



## IS COMBINATION THERAPY OF PLATELET RICH FIBRIN WITH METRONIDAZOLE OR ALLOGRAFT BETTER IN THE TREATMENT OF INFRABONY DEFECTS? - A CASE REPORT

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### ABSTRACT

**Introduction:** Endogenous regenerative technology (ERT) such as platelet rich fibrin triggers the self-repair mechanism and promotes the host's innate potential for regeneration. Modification of ERT by incorporation of drugs or in conjunction with other regenerative materials have gained interest recently.

**Objective:** To comparatively evaluate the efficacy of platelet rich fibrin (PRF) with metronidazole, PRF with demineralized freeze-dried bone allograft (DFDBA) and PRF alone in the treatment of infrabony defects both clinically and radiographically.

**Methodology:** A 48-year-old patient having infrabony defects in four sites was selected using grid IOPA. Clinical parameters like Plaque index, Gingival index, Probing pocket depth and Clinical attachment level was recorded at baseline, 1month, 3months and 6months. The defects in 2 sites were treated with PRF+Metronidazole (MTZ) and either of the other 2 sites with PRF+DFDBA and PRF alone respectively. Open flap debridement was accomplished before the placement of either of the material. Radiographic changes were recorded at 3 months and 6 months.

**Results:** The clinical and radiographic parameters showed improvement as compared to baseline in all the sites. The sites treated with PRF+MTZ and PRF+DFDBA showed better results as compared to the site treated with PRF alone.

**Conclusion:** The combination of PRF+MTZ and PRF+DFDBA were proven to be better than PRF alone. Further, long term clinical trials with larger samples should be carried out to assess a complete periodontal regeneration rather than bone regeneration.

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### INTRODUCTION

Regeneration has been defined as “the reproduction or reconstitution of a lost or injured part to restore the architecture and function of the periodontium.”<sup>1</sup> To increase the predictability of the periodontal regenerative procedures an orchestrated sequence of biologic events such as cell migration, adherence, growth and differentiation are required. Repair by the formation of long junctional epithelium occurs with the conventional technique such as open flap debridement. Thus, the objective of regeneration is not fulfilled with conventional method.

In the field of regeneration, endogenous regenerative technology (ERT) has acquired its place as it can initiate latent self-repair mechanisms in patients and promote the host's innate capacity for regeneration.<sup>2</sup>

Platelet-rich fibrin (PRF) is the most widely used ERT. It was first described by Choukroun *et al.* in 2004 in France.

It has been referred to as a second-generation platelet concentrate because the natural concentrate is produced without any anticoagulants or gelifying agents.<sup>3</sup> The PRF composition consists of an intimate assembly of structural glycoproteins, cytokines, and glycanic chains enmeshed within a slowly polymerized fibrin network.

The preparation and the use of PRF, a concentrated suspension of the growth factors found in platelets is being widely used in dentistry. These growth factors are postulated as promoters of tissue regeneration for its role in wound healing. Platelet concentrate contains platelet-derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), etc. growth factors that modulate and up-regulate growth factor function.<sup>4</sup>

Currently, drugs have also been incorporated into ERT to create a material alcove in an injured site where the progenitor/stem cells from neighbouring tissues can be employed for in situ periodontal regeneration.<sup>5</sup>

Metronidazole (MTZ) is a broad-spectrum antimicrobial drug mainly acting against protozoal and anaerobic bacterial infections (Tracy and Webster 1996, Lamp *et al.* 1999).

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MTZ is very effective against periodontic pathogens and is used solely or in combination with amoxicillin in the treatment of periodontal diseases (Winkelhoffvan *et al.* 1989, American Academy of Periodontology 1996, Elter *et al.* 1997, Winkelet *al.* 2001, Slots and Ting 2002). Hence, MTZ is a drug of interest for periodontist for treating periodontitis-induced alveolar bone loss.

The use of bone graft in ERT has also been proven to have potential regenerative properties that helps to achieve the goal of periodontal regeneration. The bone graft used in this case is demineralized freeze-dried bone allografts (DFDBA), an allograft which has osteogenic potential.

