

## **The uses and application of Platelet Rich Fibrin in clinical practice**

### **ABSTRACT**

Platelet derivatives are commonly used in wound healing and tissue regeneration. Different procedures of platelet preparation may differentially affect growth factor release and cell growth. Preparation of platelet-rich fibrin (PRF) is accompanied by release of growth factors, including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF) and transforming growth factor b1 (TGFb1), and several cytokines. When compared with the standard procedure for platelet-rich plasma (PRP), PRF released 2-fold less PDGF, but 415-fold and 42-fold VEGF and TGFb1, respectively.

**KEYWORDS:** "Wound healing", "Platelet rich fibrin", "Bone regeneration"

### **INTRODUCTION**

The maxillofacial bone that is lost as a result of conditions such as tumour surgery, alveolar bone atrophy succeeding tooth loss, periapical periodontitis resulting in periapical bone deterioration, and alveolar cleft has a significant impact on the individual physical and mental health. The biggest obstacle in clinical research is the creation of biologically active operative additive that may control inflammation and promote healing. As a result, there is a greater need for bone regeneration research.<sup>[1]</sup> Tissue engineering is a multidisciplinary area that tries to anticipate regeneration restoring damaged and supportive tissue, such as cells, tissues, and organs, due to a variety of biological situations, such as congenital anomalies, injury, disease, and aging<sup>[2]</sup>. Platelet Rich Fibrin (PRF), which has been used in a variety of applications, is one area of research that has gotten a lot of interest in recent years<sup>[3]</sup>. PRF is a second-generation platelet concentrate which does not contain anti-coagulating factors, the first generation being the Platelet Rich Plasma. Choukron et al. was the first person to define platelet-rich fibrin.<sup>[4]</sup>

Platelet Rich Plasma (PRP) was formerly a popular platelet aggregate. Despite its extensive usage, one of its most serious flaws was the presence of anticoagulant factors, which slowed normal wound healing.<sup>[5]</sup> Further research was focused on generating a second generation platelet concentrate without the usage of anticoagulant agents due to the identified limitations.<sup>[6]</sup>

PRF has the ability to facilitate wound closure, accelerate bone healing, and improve graft survival without causing complications.

PRF has several advantages over PRP which include <sup>[7]</sup>

- Easy and less time-consuming preparation time
- Better handling and utilization properties
- Economic
- No additional additives such as anticoagulant or thrombin or calcium chloride needed unlike PRP
- Simple processing and carriage to the operating site

PRF cannot be stored in tissue banks as it has circulated immune cells and all the antigenic plasmatic molecules is strictly donor specific so it cannot be used as allogenic graft material.<sup>[8]</sup> PRF can be used as a wound adjuvant since it has all of the critical criteria for successful wound healing. However various parameters of PRF still need to be clinically tested before it can be incorporated in routine practice.<sup>[8]</sup>

### Wound healing

Rapid wound healing is desirable in order to achieve optimal functional repair. The ultimate alveolar bone density and architecture are influenced by the wound healing process following tooth extraction. Wound healing takes place in multiple steps namely haemostasis, inflammation, proliferation, and remodelling. It's a meticulously planned affair, and adequate wound care is critical to speed up the healing process. Wound healing is a complex process and any interruption or failure leads to delayed healing or non-healing wound.<sup>[4]</sup> Platelets are known to have a role in haemostasis regulation by obliterating arteries and facilitating fibrin clot formation.

Platelets release various growth factors that speed up healing, including platelet derived growth factor, vascular endothelial growth factor, epidermal growth factor, fibroblast growth factor, transformin growth factor, and insulin like growth factor..<sup>[4]</sup>

PRF is a promising biomaterial for unmistakable improvement and quicker recovery of bone after exodontia strategy.

### Bone Regeneration

Bone loss after transalveolar extraction is a topic of consent for all maxillofacial surgeon. Autologous bone grafting is a method most commonly and successfully is used for such bone defect but it has is a disadvantage of donor site morbidity which can create complication. Tissue regeneration is an area that attempts to repair, restore or regenerate cells, tissues, and organs. Platelet -Rich Plasma (PRP), is an upcoming adjunct to promote bone repair and regeneration. It is a platelet concentrate that contains a variety of bone healing growth factors (GFs), including GF- $\beta$ , vascular endothelial growth factor (VEGF), and epithelial growth factor (EGF). PRF possesses regenerative and stimulatory qualities, making it an excellent biomaterial for tissue repair and regeneration. It has a three dimensional structure that promotes bone growth by creating a conductive microenvironment<sup>[9]</sup>. PRF possesses the

potential to improve cellular migration, proliferation, differentiation, and mineralization during osteogenesis. When placed in tissues PRP resorbs completely, thus avoiding the need for a second surgery for its retrieval. Additionally, it can be used in a gel consistency or as a filler in the split crest bone gap.

