Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies

Journal home page: www.jamdsr.com doi: 10.21276/jamdsr UGC approved journal no. 63854

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Review Article

A Novel Healing Platelet Rich Fibrin (PRF) Matrix and its Role in Dentistry

Rahul Srivastava[1], Sekhar Mukherjee[2], Shubhra Saxena[3], Saheli Saha[4]

[1]Reader, [2,34]Post graduate student, Department of Oral Medicine & Radiology, Rama Dental College, Hospital & Research Centre Kanpur (U.P.), India

ABSTRACT

Platelet-rich fibrin (L-PRF) is an autogenous matrix derived from the concentration of the patient's blood platelets. A simplified chair side procedure results in the production of a fibrin membrane that is capable of stimulating the release of many important growth factors involved during wound healing processes that take place after surgery. Platelet-rich fibrin can play an important role in oral and maxillofacial surgery, implant dentistry, periodontal regeneration and post-extraction site preservation. The fibrin is a reservoir of platelets that will slowly release growth factors and cytokines, which are the key factors for regeneration of the bone and maturation of the soft tissue. Platelet-rich fibrin (PRF) is an autologous platelet concentrate prepared from the patient's own blood at the dentist's office just before the oral/dental procedure. This review highlights the brief about PRF, advantages, disadvantages and it's applications in dentistry.

Key words: Blood clot, Platelet-rich fibrin, Regenerative endodontic treatment, Fibrin, Platelet concentrate.

Received: 8 February, 2019 Revised: 27 February, 2019 Accepted: 28 February, 2019

Corresponding Author: Dr. Rahul Srivastava, Reader, Department of Oral Medicine & Radiology, Rama Dental College, Hospital & Research Centre Kanpur (U.P.), India

This article may be cited as: Srivastava R, Mukherjee S, Saxena S, Saha S. A Novel Healing Platelet Rich Fibrin (PRF) matrix and its Role in Dentistry. J Adv Med Dent Scie Res 2019;7(4): 19-22.

INTRODUCTION

Wound healing is a process which includes a multi-staged approach and interaction of a complex cascade of cells and molecules in the host's defense mechanism. As body engrosses in wound healing, a captivating process occurs throughout each of the systems that constitute the body. Wound healing is initiated by clot formation, followed by proliferative stage which comprises of epithelialization, angiogenesis, granulation tissue formation, collagen deposition and finally collagen maturation and contraction. This involves adherence and aggregation of platelets favoring formation of thrombin and fibrin. Platelets contain biologically active proteins, binding of these proteins within a developing fibrin mesh or to the extracellular matrix can create chemotactic gradients favoring recruitment of stem cells, stimulating cell migration, differentiation, and promoting repair.[1,2,3]

The development of bioactive surgical additives, which are being used to regulate the inflammation and increase the speed of healing process, is one of the great challenges in clinical research. In this sense, healing is a complex process, which involves cellular organization, chemical signals, and the extracellular matrix for tissue repair.[4] The world of dentistry was first familiarized with the regenerative capacity of platelets in the 70s. As per its first definition in 2007, it is a preparation of platelets present in a small volume of plasma containing a large amount of growth factors (GFs), which is essential for bone growth and regeneration. Platelet-rich fibrin (PRF) is frequently named as Choukroun's PRF after its inventor, and was described as a second-generation platelet concentrate which contains platelets and growth factors in the form of fibrin membranes prepared from the patient's own blood free of any anticoagulant or other artificial biochemical modifications.[5,6]

Nowadays in oral surgery there are two kinds of platelet concentrates for in vivo tissue engineering applications: platelet-rich plasma (PRP) and platelet-rich fibrin (PRF). Platelet concentrates are a concentrated suspension of growth factors found in platelets, which act as bioactive

surgical additives that are applied locally to induce wound healing. PRF was first used specifically in oral surgery by Dohan et al. and is currently considered as a new generation of platelet concentrate. It consists of a matrix of autologous fibrin and has several advantages over PRP, including easier preparation and not requiring chemical manipulation of the blood, which makes it strictly an autologous preparation.[7]

