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I-PRF SUPER PRF AS PERIODONTAL REGENERATIVE MATERIAL- A SHORT REVIEW & CASE REPORT.

Dental Science

Dr. Prashansa Sharma	BDS MDS (Department of Periodontology) Sr. Lecturer, I.T.S Dental College Muradnagar, Ghaziabad.
Dr. Surinder Sachdeva	BDS MDS (Department of Periodontology)Head & Professor , MMCDSR.
Dr. Shivam Agarwal	BDS MDS (Department of Oral And Maxillofacial Surgery), Sr. Lecturer I.T.S Dental College Muradnagar, Ghaziabad.
Dr. Tarun Gaur	BDS MDS (Department of Prosthodontics) Sr. Lecturer, I.T.S Dental College Muradnagar, Ghaziabad.
Dr. Sanjay Talnia	BDS MDS (Department of Oral And Maxillofacial Surgery) Sr. Lecturer, Swami Devidayal Dental College & Hospital, Haryana.

ABSTRACT

Search for various biomaterial for periodontal regeneration is always the topic of interest. Most important requirement for biomaterial is presence of good amount of growth factors that can promote periodontal regeneration that to at fast rate. In this review, new bioactive material i-PRF (injectable platelet rich fibrin) that is autologous, rich in growth factors and stem cells with wide range of clinical implications has been discussed.

KEYWORDS

Platelet Concentrate, i-PRF, Biomaterial, Sticky Bone, Injections

INTRODUCTION

Among the great challenges facing clinical research is the development of bioactive surgical additives regulating inflammation and increasing healing. The healing of hard and soft tissue is mediated by a wide range of intra and extracellular events that are regulated by signaling proteins. Understanding the entire process is still incomplete. However, it is known that platelets play a crucial role not only in hemostasis, but also in the wound healing process

A blood product prepared from a single donor, which increases platelet count by 5-10 x 109/L/m2 body surface area (5-10,000/μL) is called Platelet Concentrate.[1]

With our improved understanding regarding cellular and molecular mechanism involved in periodontal wound healing application of platelet concentrates have been introduced to achieve maximum periodontal regeneration. Platelet concentrates are the blood extracts obtained after various processing of a whole blood sample, mostly through centrifugation. The objective of the processing is to separate the blood components in order to discard elements considered as not usable (mostly the red blood cells, heavy and easily separated) and to gather and concentrate the elements that may be use for therapeutic applications (fibrinogen/fibrin, platelets, growth factors, leukocytes and other forms of circulating cells, in solution in liquid plasma).[2] With time, this concept of optimization of healing evolved to a more sophisticated concept of tissue regeneration promoted by the growth factors and the cells contained in these preparations: initially considered as surgical adjuvants, the PRP/PRF became the promoted glorious instruments of new regenerative medicine strategies. The rationale behind use of platelet concentrate is to provide these growth factors in high concentrations in the healing area.[3,4]

Research of i-PRF («i» as injectable) has been directed towards obtaining a blood concentrate with very high leukocyte content but which coagulates few minutes after the end of spin. The use of platelet concentrates in «liquid» and not coagulated remains an important indication in various medical and dental applications.[3]

TECHNIQUE

The classical technique for PRF preparation was invented by Dr. Choukroun in 2000. It is the current PRF technique authorized by the French Health Ministry in which PRF is prepared without using an anticoagulant during blood harvesting or bovine thrombin during gelling. Blood specimen is collected or drawn from the patient intravenously. The blood specimen is drawn in the test tube and centrifuged and allowed to spin immediately for the stipulated time. Following this the blood sample settles into various layers. Three different layers are formed which are as follows:

- Red colored lower fraction containing the RBCs
- Middle fraction containing the fibrin clot
- Straw-colored upper fraction contains acellular plasma or platelet poor plasma.

The results of this technique depend on speed of blood collection and its transfer to centrifuge. The upper portion of the test tube contains the acellular plasma which is removed. The middle portion containing the fibrin clot is then removed by the help of tweezer and is been squeezed off from the lower part that contains the red blood cells.