In the present 6 months follow-up study, we aim to compare the regenerative potentials of PRF with Metronidazole, with bone graft and PRF alone in the treatment of infrabony defects.

**Case Report**

A 48-year-old male patient reported to the Department of Periodontics, A J Institute of Dental Sciences, with a chief complaint of food lodgement and pain in the upper and lower, right and left back tooth region since 4 months. Patient did not give any relevant medical history or history of dental trauma, orthodontic treatment, and no injurious habit was reported.

On intra oral examination, bleeding on probing was present, with probing pocket depth of 7mm, 6mm, 10mm, 8mm, 7mm, 6mm in respect to 16,17,27,37,47and 48 respectively. No mobility was detected. Pulp vitality was negative.

Grid IOPA was taken, which revealed presence of interproximal angular bone loss. The defects were measured as follow 6mm in 16 and 17, 5mm in 27 ,4mm in 37, 3mm in 46 and 4mm in 47.

**The Periodontal Therapy was Planned**

1. Conventional scaling and root planning using ultrasonic instruments and curettes was done as part of non-surgical therapy.
2. The patient was recalled after every week and re-examined for 4 weeks.
3. Surgical periodontal therapy was planned since, pocket persisted even after the non-surgical periodontal therapy.

Haematological evaluation was carried out and was found to be within normal limits.

**PRF Preparation**

In accordance with the protocol developed by Choukroun *et al.* PRF (Fig. 1) was prepared just prior to surgery, intravenous blood from antecubital vein was collected in the 10 ml of sterile tube without an anticoagulant and centrifuged immediately. Blood was centrifuged using a tabletop centrifuging machine for 10 min at 3000 rpm.

**The Resultant Product Consists of Three Layers**

1. Topmost layer consist of acellular platelet poor plasma (PPP).
2. PRF clot in the middle.
3. Red blood cells (RBCs) at the bottom.

PRF was separated from RBCs after removal of PPP and then transferred on to the sterile dappen dish.

**Surgical Procedure**

Intraoral antiseptics was performed using 0.2% chlorhexidine digluconate rinse and iodine solution was used to carry out extra oral antiseptics. Following administration of local anaesthesia, sulcular incisions were made, and mucoperiosteal flap were reflected. Meticulous defect debridement and root planning was carried out with the help of area specific curettes. The direct examination after debridement, confirmed the presence of three walled bony defect. PRF mixed with Metronidazole gel 1% w/w (Metrohex gel) was filled into the infrabony defect of 16 and 17 region. The mucoperiosteal flap were repositioned and secured in place using 3-0 nonabsorbable black silk surgical suture. The simple interrupted sutures were placed. Periodontal dressing was placed. Same procedure was done for the infrabony defect of 47and 48 Fig. 2. The infrabony defect in the region of 27 was filled with PRF mixed with DFDBA bone graft (Fig. 3) and that of 37 was filled with PRF alone (Fig. 4).

**Post-Operative Care**

Antibiotics and analgesics (Amoxicillin 500 mg three times a day for 5 days and Imol plus two times a day for 3 days) were prescribed along with 0.2% chlorhexidine mouth wash twice daily, for 1week. Periodontal pack and sutures were removed after 1 week postoperatively. The patient was instructed for gentle brushing with soft toothbrush. Patient was instructed for oral hygiene maintenance and re-evaluated weekly for 1 month for clinical changes and then 3 and 6 months for radiological changes.

**RESULTS**

On intragroup comparison the clinical parameters like the Plaque index, Gingival index, probing pocket depth and clinical attachment level showed improvement at 3months and 6 months from baseline and at 6 months from 3months. There was greater reduction in the probing pocket depth and clinical attachment gain at the sites that received combination therapy (PRF + MTZ and PRF +DFDBA) (Table 1).The radiographic parameters at 3months and 6 months from baseline showed improvement in all the defect sites (Fig.5-8). The sites treated with combination therapy showed better results (Table 2).