PRF seems to be a reliable material for promoting faster bone regeneration after extractions. It also increases bone density which makes it useful in accelerating hard tissue regeneration.<sup>[11]</sup>

According to Nesligul Niyaz Kokdere, Timucin, Yavuz Findik that PRF favours new bone formation and osteoblasts when combined with autogenous bone grafts. PRF has haemostatic effect which is important for keeping the particles of graft together in defect. This implies that using PRF reduces the need of a membrane for stabilizing graft particles. Further studies need to be done to assess the combined application of PRF and autogenous grafts<sup>[13]</sup>.

The study conducted by Nesligul Niyaz Kokdere, Timucin, Yavuz Findik states that when PRF is used in bony defects there is faster healing of the bone and less time is needed for rehabilitation. Keeping in view of its benefits there is a greater need for bone regeneration research pertaining to the use of PRF in routine practice<sup>[12]</sup>. After bone augmentations, platelet products are added to various types of graft materials, resulting in a more predictable outcome<sup>[14-17]</sup>.

### **Literature searched**

According to Manzoor Mohammad Dar in his study, to determine healing potential of platelet rich fibrin in extraction sockets of impacted mandibular third molar. He did study on 30 patient(60 sockets) requiring removal of mesioangular impacted mandibular third molar bilaterally the target population was divided into two groups : test group and control group. Out of two extraction socket in each patient one side belong to test group and other to control. Test group was the one which received PRF in extraction socket and in control group's extraction socket spontaneous healing was allowed to occur. Post operatively patients were evaluated for pain, swelling, periodontal health and bone healing. The results of the study showed less pain, swelling and improved bone healing in test groups. Bone healing and lamina dura formation was more significant at the end of fourth week than twelve week postoperatively.<sup>[10]</sup>

According to Amit Shrivastava, Ramakrishna Shenoi, and Anup Garg Purpose of this clinical trial was to compare how capable healing and bone regeneration is through PRF as compared to naturally healing socket. Platelet-rich fibrin looks to be a good alternative for extraction socket repair, with good results and few concerns. In this study, bone density was assessed and compared in total 120 participants to evaluate extraction wound healing using PRF gel and the control group on RVG. STATA Version10 was utilised for statistical analysis<sup>[4]</sup>.

According to Shahram Ghanaati, Patrick Booms, Advanced PRF was the subject of a study Lowering the rpm and increasing the centrifugation duration enhanced the presence of neutrophilic granulocytes in the distal region of the produced clot in the A-PRF group. In the S-PRF group, neutrophils were mostly found near the red blood cell (RBC)-BC interface. Monocyte transformation into macrophages is aided by neutrophilic granulocytes. The PRF scaffold was made as per the methodology that has previously been published. This study included four healthy individual ranging from 18 to 60 years old. Four tubes containing peripheral blood were taken from each participant and put in a centrifuge that had been pre-programmed (PC-O2, PROCESS for PRF, Nice, France). The following two methods were

employed for centrifugation: (1) sterile glass coated plastic tube, standard PRF S-PRF (9 mL; for 12 minutes at 2700 rpm), and (2) advanced PRF, sterile plain glass-based vacuum tubes (10 mL; for 14 minutes at 1500 rpm). A-PRF results to be an optimal source of autologous cells (particularly macrophages and neutrophils), allowing mutual stimulation and result in a rapid connection for tissue regeneration<sup>[12]</sup>.

## Conclusion

The loss of bones in the maxillofacial area due to surgery, periapical bone loss, alveolar bone atrophy after tooth loss, and alveolar cleft has an impact on a person's physical and mental well-being.

PRF is a platelet aggregate that can be used with grafts for promoting bone growth, stabilisation wounds, provide haemostasis and improve handling properties of grafts. It provides significant postoperative protection of the wound and surgical site. PRF as a platelet gel can be used for bone healing and development, wound fixing, haemostasis and improve the working of particulate graft materials.