The centrifugation time for i-PRF varies from 2-12 minutes at 3300 rpm.(Fig 1) To get higher growth factors, the centrifuge is stopped after 2 minute-centrifugation and take i-PRF tube out of the centrifuge first. The non-coated tube shows 2 different layers. The upper layer is i-PRF layer and red blood cell is collected in bottom layer which will be is discarded. Upon termination of this process, it is possible to observe an orange color area in the tube (i-PRF) and the remaining blood materials below. Then, the tubes were opened carefully, to avoid homogenization of the material. We collected 5 ml of i- PRF from the tubes using a 20ml syringe with a 18G hypodermic needle.[5] i-PRF has property of getting polymerized when mixed with bone graft in 7-10 mins. Resulting in bone graft with superior handling property and is famous by name STICKY BONE GRAFT.(Fig 2,3)

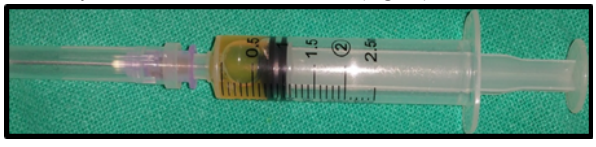

Fig1 Liquid (i-PRF)

Fig 2 Polymerized (clot) forms with bone graft

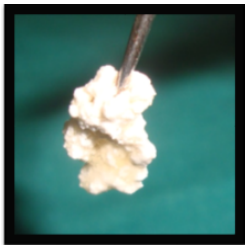

Fig 3 Sticky bone or steak technique .

CASE REPORT
Case 1: Patient name Satish kumar aged 42 Years reported to department of Periodontology with chief complain of missing tooth and wanted to get new set of artificial teeth. On radiographic examination revealed very less bone support for any further treatment. Patient had no contraindication to surgery.(Fig 4)

CASE MANAGEMENT Ridge augmentation using sticky bone (FDBA AND i-PRF) and PRF Membrane was planned. Two vertical incision to expose the site were given, corticotomy was done to induce fresh bleeding. Sticky bone was formed using the above discussed protocol. FDBA Bone graft was procured from TATA Memorial tissue bank which was combined with i-PRF to form Sticky Bone. Suture were given to close the site.(Fig 5,6,7) After 6 months post operative IOPA was taken which showed marked improvement in bone density.(Fig 8,9)

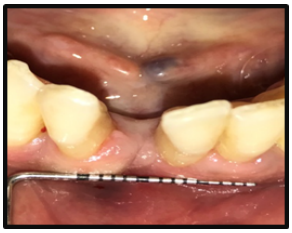

Fig 4 Ridge Defect

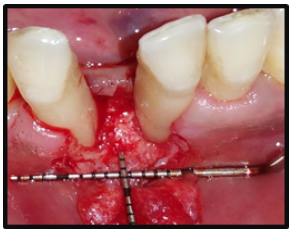

Fig 5 Intraoperative defect

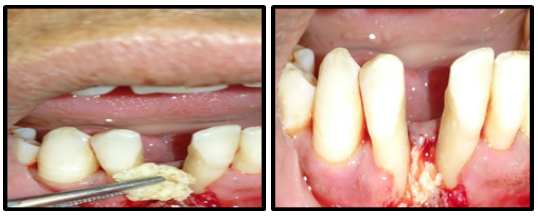

Fig 6 Sticky Bone Placement

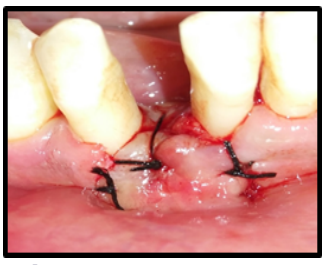

Fig 7 Suture placed.

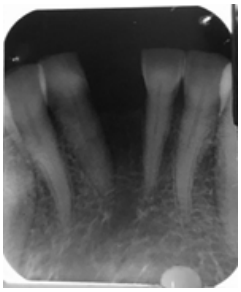

Fig 8 Pre-Operative

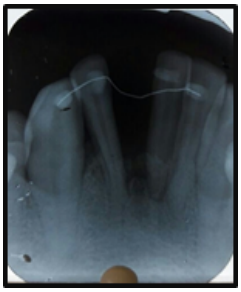

Fig 9 Post-Operative

Case 2:
Patient name Saloni Sharma aged 37 Years reported to department of Periodontology with chief complain of sensitivity in lower anteriors. Clinically there was recession of 2mm in 41 and 1mm in 31.(Figure 10)

CASE MANAGEMENT As a treatment modality Coronally advanced flap with PRF membrane saturated with i-PRF as graft material was used. After 5 days results showed marked improvement in Gingival Biotype. (Fig 11,12,13,14)

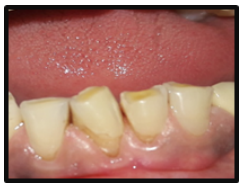

Fig 10:Recession Defect

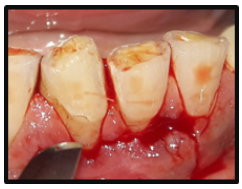

Fig 11: Incision given.

