Review Article

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Platelet Rich Fibrin: A Review Article

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ABSTRACT

Background: Platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) are autologous platelet concentrates prepared from patient's own blood. Recent researches are being focused on the development of therapeutic alternatives which are easy to prepare, non-toxic or biocompatible to living tissues and economically cheap that might result in the local release of growth factors accelerating hard and soft tissue healing. Platelet concentrates is one of these various growth factors and platelet rich fibrin (PRF) is one of the recent innovation of various platelet concentrates. This article describes the method of preparation, technique of using PRF, advantages and disadvantages of using it in clinical researches.

Keywords: Blood platelet, platelet rich fibrin, growth factors, bone regeneration.

INTRODUCTION

Healing is a complex process that involves cellular organization, chemical signals, and the extra-cellular matrix for tissue repair. Platelets play a very important role in both tissue hemostasis and wound healing. The use of platelets concentrates in many field-related protocols is well documented from the past years, but it remained controversial owing to the complexity of the production protocol or risk of cross-infection.[1] With the introduction of potential of platelets regeneratives in 70's, it was found that they contains growth factors that are responsible for increase collagen production, cell mitosis, blood vessels growth, recruitment of other cells that migrate to the site of injury, and cell differentiation induction, among others.[2]

One of the last achievements in dentistry is the use of platelet concentrates for the improvement of reparation and regeneration of the soft and hard tissues after different surgical procedures. Two types of such platelet concentrates are available: 1) platelet-rich plasma (PRP) and 2) platelet-rich fibrin (PRF). Various growth factors are expressed during different phases of tissue healing and could serve as therapeutic agents to enhance both soft and hard tissue repair. Platelet concentrates is one of these various growth factors and platelet rich fibrin (PRF) is one of the recent innovation of various platelet concentrates.[3, 4]

PRF was developed in France by Joseph Choukroun et al. in 2001 was used to improve bone healing in cases of implants. It is a fibrin matrix in which platelet cytokines, growth factors and cells are trapped and may be released after a certain time and that can serve as a resorbable membrane. Growth factors are released after activation from the platelets trapped within fibrin matrix, and have been shown to stimulate the mitogenic response in

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the periosteum for bone repair during normal wound healing.[5]

PLATELETS and FIBRIN

Platelets were first described by the remarkably early observations of Bizzozero in the late 1800s.[6] Human platelets are small and discoid in shape, with dimensions of approximately 2.0–4.0 by 0.5 μm, and a mean volume of 7–11 fl. They are the second most numerous corpuscle in the blood normally circulating at between 150–450×10^9/litre. Platelets are enucleated cells derived from megakaryocytes and typically circulate for 10 days. Their shape and small size enables the platelets to be pushed to the edge of vessels, placing them in the optimum location required to constantly survey the integrity of the vasculature.[7]

Fibrin is the activated form of a plasmatic molecule called fibrinogen. This soluble fibrillary molecule is massively present both in plasma and in the platelet alpha-granules and plays a ascertain role in platelet aggregation during hemostasis. It is transformed into a kind of biologic glue capable of consolidating the initial platelet cluster, thus constituting a protective wall along vascular breaches during coagulation. In fact, fibrinogen is the final substrate of all coagulation reactions. Being a soluble protein, fibrinogen is transformed into an insoluble fibrin by thrombin while the polymerized fibrin gel constitutes the first cicatricial matrix of the injured site.[1]

The crucial role of platelets in inflammation and wound healing is due to the presence of several growth factors and cytokines. Furthermore, they contains fibrin, fibronectin that provide connective tissue, a matrix and creates an efficient network for cell migration.[1] Platelet-rich fibrin (PRF) being a second generation concentrate, consist of platelets, leukocytes, and fibrin matrix which enhances the healing process of tissue.[8] The various cytokines that are involved in PRF and their roles in wound healing is described in figure 1.

PLATELET RICH FIBRIN

Platelet rich fibrin (PRF) is a fibrin matrix in which platelet cytokines, growth factors and cells are trapped and may be released after a certain time and that can serve as a resorbable membrane.[5] The ability of PRF in accelerating soft and hard tissue healing has stimulated the research of its clinical applications which includes healing of extraction sockets, including impacted tooth, implantology, cleft lip and palate, ulcer management, and bisphosphonate-related osteonecrosis of the jaw. Studies shows that PRF can be used as filling material in extraction socket. In extraction socket, it will act as a stable clot for neovascularization and accelerates tissue healing.[9]

Some in-vitro studies demonstrate that PRF shows more proliferation and differentiation of osteoblast than PRP[10] and suggests a potential role for new bone formation.[11] Su et al.[12] stated that PRF membrane should be used immediately after formation to maximize release of growth factors to surgical site. The remaining fluid can be recovered as an additional source of growth factors for grafting.