**Table 1** Comparison of the clinical parameters using three different regenerative materials

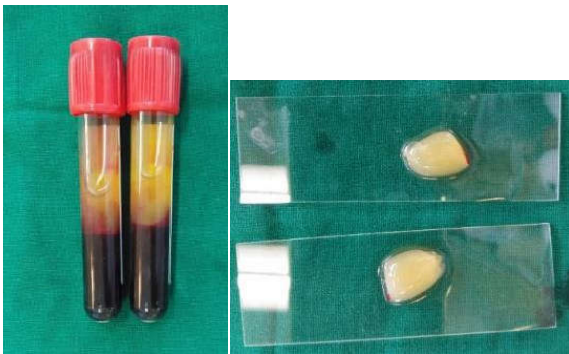
Regenerative material used		Gingival index score	Plaque index score	Probing pocket depth and Clinical attachment level
PRF + Metronidazole	Baseline	3	2	7mm (16) 6mm (17) 7mm (47)
	1 month	2	1.5	
	3 months	1	1	4mm
	6 months	1	1	3mm
PRF + DFDBA	Baseline	3	2.25	10mm (27)
	1 month	2	1.25	
	3 months	1	1	4mm
	6 months	1	1	3mm
PRF	Baseline	3	2	8mm (37)
	1 month	2	1	
	3 months	1	1	5mm
	6 months	1	1	4mm

**Table 2** Comparison of the bone regeneration attained using three different regenerative materials

Regenerative material used	Defect depth at baseline	Bone fill after 3 months	Bone fill after 6 months
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PRF +	7mm (17)	5mm	6mm
Metronidazole	6mm (16)	4mm	5mm
PRF + DFDBA	5mm (47)	5mm	5mm
PRF + DFDBA	6mm (27)	4mm	5mm
PRF	5mm (37)	1mm	2mm



**Fig 1** Platelet-rich fibrin



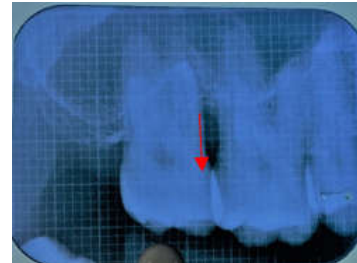
**Fig 2** First and fourth quadrant defect being filled with PRF and Metronidazole gel 1%



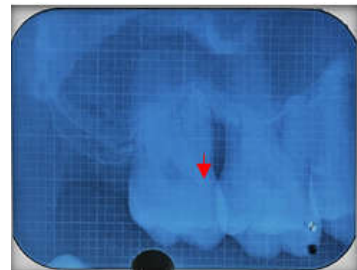
**Fig 3** Second quadrant defect being filled with PRF and DFDBA



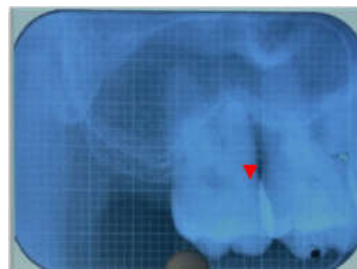
**Fig 4** Third quadrant defect being filled with PRF



**Fig 5a** At baseline

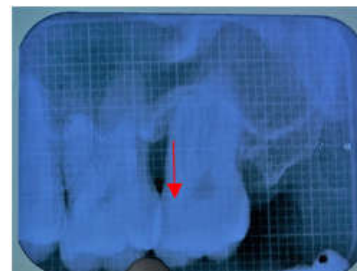


**Fig 5b** 3<sup>rd</sup> month

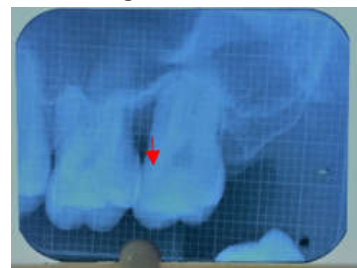


**Fig 5c** 6<sup>th</sup> month

**Fig 5(a-c)** Grid IOPA of the defect in the First Quadrant at baseline, 3<sup>rd</sup> month and 6<sup>th</sup> month



**Fig 6a** At baseline



**Fig 6b** 3<sup>rd</sup> month

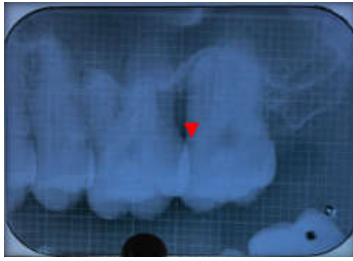


Fig 6c 6<sup>th</sup> month

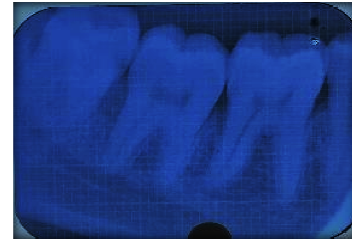


Fig 8c: 6<sup>th</sup> month

Fig 6(a-c) Grid IOPA of the defect in the Second Quadrant at baseline, 3<sup>rd</sup> month and 6<sup>th</sup> month

