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Journal homepage: www.joooo.org**Review Article****Platelet rich fibrin (PRF) and its application in oral surgery: A literature review****Diwakar Vasudev^{1,*}, Dhananjay Vasudeva², Akanksha Garg³, Manisha Rani⁴**¹Dept. of Oral and Maxillofacial Surgery, Dasmesh Institute of Research and Dental Sciences, Faridkot, Punjab, India²Dept. of Prosthodontics Crown & Bridge, Desh Bhagat Dental College and Hospital, Mandi Gobindgarh, Punjab, India³Dept. of Paedodontics & Preventive Dentistry, Inderprastha Dental College & Hospital, Ghaziabad, Uttar Pradesh, India⁴Dept. of Periodontology and Oral Implantology, Bhojia Dental College and Hospital, Baddi, Himachal Pradesh, India**ARTICLE INFO***Article history:*

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ABSTRACT

Platelet rich fibrin (PRF) is an autogenous platelet concentrate containing growth factors and cytokines, trapped in fibrin matrix. Growth factors which are present provides ideal environment for wound healing and regeneration of the tissues. Platelet Concentrate have evolved a long way since 1954. In recent time it has been used in the field of medical science including dentistry, oral surgery, plastic surgery, orthopaedic surgery etc. This review discuss the evolution of platelet concentrate, its preparation technique and its application in the field of dentistry and oral surgery.

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For reprints contact: reprint@ipinnovative.com**1. Introduction**

Platelet rich fibrin (PRF) was first mentioned by Dr. Joseph Choukroun et al. in 2001. It is the second generation platelet concentrate containing platelets and growth factors which is prepared from the patient's own blood without adding any anticoagulant or other artificial biochemical modifications.¹ PRF speeds up the healing process and has potential for generating both hard and soft tissues, it can be used alone or can be used along with bone substitute.^{2,3}

Regenerative potential of platelets is known since 1974 in medical science. Platelets provide a rich amount of various growth factors such as platelet derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factors (VEGF), insulin like growth factors, fibroblast growth factor, connective tissue growth factor, epidermal growth factor, etc.

In recent times, various types of platelet concentrates has been developed and has shown desired results. Platelet rich

plasma (PRP), was the first generation platelet concentrate, that was become quite popular in 1970s.⁴ However, the protocol for the preparation was quite complex and there was the risk of cross infection due to the use of bovine thrombin, because of these reasons researchers developed the newer generation of platelet concentrate which is completely autologous that is platelet rich fibrin (PRF) also called as Choukroun's platelet rich fibrin.

2. Preparation of PRF

For preparation of PRF, 10 ml of blood sample is collected from the patient's body without adding any anticoagulant in blood collection tubes with the help of butterfly needle. After the collection of blood in the test tube, it is centrifuged immediately at the rate of 3000 rpm for 10 minutes. After centrifugation, 3 layers will obtained in the test tube (Figure 1). The topmost layer is made up of acellular PPP (platelet poor plasma), middle layer is of PRF clot and and the lowermost layer is of RBCs. The middle layer of PRF clot is removed with the help of sterile tweezers

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and separated from the underlying RBC layer by cutting it with scissors.⁵ Once separated, the PRF may be used immediately or may be stored in refrigerator. This PRF clot (Figure 2) can be shaped into PRF plug or can be compressed into a membrane depending upon the patient requirement.

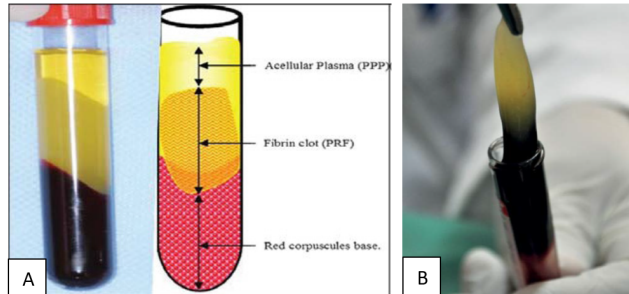


Fig. 1: A): Layers of PRF; **B):** Layers of PRF



Fig. 2: PRF clot removal

3. Advantages of PRF

1. Single step and simplified process of preparation.
2. Bovine thrombin is not required, which reduces the chance of crossinfection.
3. Blood sample is autologous with least blood manipulation.
4. Natural polarization with minimum immunological reaction.
5. Can be used along with bone grafts.
6. Helps in hemostasis.

4. Disadvantages of PRF

1. The success rate of the PRF formation depends directly on its handling, mainly, at the time of blood collection and its placement in centrifuge machine.
2. Glass-coated tube is required for polymerization of clot.
3. Patient may refuse the treatment because of the puncture required for the collection of blood.

5. Role of PRF in Wound Healing

PRF consists of fibrin matrix which is a polymerized tetra molecular structure having platelets, leukocyte, circulating stems cells and cytokines.⁶ PRF stimulates, osteoblasts, fibroblasts, and periodontal ligament cells proliferation as mitogen. Its molecular structure is such which promotes the migration of endothelial cells and fibroblasts towards the healing site.⁷ It causes angiogenesis rapidly and remodelling of fibrin easily. All these parameters are optimal for wound healing.

Various types of growth factors and cytokines are released from the PRF matrix locally at the site of wound for prolonged period of time, which helps in the wound healing at its various stages for tissue regeneration. Alpha granules present in the platelets releases the growth factors, when they are activated. Transforming growth factor beta (TGF-beta) and Platelet-derived growth factor (PDGF) are typical two growth factors which promotes the healing of hard tissues (bone) and soft tissues by production of collagen.⁷

Platelet-derived growth factor (PDGF) activates the cells of mesenchymal origin. PDGF act mostly on the osteoblastic cell proliferation, exerting most of its effects during early phases of wound healing.¹ It also stimulate chemotaxis, proliferation and new gene expression in monocytes-macrophages and fibroblasts that is considered for tissue repair.