Some clinical studies used PRF membrane as a sole or with grafting material to achieve maxillary sinus floor augmentation, presenting promising results.[13,14,15,16] Choukroun et al.[17] evaluated the potential of PRF in combination with FDBA to enhance bone regeneration in sinus floor elevation. The results showed that healing period is reduced from 8 months to 4 months between sinus floor procedures and implant placement. Furthermore, the quantity of bone material used to fill the sinus cavity can be safely reduced without injuring the final bone density.

The use of platelet-rich fibrin in the treatment of intra-bony defects showed an greater reduction in Pocket depth, more clinical attachment level (CAL) gain, and greater intrabony defect fill.[18,19] According to Chang et al.[20] PRF promotes expression of phosphorylated extracellular signal-regulated protein kinase (p-ERK), osteoprotegerin (OPG), and alkaline phosphatase (ALP) activity that will help in periodontal regeneration. Simonpieri et al.[21] mentioned the concept of "natural bone Regeneration" (NBR), which includes regeneration through PRF membranes both the bone volume and gingival tissue. The same authors reported satisfactory clinical results related to reshaping the whole alveolar bone and the restoration of gingival volume and peri-implant bone, achieving adequate mechanical and aesthetic properties.

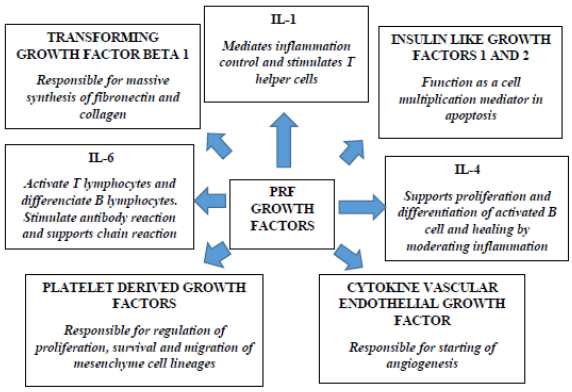

Fig 1: Platelet-rich fibrin growth factors

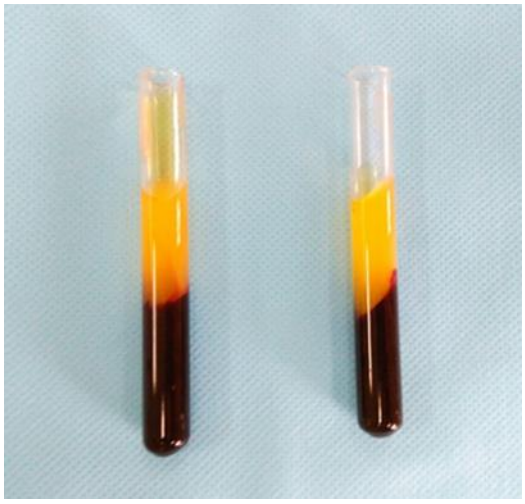

Fig 2: PRF Layer.

The use of PRF as a tissue engineering scaffold was investigated by many researchers for the past few years. In a study by Gassling et al. reported that PRF appears to be superior to collagen as a scaffold for human periosteal cell proliferation and PRF membranes can be used for in vitro cultivation of periosteal cells for bone tissue engineering. Thus PRF is a potential tool in tissue engineering but clinical aspects of PRF in this field requires further investigation.[22]

According to Boora et al[23] PRF could be considered as a healing biomaterial with potential beneficial effect on peri-implant tissue and can be used as a therapeutic adjuvant in clinical scenario of one stage, single tooth implant placement procedure in maxillary anterior region. Other authors including Tomar et al.[24] stated that PRF is efficacious material for cell proliferation and differentiation of human dental pulp stem cells with minimal threat of disease transfer. PRF is an autologous preparation and found to be clinically effective and economical biomaterial than any other available regenerative materials including PRP.

PRF PREPARATION

The classical technique for PRF preparation was described by Dr. Joseph Choukroun in 2000. For preparation of PRF, blood sample is collected from the patient without anticoagulant using a butterfly needle and 10 ml blood collection tubes. After collection of blood, it is immediately centrifuged on a table-top centrifuge at a rate of 3000 rpm for 10 minutes. After centrifugation, 3 layers are obtained in the test tube (Figure 2). The topmost layer consisting of acellular PPP (platelet poor plasma), PRF clot in the middle and RBCs at the bottom of the test tube. The middle layer of PRF clot is then removed with sterile tweezers and separated from the underlying RBC layer using scissors and then transferred on a sterile dish and stored in a refrigerator. It is supposed that the junction of PRF to the RBC layer is rich in growth factors and therefore this region is preserved.[25]

Currently used centrifugation protocols

There are various centrifugation processing-protocols that are currently being used.