Fig 8(a-c) Grid IOPA of the defect in the Fourth Quadrant at baseline, 3<sup>rd</sup> month and 6<sup>th</sup> month



Fig 7a At baseline

## DISCUSSION

The success of periodontal therapy is the ability to achieve regeneration of the lost tissues. Over the years many regenerative materials have been used to achieve this goal. In the present study, the effective regeneration of the periodontal tissues using different treatment modalities was compared. It was seen that combination therapy such as metronidazole and DFDBA with PRF showed greater improvement in the clinical and radiographic parameters when compared to that of PRF alone.



Fig 7b 3<sup>rd</sup> month

PRF when used in combination with other regenerative materials has shown significant improvement in its potential to regenerate the lost tissues.



Fig 7c 6<sup>th</sup> month

PDGF and TGF- $\beta$  are the growth factors present in PRF. They help in the protein synthesis in osseous tissues, stimulates angiogenesis, and enhance woven bone formation, etc.

Fig 7(a-c) Grid IOPA of the defect in the Third Quadrant at baseline, 3<sup>rd</sup> month and 6<sup>th</sup> month

The breakthrough in vitro study that introduced PRF in medical field was conducted by Choukran *et al.* It highlighted improved neovascularization, wound closing with accelerated tissue remodelling in the absence of infectious events.<sup>6</sup>

The soft tissue healing and the bone regeneration potential of PRF infused with metronidazole in transalveolar extraction was proven in a study by Tripathi *et al* 2014.<sup>7</sup>

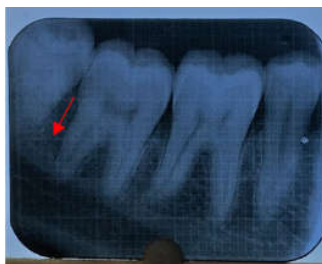


Fig 8a At baseline

Similar results were achieved by Needleman IG *et al.* 2005<sup>8</sup> and Vinayak KS *et al.* in 2014<sup>9</sup>, in the treatment of osseous defects by beneficial osseous and soft tissue regeneration.

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.<sup>(10,11)</sup>



Fig 8b 3<sup>rd</sup> month

The immunomodulatory effects of antibiotics influence the degree of the local response to infection on the human periodontal ligament cell (HPLC). HPLCs play a role in the immune response by the production of cytokines. In periodontal therapy, MTZ is used either with a systemic administration or with local biodegradable sustained-release agents. Significant reduction in the systemic side effects is seen on administration of MTZ gel locally.

In an in vivo study done by Rizzo A *et al.* 2010, MTZ showed no cytotoxic effect on HPLC and it enabled to inhibit the production of pro-inflammatory cytokines thus affecting the immunomodulation in periodontal therapy.<sup>12</sup>



Bansal *et al.* (2013)<sup>13</sup> and Khattar Sakshi *et al.* (2014)<sup>14</sup> had done a study to evaluate the efficacy of autologous PRF with the DFDBA, in the treatment of periodontal intrabony defects. They concluded that a combination of PRF and DFDBA demonstrated significant improvement in the clinical probing depth, relative attachment level, and radiographical bone fill.

## CONCLUSION

All the treatment modalities (PRF + MTZ, PRF + bone graft and PRF alone) were found to be effective both clinically and radiographically in the treatment of intrabony defects. However, the combination of PRF +MTZ and PRF + bone graft was proven to be better than PRF alone.

There are wide range of regenerative procedures that have been developed over the years. It is important to cognize and channel the use of various regenerative materials available as the need arises.

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