What are the Platelets

Platelets are anucleate cytoplasmic fragments derived from bone marrow megakaryocytes and measure 2–3 μm in diameter. They contain many granules, few mitochondria and prominent membrane structures, the surface-connected canalicular system and the dense tubular system. The α granules are spherical or oval structures with diameters ranging from 200 to 500 nm each, enclosed by a unit membrane. They form an intracellular storage pool of proteins vital to wound healing, including platelet-derived growth factor (PDGF), transforming growth factor (TGF-β), and insulin-like growth factor (IGF-I).[3] Biologic action of PDGF is stimulation of DNA and protein synthesis in osseous tissues; mitogenic effects on mesenchymal cells; angiogenic effect on endothelial cells. TGF-β stimulates angiogenesis and matrix synthesis; enhanced woven bone formation; chemotactic effect on osteoblastic cells; stimulates endothelial chemotaxis and bone formation by inhibitory effects on osteoclasts. IGF-1 stimulates proliferation of osteoblasts and matrix synthesis, increases expression of bone matrix proteins, such as osteocalcin; in combination with PDGF it enhances the rate and quality of wound healing.[8,9]

What is Platelet rich fibrin (PRF)???

PRF demonstrates a novel shift in the therapeutic development of platelets. PRF is routinely called Choukroun's PRF, after its inventor, as there are varied platelet concentrates with corresponding names. Choukroun's platelet-rich fibrin (PRF) is a leukocyte and platelet rich fibrin biomaterial with a distinct arrangement and three dimensional framework. PRF is distinguished as a second generation framework as it is primed as an elemental condensed form minus the accretion of any anticoagulants. PRF is also observed to have a packed fibrin complex, containing leukocytes, cytokines and glycoproteins such as thrombospondin. Leukocytes that are condensed in PRF scaffold hold a necessary position in growth factor release along with immune administration.[10]

Preparation of PRF

The procedure involves drawing of blood that is collected into test tubes without an anticoagulant and needs to be centrifuged instantaneously. A tabletop centrifuge can be used for this purpose for 2 minutes at 2,700 rpm. The resultant product consists of the three layers.

1. Straw colored fraction of acellular platelet poor plasma (PPP) at peak level.
2. PRF clot in intermediate level.
3. Red fraction of red blood cell (RBCs) at the base level.

The blood coagulation starts instantaneously as it comes in contact with the glass surface due to the lack of anticoagulant. If the time necessary to collect blood and launch centrifugation is exceedingly prolonged, the fibrin will polymerize in a diffuse way in the tube and only a small blood clot without consistency will be obtained. Consequently, blood collection should be prompt and instant centrifugation is a prerequisite in the production protocol for PRF.

Recently, PRF box (Process, Nice, France) has been announced. It is formulated to produce homogenously thickened hydrated membrane and an exudate rich in platelets, leukocytes, vitronectin and fibronectin expressed from the fibrin clots. It has improved the issues regarding the handling of the PRF clot.[11]

Mechanism of Action

In vitro release of growth factors from PRF and the results of in vivo studies have now put forward a proposal to optimize the clinical application of PRF. PRF is a concentrated suspension of the growth factors found in platelets. These growth factors are involved in wound healing and are postulated as promoters of tissue regeneration.[11] (Table:1)

Factor	Action
Interlukin-1 (IL-1)	• Key mediator of inflammation control • Stimulates T-helper lymphocyte
Interleukin-6 (IL-6)	• Differentiation factor for B-lymphocytes • Activator for T lymphocytes • Stimulates the secretion of antibodies • Supports the chain reaction leading to inflammation, destruction and remodeling
Tumor necrosis factor alpha (TNF alpha)	• Activates monocytes • Stimulates the remodelling capacities of fibroblasts. • Increases phagocytosis and neutrophil cytotoxicity. • Modulates the expression of IL-1 and IL-6.
Interleukin-4 (IL-4)	• Supports proliferation and differentiation of activated B cells. • Supports healing by moderating inflammation increases fibrillary collagen synthesis by fibroblast.
Cytokine vascular endotheilial growth factor (VEGF)	Functions to start angiogenesis
Transforming growth factor β1(TGF β1)	Can induce a massive synthesis of collagen and fibronectin.
Platelet derived growth factors (PDGF)	• Regulates migration, proliferation and survival of mesenchymal cell lineages • Plays an essential role in physiologic cicatrisation and pathogenesis of atherosclerosis and other fibroproliferative diseases.
Insulin like growth factors (IGFs) 1 and 2	• Cell multiplication mediator in apoptosis • Exerts chemotactic effects towards human osteoblast