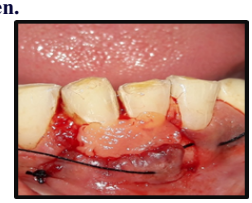

Fig-12 PRF membrane saturated with i-PRF

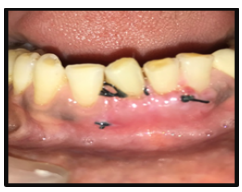

Fig- 13 one day Postoperative

Fig 14 Ten day Postoperative

DISCUSSIONS
According to the results of this study, Injectable-PRF is effective in treating various regenerative treatment modalities. Significant improvements in clinical parameters were observed. Further long term studies are needed. The protocol i-PRF is a real scientific and clinical innovation and will allow many practitioners to improve their results in bone grafting.

The concept behind the injectable form of i-PRF is to include the majority of the cells from the blood. As recently the role of WBC as monocytes on bone regeneration and vessel growth emerged. Monocytes play an essential on bone growth, vascularization and production of vascular endothelial growth factors (VEGF). They also have receptor for BMP and can produce BMP-2.6 we are not only getting whole amount of cells from the blood, white cells, platelets but also other cells like circulating stem cell and endothelial cells both of which are essential fuel for any regenerative procedure. So, we should consider the i-PRF as "Blood concentrate" and not platelet concentrates.7

The possibility of bonding of i-PRF with biomaterials for bone grafting creates an alternative to PRP as a platelet aggregate for bone regeneration in liquid form. Sticky bone is biologically solidified bone graft which is entrapped in fibrin network. Sticky bone graft doesn't scatter even upon being shaken with cotton plier because particulate bone powders are strongly interconnected each other by fibrin network. As alternative to titanium mesh or block bone procedure, sticky bone was introduced in 2010.

Sticky bone has numerous **ADVANTAGES:**

- it is moldable, so well adapted over various shape of bony defect
- Micro and macro movement of grafted bone is prevented. So the volume of augmentation is maintained during healing period, therefore the need of block bone and titanium mesh is minimized
- Fibrin network entraps platelets and leukocytes to release growth factors, so bone regeneration and soft tissue is accelerated
- No biochemical additives are needed to make sticky bone unlike PRP or PRGF
- Fibrin interconnection minimizes soft tissue ingrowth into the sticky bone graft.

CONCLUSION

The recent advances in PRF technology are based on the concept which enables the scaffold of PRF to be tailored for specific clinical applications by changing the centrifugation protocol and time. These super PRFs are said to contribute for faster and effective handling characteristics and bonding with the biomaterials. However, as these studies on advanced PRFs are still in infancy, many more multi-centered, randomized clinical trials using different forms of PRF are required to assess the superiority of each of these super PRFs in effective and faster wound healing. In both the case reports i-PRF have yielded good clinical results

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CONFLICTS OF INTEREST:

There are no conflicts of interest.