The prime advantage of PRF over PRP are that PRF requires no biochemical handling of blood, it's made in a simplified and cost-effective manner with no requirement of bovine thrombin and anticoagulant. Despite its several advantages the method of its preparation is not always feasible because it requires an expensive centrifuge machine. Furthermore, PRF cannot be stored in tissue banks. As it has antigenic potential PRF films are recipient specific and cannot be used as a universal graft material.

Hence more research is needed to find alternative economic solutions for preparing PRP as well as finding more ways to develop it as an allogeneous graft material.

### **COMPETING INTERESTS DISCLAIMER:**

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## References

1. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, Gogly B. Platelet rich fibrin (PRF): a second-generation platelet concentrate. Part 1 : technological concepts and evolution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:e37-44.
2. Coury, A.J. Expediting the transition from replacement medicine to tissue engineering. Regen Biomater 3, 111, 2016.
3. Rouwkema, J., and Khademhosseini, A. Vascularization and angiogenesis in tissue engineering: beyond creating static networks. Trends Biotechnol 34, 733, 2016.

4. Shrivastava A, Shenoi R, Garg A, Vats V, Gadve V, Siddiqui A. Role of Platelet Rich Fibrin in Healing of Extraction Socket. IJCMR. 2018;5:E6-10.

5. Miron RJ, Fujioka-Kobayashi M, Bishara M, Zhang Y, Hernandez M, Choukroun J. Platelet-rich fibrin and soft tissue wound healing: a systematic review. Tissue Engineering Part B: Reviews. 2017 Feb 1;23(1):83-99.

- 6. Choukroun J., 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 101, e56, 2006

7. Toffler M, Toscano N, Holtzclaw D, Corso MD, Dohan Ehrenfest D. JIACD Continuing education. Introducing Choukroun's platelet rich fibrin (PRF) to the reconstructive surgery milieu. J Implants Advan Clin Dent 2009;1:21-31

8. Anantula K, Annareddy A. Platelet-rich fibrin (PRF) as an autologous biomaterial after an endodontic surgery. Journal of Dr. NTR University of Health Sciences. 2016 Jan 1;5(1):49.

9. Liu Y, Sun X, Yu J, Wang J, Zhai P, Chen S, Liu M, Zhou Y. Platelet-rich fibrin as a bone graft material in oral and maxillofacial bone regeneration: classification and summary for better application. BioMed research international. 2019 Dec 6;2019.

10. Dar MM, Shah AA, Najjar AL, Younis M, Kapoor M, Dar JI. Healing potential of platelet rich fibrin in impacted mandibular third molar extraction sockets. Annals of maxillofacial surgery. 2018 Jul;8(2):206.

11. Dambhare, A., Bhongade, M.L., Dhadse, P., V., Sehdev, B., Ganji, K.K., Thakare, K., Murakami, H., Sugita, Y., Maeda, H., Alam, M.K., 2019. A Randomized Controlled Clinical Study of Autologous Platelet Rich Fibrin (PRF) in Combination with HA and Beta-TCP or HA and Beta-TCP Alone for Treatment of Furcation Defects. JOURNAL OF HARD TISSUE BIOLOGY 28, 185–190

12. Ghanaati S, Booms P, Orlowska A, Kubesch A, Lorenz J, Rutkowski J, Landes C, Sader R, Kirkpatrick CJ, Choukroun J. Advanced platelet-rich fibrin: a new concept for cell-based tissue engineering by means of inflammatory cells. Journal of Oral Implantology. 2014 Dec;40(6):679-89.

13. Kökdere NN, Baykul T, Findik Y. The use of platelet-rich fibrin (PRF) and PRF-mixed particulated autogenous bone graft in the treatment of bone defects: An experimental and histomorphometrical study. Dental research journal. 2015 Sep;12(5):418.

14. Toffler M, Toscano N, Holtzclaw D, Corso MD, Dohan DM. Introducing Choukroun's platelet rich fibrin (PRF) to the reconstructive surgery milieu. J Implant Adv Clin Dent. 2009;1:22–31.

15. Dohan DM, Del Corso M, Diss A, Mouhyi J, Charrier JB. Three-dimensional architecture and cell composition of a choukroun's platelet-rich fibrin clot and membrane. Ann Maxillofac Surg. 2011;1:53–7.

16. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, et al. 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.

17. Sohn DS, Moon JW, Moon YS, Park JS, Jung HS. The use of concentrated growth factor (CGF) for sinus augmentation. *J Oral Implant.* 2009;38:25–38.

UNDER PEER REVIEW