- Original Choukroun's PRF protocol (standard protocol): 10 ml at 3000 rpm / 10minutes
- Dohan Ehrenfest's Group - Leukocyte- and Platelet-Rich Fibrin (L-PRF): 9ml at Speed 2700 rpm / 12 minutes)
- Choukroun's advanced PRF (A-PRF), enriched with leukocytes: 1300 rpm / 8 minutes
- Choukroun's i-PRF (solution/gel): 700rpm/3 minutes

Advantages of using PRF

Some advantages are reported in the literature related to the use of PRF, such as the following:

1. PRF preparation technique is simple and cost effective.

2. It is obtained by autologous blood sample.

3. Minimized blood manipulation.

4. It does not require the addition of external thrombin and thereby reduce the chances of crossinfection.5

5. It has a natural fibrin framework with growth factors and shows slow polymerization.8

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. PRF helps in hemostasis.[26]

9. PRF membrane avoids a donor site surgical procedure and results in a reduction in patient discomfort during the early wound-heal¬ing period.[27]

10. The present studies of PRF shows that it is more effi¬cient and less controversial than PRP.[21]

Disadvantages of using PRF

PRF may present some disadvantages as follows:

1. Minimal experience of clinician is required for PRF manipulation.[21]

2. After centrifugation the final amount of PRF obtained is low.[3]

3. Glass-coated tube is required to achieve clot polymerization.[28]

4. Successful PRF preparation depends on the handling, blood collection time and its transference for the centrifuge.[1]

Application of PRF

The literature reports some applications of PRF clot and PRF membrane, such as:

1. PRF has been used for treatment of gingival recession, intrabony defects, periapical lesions and guided tissue regeneration.[29]
2. It can be used as filling material in avulsion sockets and bony defects.
3. PRF has been used for ridge preservation and bone augmentation in sinus lifts procedures.[5]
4. PRF can be used as a scaffolding material in an infected necrotic immature tooth for pulpal regeneration and tooth revitalization.[30]
5. PRF membranes can be used for in vitro cultivation of periosteal cells for bone tissue engineering.

CONCLUSION

In vitro and *in vivo* studies have demonstrated safe and promising results, without contradictory findings, related to the use of PRF alone or in combination with other biomaterials. It has several advantages and possible indications to be used both in medicine and dentistry. Currently, platelet-rich fibrin seems to be an accepted minimally invasive technique with low risks and satisfactory clinical results.[31]

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

REFERENCES

1. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, *et al.* Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part I: Technological concepts and evolution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:e37-44.
2. Kiran NK, Mukunda KS and Tilak Raj TN. Platelet concentrates: A promising innovation in dentistry. J Dent Sci Res 2011; 2: 50-61.
3. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, et al. Platelet rich fibrin (PRF): A second-generation platelet concentrate. Part IV:clinical effects on tissue healing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101(3):56–60.
4. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, et al. Plateletrich fibrin (PRF): A second-generation platelet concentrate. Part II: plateletrelated biologic features. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101(3):45-50.
5. Gupta V, Bains VK, Singh GP, Mathur A, Bains R. Regenerative Potential of Platelet Rich Fibrin In

Dentistry: Literature Review. Asian J Oral Health Allied Sci 2011; 1(1):22-28

6. de Gaetano G. A new blood corpuscle: an impossible interview with Giulio Bizzozero. Thromb Haemost 2001;86:973–9.

7. Harrison P. Platelet function analysis. Blood Rev 2005; 19: 111-123.

8. Prakash S, Thakur A. Platelet concentrates: Past, present and future. J Maxillofac Oral Surg 2011;10:45-9.

9. Corso MD, Toffler M, David M, Ehrenfest D. Use of autologous leukocyte and platelet rich fibrin (L-PRF) membrane in post avulsion sites: an overview of Choukroun's PRF. The journal of implant and advanced clinical dentistry 2010; 1(9):27-35.

10. He L, Lin Y, Hu X, Zhang Y, Wu H. A comparative study of platelet-rich fibrin (PRF) and platelet-rich plasma (PRP) on the effect of proliferation and differentiation of rat osteoblasts in vitro. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;108:707–13.

11. Chang IC, Tsai CH, Chang YC. Platelet-rich fibrin modulates the expression of extracellular signal-regulated protein kinase and osteoprotegerin in human osteoblasts. J Biomed Mater Res Part A: 2010;95A: 327–332.

12. Su CY, Kuo YP, Tseng YH, Su CH, Burnouf T. In vitro release of growth factors from platelet-rich fibrin (PRF): a proposal to optimize the clinical applications of PRF. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:56-61.