Table 1: PRF growth factors and their specific role

Advantages of PRF

1. It's preparation is a simplified and efficient technique, with centrifugation in a single step, free and openly accessible for all clinicians.
2. It is obtained by autologous blood sample.
3. Minimized blood manipulation.
4. It does not require the addition of external thrombin because polymerization is a completely natural process, without any risk of suffering from an immunological reaction.
5. It has a natural fibrin framework with growth factors within that may keep their activity for a relatively longer period and stimulate tissue regeneration effectively.
6. It can be used solely or in combination with bone grafts, depending on the purpose.
7. Increases the healing rate of the grafted bone.
8. It is an economical and quick option compared with recombinant growth factors when used in conjunction with bone grafts.
9. Used as a membrane, it avoids a donor site surgical procedure and results in a reduction in patient discomfort during the early wound-healing period.
10. The studies of PRF present it to be more efficient and with less controversies on its final clinical results when compared to PRP.

Disadvantages of PRF

1. The final amount available is low because it is autologous blood.
2. The success of the PRF protocol depends directly on the handling, mainly, related to blood collection time and its transference for the centrifuge.
3. Need of using a glass-coated tube to achieve clot polymerization.
4. Possible refusal of treatment by the puncture required for blood collection.
5. Only needs a minimal experience of clinician for PRF manipulation.[12]

Role of PRF in Dentistry

In Oral and Maxillofacial Surgery

PRF has been commonly used in sinus lift procedures. Besides that, the use of PRF as the sole filling material during sinus lift and implantation.[13]

PRF-based membranes are used for masking the alveolar ridge augmentation side in several in vivo studies. L-PRF is a new platelet concentrate used with a great success in a number of surgical procedures to optimize the wound healing. Numerous studies showed that LPRF has the property of the new bone formation.[14]

PRF could be useful for small otologic surgery. Sports-related soft tissue injuries cause athletes to lose a significant amount of time from their sports and represent a significant burden to society in terms of health-care resources, personal disability, and activity restriction. By using PRF and piezo surgery, the healing time is reduced, compared to 150 days, favoring optimal bone regeneration.[15]

In Periodontics

The regeneration of the lost periodontal structures is the ultimate aim of the periodontal therapy to restore the health, function, and esthetics of periodontium.

PRF used either in combination with bone grafts (bovine porous bone mineral, nanocrystalline hydroxyapatite, and demineralized freeze-dried bone allograft [DFDBA]) or pharmacologic agents such as metformin gel was found to be more effective in terms of improvements in clinical parameters and radiographic defect depth reduction compared to when bone grafts or metformin used alone.

PRF being a reservoir of soluble growth factors and cytokines (transforming growth factor beta-1, insulin-like growth factor 1 and 2, platelet-derived growth factor, cytokine vascular endothelial growth factor, and interleukin 1, 4, and 6) that not only help in tissue regeneration but also accelerate wound healing. Studies have shown that PRF, when used with coronally advanced flap for recession coverage, has shown to decrease matrix metalloproteinase-8 (MMP-8) and interleukin beta levels but increase in tissue inhibitor of MMP-1 levels at 10 days, thereby promoting periodontal wound healing in the earlier phase of the process. On comparing with PRF and connective tissue graft (CTG) in gingival recession procedures, it was found that there was a greater gain in keratinized tissue width in CTG group but better wound healing in PRF group.[16]

In Endodontics

Jayalakshmi et al. used PRF in combination with beta tricalcium phosphate (β-TCP) bone graft in the treatment of periapical cyst. The authors reported progressive, significant, and predictable clinical and radiographic bone regeneration/healing with the use of PRF. It was concluded that the combined use of PRF and β-TCP for bone augmentation in treatment of periapical defects is a potential treatment alternative for faster healing than using biomaterials alone.[17]

Keswani et al. reported that PRF might serve as a potentially ideal scaffold in revascularization of immature permanent teeth with necrotic pulps as it is rich in growth factors, enhances cellular proliferation and differentiation, and acts as a matrix for tissue in growth.[18]

Huang et al. conducted an investigation into the biological effects of PRF on human dental pulp cells. PRF was found to increase dental pulp cell proliferation as well as osteoprotegerin (OPG) expression in a time-dependent manner. Alkaline phosphatase (ALP) activity was also significantly up-regulated by PRF. These findings might serve as a basis for preclinical studies that address the role of PRF in reparative dentin formation.[19]

Role of PRF in regenerative endodontics

1. Post enucleation of large periapical lesions.
2. Apical matrix barrier for in root end apexification.
3. Revascularization in immature teeth with a necrotic pulp.
4. Apical plug in apexification.
5. Pulpal floor perforation repair.
6. Pulpotomy in young permanent teeth.
7. As a scaffold for dentin pulp regeneration.[17,18,19]