Vascular endothelial growth factor (VEGF) is an growth factor which is responsible for angiogenesis. It acts on endothelial cells, vascular smooth muscle cells, fibroblasts etc. for initiating blood vessel formation.

Transforming growth factor Beta-1 (TGF beta-1), which is an inflammatory regulator, is the most powerful fibrosis agent and it can induce a massive production of fibronectin and collagen either from fibroblast or osteoblast.²

Fibrin matrix has mechanical adhesive properties and biologically it functions like a fibrin glue, due to this adhesive properties PRF can maintain soft tissue flaps in a stable position with very less shrinkage. Circulating stem cells traps in the PRF because of initial neovascularisation during healing process also promotes the healing.⁸

6. Applications of PRF in oral Surgery

In past few years a lot of research has been done on PRF & numerous cases have been published regarding the use of PRF clot and PRF membranes. Majority of research work has been done on the use PRF in oral surgery for bone augmentation, socket preservation, sinus lifts and the periodontics for correction of intra bony defects, gingival recession, periapical lesions, guided bone regeneration. It has also been used for regenerative pulpotomies, periapical surgeries. Besides oral surgery it has been used for healing of facial wounds, in the treatment of alopecia and for necrotising fasciitis treatment.

7. In Oral & Maxillofacial Surgery

PRF can be used in the extraction socket as filling material. In socket preservation it can be used along with bone graft which accelerate the healing process. In diabetic and immunocompromised patients, PRF can be used for acceleration of oral and facial wound healing. PRF also stimulates the blood coagulation (used with thromboplastin) so it can be used in those patients who are on anticoagulant therapy.⁹

Studies showed that PRF alone or along with other bone graft material can be used in sinus lift procedures. It can be used in various direct and indirect sinus lift procedures like osteotome – mediated sinus floor elevation, bone added sinus floor elevation, minimally invasive antral membrane ballon elevation etc.²

In cases of wide extraction sockets where primary closure is difficult, PRF membrane can be used as protective covering membrane that promotes the reepithelization of extraction site and merges the wound margins at a faster rate. PRF can be sutured easily because it has strength and elasticity. In guided bone regeneration (GBR) it can be used, where PRF membrane covers, stabilizes and protects bone graft material.

Over the facial skin wounds studies has shown that PRF can be used with promising results, studies proven that autologous gel enhances wound closure and healing velocity over the avulsive wounds. PRF membrane placement is simple technique by which we can concentrate platelets and natural blood clot over the wound which promote more rapid and complete wound healing. PRF membrane favours three keys of healing naming immunity, angiogenesis and epithelial cover. All this protects, open wound and accelerates healing and promote development of microvascularization and guides the migration of epithelial cells to the surface of wound.¹⁰

For treating Alopecia it has been used, in males hair loss is very common, till now PRP has been used in medical science for hair growth and regeneration and shown good results but it has been seen that regenerative potential of PRF is more as compared to PRP. Injectable PRF (i-PRF) is the advanced and the liquid form of PRF which can be injected in the scalp. i-PRF contains stem cells having regenerative potential. Type VI and Type VII alopecia are difficult to treat, but i-PRF has shown very good results in these cases. Numerous case reports have been published in which it has been shown that i-PRF has better regenerative potential for treating alopecia.¹¹

8. In Periodontics

In periodontics, PRF has been used to treat various periodontal problems, including gingival recession, intrabony defects, periapical lesions, and for periodontal bony regeneration.

In the treatment of gingival recession PRF membrane can be used as subepithelial connective tissue graft along with coronally advancement flap.¹²

For the treatment of intrabony defects (IBD), PRF gel along with hydroxyapatite graft and guided tissue regeneration (GTR) membrane can be used collectively to fill the bony defects.¹³

PRF can also be used in the regeneration of peri-implant bone defects. PRF not only improve osseointegration of implant but also helps in the regeneration of peri-implant bone defects, PRF along with bone grafts can be used to fill the bony defect where bone is lost due to peri-implantitis, it can also be used during the immediate implant placement where the implant is placed immediately in extraction socket and bone around the implant is not adequate.¹⁴

9. In Endodontics

Studies have shown that PRF can be used in infected necrotic immature tooth for the regeneration of pulp and revitalization of tooth.¹⁵

Case reports have been published that showed that PRF membrane along with MTA can be used for apexification procedures and induces the faster healing in periapical areas.

PRF has also been used in the pulpotomy procedures. It has been used where coronal pulp is removed and the pulpal wound is covered by PRF followed by sealing it with MTA and GIC.⁶

To fill the bony defects after periapical surgeries PRF has also been used, like in case of periapical infection, or where root resection is required, and it has been proven by studies that it promotes faster healing in large periapical lesions.

10. In Tissue Engineering

In the past few years so many researchers have worked on the use of PRF in tissue engineering. Study conducted by Gassling et al. showed that PRF membranes can used for cultivation of human periosteal cells for bone tissue engineering in vitro, but further investigation is required regarding the use of PRF in tissue engineering in clinical aspects.

11. Conclusion

PRF is a new generation platelet concentrate whose preparation technique was given by Choukroun in 2001 which is a simple and inexpensive technique. It has been used successfully in various oral surgical procedures, in oral and maxillofacial surgery, implant surgery and in the field of orthopaedic and plastic surgery. PRF promotes both hard as well as soft tissue healing proven by studies. In the field of Endodontics for regeneration of pulp-dentin complex it has been used. However, to get the deeper knowledge regarding the efficacy of PRF, more long term clinical trials are required.

12. Source of Funding

None.

13. Conflicts of Interest

The authors report no conflicts of interest related to this review.

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