes in the bone marrow.[9]

According to Schwertz et al.,[2,3] platelets from sites other than the bone marrow have been found to promote tissue regeneration. The ability of platelets to clot blood is widely known. Platelets function in inflammatory processes, angiogenesis, cell proliferation, and differentiation in addition to stopping bleeding.[2,3]

4. Studies Outlining PRP'S Results for Periodontal Regeneration[30]

(Sánchez-González DJ, Méndez-Bolaina E and Trejo-Bahena NI. Platelet-rich plasma peptides: key for regeneration. Int J Pept 2012; 2012: 1–10.)

1. Improves periodontal intrabony deficiencies, however outcomes were heterogeneous, with no unambiguous conclusions reported by Roselló-Camps et al.[30]
2. It can be employed as an adjuvant to grafting materials in periodontal intrabony defects, except in the case of guided tissue regeneration (GTR), according to Verma et al.[30]
3. In a clinical experiment for the treatment of intrabony abnormalities, PRP alone demonstrated substantial benefitsin contrast to PRP with demineralized dried bone allograft as per Agarwal et al.[30]
4. Promotes periodontal tissue regeneration and lowers patient morbidity. It could be useful; additional evidence is required. Platelet regeneration capacity is limited as quoted by Agarwal et al., Roselló-Camps et al.[30]
5. According to Bajaj et al., there was a lack of furcation closure in the treatment of furcation problems, despite improvements in periodontal health.[30]
6. PRP releasing growth factors in a continuous manner is significant in periodontal tissue engineering according to Fernandes et al.[30]
7. PRP demonstrated antibacterial activity against periodontal pathogens in addition to regeneration according to Badade et al.[30]
8. According to Agarwal et al., Yamada et al., Roffi et al.good benefits were seen with PRP in periodontal regeneration with other graft materials but no added advantagewas seen with PRP alone in the treatment of infrabony defects.[30]

5. PRF Over PRP

When compared to PRP, PRF has a number of advantages, including lower levels of polymerization, simplicity of manipulation, no biochemical processing of patient blood samples, support for the immune system, and comparatively better wound healing capacity. Utilizing the PRF has less risks than utilizing PRP[31] since it lacks anticoagulants and bovine thrombin and is more effective at promoting cell migration and proliferation.[31]

Due to its beneficial qualities, which are outlined below, the PRF has been the subject of several studies looking at its potential for usage in various tissue regeneration applications in dentistry.[31]

6. The Use of PRF in Other Dental Applications, According to Various Studiess[31]

(Deeb MA. Role of platelet-rich fibrin (PRF) and platelet-rich plasma (PRP) in oro-facial tissue regeneration: a narrative review. Journal of Advanced Oral Research. 2020 May;11(1):5-11)

1. According to Mazor et al, materials utilized in sinus lifting and implantation.[31]
2. According to Najeeb et al., aids in the regeneration of the bone around the immediate implant.[31]
3. "Alveolar height preservation during successive extractions," Borie et al., Naik et al.[31]
4. To treat gingival recession in the mandibular anterior teeth, Mishra et al. performed flap surgery.[31]
5. Mishra et al. used PRF to successfully treat periodontic endodontic furcation problems.[31]
6. According to Gupta et al. and Borie et al. (2017) Miron Fujiioka and colleagues, PRF positioned beneath a modified coronal advanced flap had excellent outcomes after a 6-month follow-up.[31]
7. According to Keswani et al., sufficient bone filling was shown in PRF in sockets with titanium membranes placed to the walls and primary closure after 8 weeks.[31]
8. In reconstructive surgeries using freeze-dried bone allograft with graft or implant loss, Simonpieri et al. employed PRF.[31]
9. In situations of localized osteitis, Hoaglin and Lines surgical sites showed 90% closure.[31]
10. According to Suchetha et al., the impact of PRP and PRF on periodontal regeneration is essentially identical.[31]

11. The primary option for therapy in elderly patients due to PRF's strong healing and regeneration properties and complete resorption after surgery, according to Cortese et al.[31]
12. A possible appropriate scaffold for revascularizing young permanent teeth with necrotic pulp tissues was presented by Keswani et al.[31]
13. According to Hotwani and Sharma, PRF promotes the growth of dental pulp and the regeneration of teeth with necrotic pulp tissues.[31]
14. Sarkarat et al. reported that using PRP/PRF to treat jaw osteonecrosis brought on by bisphosphate.[31]

7. Conclusion

In the field of dentistry, PRF and its variations provide improved regeneration potential. The formation of the PRF membrane aids in the healing process.[28] In the majority of medical specialties, PRP and PRF are utilized or are being explored as adjuvants for surgery or as preparations for regenerative medicine. Natural growth factors included in platelet concentrates support physiological tissue repair.[31]

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None.

9. Conflict of Interest

None.

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