Conclusion

Presence of growth factors and cytokines in platelets play key roles in inflammation and wound healing. Platelets also secrete fibrin, fibronectin and vitronectin, which act as a matrix for the connective tissue and as adhesion molecules for more efficient cell migration. This has led to the idea of using platelets as therapeutic tools to improve tissue repair during wound healing. Because of the benefits to soft tissue, PRP is now being used all over the word for facial rejuvenation, joint regeneration, hair growth stimulation. Because of the easier and less expensive alternative, PRF liquid is starting to be used instead of PRP. PRF is the newest and most popular technique to accelerate healing in dentistry. However continued research and scientific studies are required to substantiate the claims of effectiveness of this technique.

References

1. Gonzalez AC, Costa TF, Andrade ZA, Medrado ARAP Wound healing -A literature review. An Bras Dermatol 2016;91: 614-620.
2. Agrawal M, Agrawal V. Platelet rich fibrin and its applications in dentistry - A review article. Natl J Med Dent Res 2014;2:51-8.
3. Chandran P, Sivadas A. Platelet-rich fibrin: Its role in periodontal regeneration. Saudi J Dent Res 2014;5:117-22.
4. Singer AJ and Clark RA. Cutaneous wound healing. N Engl J Med 1999; 341: 738-746.
5. Wang HL, Avila G (2007) Platelet rich plasma: myth or reality?. Eur J Dent: 192-194. 15.
6. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, et al. (2006) Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part V: histologic evaluations of PRF effects on bone allograft maturation in sinus lift. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 101: 299-303.
7. A. Cortese et al. Platelet-richfibrin(PRF) in implant dentistry in combination with new bone regenerative technique in elderly patient International Journal of Surgery Case Reports 2016;2:52–56.
8. Prakash S, Thakur A. Platelet concentrates: Past, present and future. J Maxillofac Oral Surg 2011;10:45-9.
9. Sunitha Raja V, Munirathnam Naidu E. Platelet-rich fibrin: Evolution of a second-generation platelet concentrate. Indian J Dent Res 2008;19:42-6.
10. Ved V, Bhagat J, Gala V, Fernandes G Platelet Rich Fibrin and Its Role in Regenerative Dentistry: A Mini Review. J Dent Sci Med 2018;3:1-3.
11. Hotwani K, Sharma K Platelet rich fibrin - a novel acumen into regenerative endodontic therapy. Restor Dent Endod. 2014;39:1–6.
12. Borie E, DaOliví D G, Orsi I A, Garlet K, Weber B, Beltrán V, Fuentes R Platelet-rich fibrin application in dentistry: a literature review Int J Clin Exp Med 2015;8:7922-7929.
13. Del Corso M, Toffler M, Dohan Ehrenfest DM. Use of an autologous leukocyte and platelet-rich fibrin (L-PRF) membrane in post-avulsion sites: An overview of Choukroun's PRF. J Implant Adv Clin Dent 2010;1:27-35.
14. Tatullo M, Marrelli M, Cassetta M, Pacifici A, Stefanelli LV, Scacco S, et al. Platelet rich fibrin (P.R.F.) in reconstructive surgery of atrophied maxillary bones: Clinical and histological evaluations. Int J Med Sci. 2012;9:872–80.
15. Jang ES, Park JW, Kweon H, Lee KG, Kang SW, Baek DH, et al. Restoration of peri-implant defects in immediate implant installations by Choukroun platelet-rich fibrin and silk fibroin powder combination graft. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;109(6):831–6.
16. Verma U P, Yadav R K, Dixit M, Abhaya Gupta A Platelet-rich Fibrin: A Paradigm in Periodontal Therapy – A Systematic Review. J Int Soc Prev Community Dent. 2017; 7: 227–233.
17. Jayalakshmi KB, Agarwal S, Singh MP, Vishwanath BT, Krishna A, Agrawal R. Platelet-rich fibrin with beta-tricalcium phosphate-a noval approach for bone augmentation in chronic periapical lesion: a case report. Case Rep Dent 2012;2012:902858.
18. Keswani D, Pandey RK. Revascularization of an immature tooth with a necrotic pulp using platelet-rich fibrin: a case report. Int Endod J 2013;46:1096-1104.
19. Huang FM, Yang SF, Zhao JH, Chang YC. Platelet-rich fibrin increases proliferation and differentiation of human dental pulp cells. J Endod 2010;36:1628-1632.