13. Diss A, Dohan DM, Mouhyi J, Mahler P. Osteotome sinus floor elevation using Choukroun's platelet-rich fibrin as grafting material: a 1-year prospective pilot study with microthreaded implants. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;105:572-9.

14. Mazor Z, Horowitz RA, Del Corso M, Prasad HS, Rohrer MD, Ehrenfest DM. Sinus floor augmentation with simultaneous implant placement using Choukroun's platelet-rich fibrin as the sole grafting material: a radiologic and histologic study at 6 months. J Periodontol 2009;80:2056-2064.

15. Toffler M, Toscano N, Holtzclaw D. Osteotome-mediated sinus floor elevation using only platelet-rich fibrin: an early report on 110 patients. Implant Dent 2010;19:447–456.

16. Simonpieri A, Choukroun J, Del Corso M, Sammartino G, Ehrenfest DM. Simultaneous sinus-lift and implantation using microthreaded implants and leukocyte-and platelet-rich fibrin as sole grafting material: a six-year experience. Implant Dent 2011;20:2–12.

17. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, Dohan AJ, Mouhyi J and Dohan DM. 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 2006; 101: 299-303.

18. Thorat M, Pradeep AR, Pallavi B. Clinical effect of autologous platelet-rich fibrin in the treatment of intra-bony defects: a controlled clinical trial. J Clin Periodontol 2011; 38: 925–932.

19. Lekovic V, Milinkovic I, Aleksic Z, Jankovic S, Stankovic P, Kenney EB, Camargo PM. Platelet-rich fibrin and bovine porous bone mineral vs. platelet-rich fibrin in the treatment of intrabony periodontal defects. J Periodont Res 2012;47(4):409-17.

20. Chang YC, Zhao JH. Effects of platelet-rich fibrin on human periodontal ligament fibroblasts and application for periodontal infrabony defects. Aust Dent J. 2011; 56: 365–371.

21. Simonpieri A, Del Corso M, Vervelle A, Jimbo R, Inchingolo F, Sammartino G and Dohan Ehrenfest DM. Current knowledge and perspectives for the use of platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in oral and maxillofacial surgery part 2: Bone graft, implant and reconstructive surgery. Curr Pharm Biotechnol 2012; 13: 1231-1256.

22. Agrawal M, Agrawal V. Platelet rich fibrin and its applications in dentistry-A review article. Natl J Med Dent Res 2014 Apr 1;2(3):51.

23. Boora P, Rathee M, Bhoria M. Effect of platelet rich fibrin (PRF) on peri-implant soft tissue and crestal bone in one-stage implant placement: a randomized controlled trial. J Clin Diagn Res 2015 Apr;9(4):ZC18-ZC21

24. Tomar A, Bhatt A, Pant V, Pant AB. Evaluation Of Biological Effect Of Platelet Rich Fibrin on the Proliferation and Osteogenic Differenciation of Cultured Human Dental Pulp Stem Cell An- In Vitro Study. J Pharm Sci Exp Pharmacol 2016;5(3):628-648.

25. Malathi K, Muthukumaraswamy A, Beri S. Periodontal regeneration of an intrabony osseous defect with combination of platelet rich fibrin and bovine derived demineralized bone matrix: A case report. IOSR-JDMS 2013; 4(2):20-26

26. Naik B, Karunakar P, Jayadev M, Marshal VR. Role of Platelet rich fi brin in wound healing: A critical review. J Conserv Dent 2013;16(4):284-93.

27. Jankovic S, Aleksic Z, Klokkevold P, Lekovic V, Dimitrijevic B, Kenney EB and Camargo P. Use of platelet-rich fibrin membrane following treatment of gingival recession: a randomized clinical trial. Int J Periodontics Restorative Dent 2012; 32: e41-50.

28. Dohan DM, Del Corso M and Charrier J-B. Cytotoxicity analyses of Choukroun's platelet-rich fibrin (PRF) on a wide range of human cells: The answer to a commercial controversy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007; 103: 587-583.

29. Ari G, Kumar A, Ramakrishnan T. Treatment of an intrabony defect combined with an endodontic lesion: a case report . ENDO (LondEngl) 2010; 4(3):215–222.

30. Shivashankar VY, Johns DA, Vidyanath S, Kumar MR. Platelet Rich Fibrin in the revitalization of tooth with necrotic pulp and open apex. J Conserv Dent 2012;15:395-398.

31. Borie E, Olivi DG, Orsi IA, Garlet K, Weber B, Beltran V, Fuentes R. Platelet-rich fibrin application in dentistry: a literature review. Int J Clin Exp Med 2015;8(5):7922-7929.