S. No	Author/Year	Type of study& Intervention	Intervention	Results
1	Mustafa Abd El Raou(2017)	Animal study -Rabbit knee defect	i-prf vs PRP -Critical-sized osteochondral defects 5 mm in diameter and 5 mm in depth	Histological Analysis At 4 weeks-Better cartilage regeneration and maintained at b12 weeks as compared to PRP.8
2	Jonathan B. Albilia(2018)	Case Study	I-PRF Injection -temporomandibular joint (TMJ) pain and dysfunction	Thirty-three of 48 TMJs (69%) showed significant reduction in pain at 8 weeks, and at 3, 6, and 12 months (Responders). Fifteen of 48 TMJs (31%) did not improve (Non-responders). The best Responders to liquid PRF injections were ID stages Wilkes' IV (78.5%) and V (100%), compared to Wilkes' I (0%), II (47%), and III (33%). A non-significant, but notable decrease in dysfunction was found.[9]
3	Ritika Arora(2019)	Case report 3 patient	Alopecia	The results were based on the clinical outcomes and subjective questionnaire based on the patient's satisfaction. Hair growth with i-PRF has better regenerative potential.[10]
4	Xuzhu Wang(2017)	In vitro study	first cell study evaluating the potential of i-PRF on any cell-type. Human primary osteoblasts were cultured with either i-PRF or PRP and compared to control tissue culture plastic. A live/dead assay, migration assay as well as a cell adhesion/proliferation assay were investigated	The results showed that all cells had high survival rates throughout the entire study period irrespective of culture-conditions. While PRP induced a significant 2-fold increase in osteoblast migration, i-PRF demonstrated a 3-fold increase in migration when compared to control tissue-culture plastic and PRP. While no differences were observed for cell attachment, i-PRF induced a significantly higher proliferation rate at three and five days when compared to PRP.11
5	Onur Ucak Turer(2019)	Controlled randomized clinical trial	72 patients with Miller class I and II gingival recessions were enrolled. 36 patients were randomly assigned to the test group (CAF+CTG+i.PRF [700 rpm for 3 min]) or control group (CAF+CTG). Clinical evaluations were made at 6 months.	At 6 months, complete root coverage was obtained at 88% of the sites treated with CAF+CTG+i.PRF and 80% of the sites treated with CAF+CTG. Difference be. tween the two groups was not statistically significant. At 6 months, the recession depth (RD) reduction and increase in keratinized tissue height (KTH) of the test sites were significantly better compared with the control sites.[12]
6	Prerna Ashok Karde(2017)	In vitro study	To evaluate the antimicrobial property, and platelet count of i-PRF in comparison to other platelet concentrates, i.e., PRF, platelet-rich plasma (PRP), and control (whole blood).	Statistical significance was analyzed by one-way analysis of variance (ANOVA). P <0.05 was considered statistically signifi cant. Mean zone of inhibition around i-PRF ($P < 0.01$) and PRF ($P < 0.05$) showed statistical signifi cance. Although a distinct zone of inhibition was seen with PRP, it was not statistically signifi cant ($P > 0.05$). i-PRF showed statistically signifi cant difference ($P < 0.001$) in platelet count when compared to control. It was also significant when compared to PRP ($P < 0.01$), PRF ($P < 0.001$).[13]
7	Richard J. Miron(2016)	In vitro Study	Standard PRP and i-PRF (centrifuged at 700 rpm (60G) for 3 min) were compared for growth factor release up to 10 days (8 donor samples). Furthermore, fibroblast biocompatibility at 24 h (live/dead assay); migration at 24 h; proliferation at 1, 3, and 5 days, and expression of PDGF, TGF-β, and collagen1 at 3 and 7 days were investigated.	higher levels of total long-term re-lease of PDGF-AA, PDGF-AB, EGF, and IGF-1 after 10 days with i-prf.Also highest mRNA levels of TGF-β at 7 days, PDGF at3 days, and collagen1 expression at both 3 and 7 days when compared to PRP.6
8	Bozan Serhat İzol	Controlled randomized clinical trial	Therapeutic effect of Injectable Platelet-Rich Fibrin (I-PRF) as root biomodification agent on root coverage of free gingival graft surgery.	40 patients with Miller class I or II gingival recession were randomly divided into 2 groups, including control group treated only with free gingival graft (FGG) and patients in the experiment group were treated with free gingival graft and injected with I-PRF as a root surface biomodification agent (FGG+I-PRF). Showing better results in experimental group.[14]
9.	Ozsagir ZB, Saglam E, Sen Yilmaz B, Choukroun J, Tunali M	Split mouth study	33 systemically healthy patients with thin gingival phenotype were treated with i-prf on one side and Microneedling on other side of same patient at 4 session with 10 day interval.	After the evaluation of GT between the groups, a statistically significant difference was found in MN + i-PRF group at the sixth month. In the intra-group comparisons, a statistically significant increase in GT was observed within both i-PRF [from 0.43 mm ± 0.14 to 0.62 mm ± 0.11 ($p < .001$)] and MN + i-PRF [from 0.4 mm ± 0.14 to 0.66 mm ± 0.12 ($p < .001$)] groups at the sixth month.15

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