Original Article

The Combined Effect of Bioactive Glass and Platelet-Rich Fibrin in Treating Human Periodontal Intrabony Defects – A Clinicoradiographic Study

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Abstract

Background: Platelets are richest source for cytokine and growth factors which are two important components for the re-establishment of bone and maturation of the soft tissue. **Aims and Objective:** The additive effect of PRF along with a synthetic bone graft material in treating human intrabony periodontal defects has been evaluated in this study. The appropriate use of platelet-rich fibrin (PRF) as an alternate comfortable graft material to restore the lost periodontal tissues has been well documented and has given clinically promising outcome. **Materials and Method:** Platelet-rich fibrin (PRF) is prepared from patient's own blood which is autologous in nature. Perio Glas (PG) is an easy to use synthetic absorbable osteostimulative as well as osteoconductive bone graft material. The selected 30 sites were randomly divided into two groups such as Test (15 sites using PRF) and Control (15 sites without PRF). **Results:** At the end of Six months, the post-operative evaluations revealed significant reduction in PPD and gain in CAL. Radiographic evidence of bone formation was also noticed. The incorporation of PRF with synthetic bone graft (perioglas) produces effective and rapid periodontal regeneration with improved healing in intrabony osseous defects. The PRF group showed a mean Radiographic Defect Fill (RDL) of 1.24 ± 0.04 compared with 0.79 ± 0.07 of control group which is statistically significant. **Conclusion:** This combination technique can be used as an alternate grafting modality for the treatment of intrabony periodontal defects with satisfactory clinical consequences.

Keywords: *Bioactive glass, bone regeneration, periodontal disease, plasma-rich derivate, platelet-rich fibrin membrane*

Introduction

Periodontal disease is manifested as loss of connective tissue attachment with destruction of periodontal tissues. The objective of the periodontal therapy is to eliminate the inflammatory process, prevent the progression of periodontal disease and also to regenerate the lost periodontal tissues.

Regeneration is a process which includes multiple sequences of events at molecular and genetic levels in which the interpretation remains restricted.[1] Periodontal regeneration involves various biologic actions such as cell adhesion, migration, proliferation, and differentiation in an episodic manner.[2] Soft-tissue grafts, bone grafts, root biomodifications, guided tissue regeneration, and combinations of these procedures are commonly used clinical applications for periodontal tissue regeneration. The goal of the current regenerative periodontal therapy is to attain the complete periodontal restoration.[3] However, all the therapeutic modalities can only bring back a small portion of the original tissue volume.[4]

After the tissue injury in periodontal surgery, there is formation of blood clot and the wound healing process is commenced. The platelet aggregation supports the release of certain biologically active proteins which binds to the fibrin mesh or to the extracellular matrix would generate chemotactic gradients supporting the recruitment of the stem cells, stimulating cell migration, differentiation, and promoting repair.[5]

Hence, PRF can be successfully applied to replace the lost periodontium which in turn aids accelerated and comprehensive healing of the same.

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Materials and Methods

Platelet-rich fibrin and Perioglas

PRF was initially introduced in France for the use of oral and maxillofacial surgery. Choukroun's platelet-rich fibrin (PRF)[6] is a PRF biomaterial with a distinct configuration and has three-dimensional architecture.[7,8] PRF has a dense fibrin network with leukocytes, cytokines, and structural glycoproteins.[9] The grit also contains various growth factors such as transforming growth factor-β, platelet-derived growth factor, vascular endothelial growth factor, insulin growth factor-1, fibroblast growth factor, epidermal growth factor, and glycoproteins such as thrombospondin-1.[10,11] Leukocytes that are intensely found in PRF represents multiple tasks such as growth factor release,[12] immune regulation,[13] anti-infectious activities,[14] and matrix remodeling during wound healing. The steady polymerization mode of PRF and cicatricial capacity creates a physiologic architecture favorable for wound healing.[15]

Perioglas (PG) is composed of a calcium-silicate bioactive glass. It acts as an osteoconductive bone graft bioactive material and also merge with neighboring tissues and initiates an osteostimulatory effect. This would help in rapid bone regeneration than exhibited by osteoconduction which also increases the resorption rate of the implanted graft material[16] which is 100% synthetic, safe, and completely resorbable. It is designed for filling and reconstruction of bone defects in maxillofacial and dental surgeries.

Patient selection

Patients were selected from the patient pool attending RVS Dental College and Hospital for the study. Patients with ≥30% of the sites having attachment loss were considered as chronic-generalized periodontitis. The presence of suitable bony defects was confirmed with radiographs and patients were selected accordingly. Informed consent was obtained from all the patients.

Inclusion criteria

The inclusion criteria were as follows:

- Patients with chronic periodontitis within 25–50 years age and requiring periodontal therapy
- Presence of at least two interproximal periodontal pockets on contralateral sides with probing pocket depth (PPD) measuring 6 mm or more, with radiographic evidence of bone loss
- No history of use of antibiotics for the last 6 months
- No pregnancy or lactation
- Agree to follow-up compliance.

Exclusion criteria

The exclusion criteria were:

- Any systemic diseases that affect the periodontium and contraindicate for periodontal surgery
- Patients having deficient platelet count for PRF preparation
- Patients with coagulation defect or on anticoagulant treatment
- Carrying and nursing mothers
- History of heavy smoking
- History of alcohol abuse.

Clinical parameters

A single calibrated examiner evaluated the clinical parameters at baseline before regenerative therapy and 6 months after the surgery.

Clinical parameters such as PPD, clinical attachment level (CAL), and radiographic bone level (RBL) were recorded. An acrylic stent was used to measure the CAL.

Stent fabrication

Alginate impressions were taken, casts were poured, and a stent was fabricated using acrylic. A groove was made to duplicate the placement of the probe at the end of the 6 months to minimize the errors in postoperative measurement.

Study design

The selected patients were assessed with history, clinical examination, and routine investigations. Phase I therapy such as oral hygiene instructions, scaling, and root planing were done for all the patients. The patients were reevaluated after a month period and selected for the study according to the selection criteria. The Oral Hygiene Index (simplified) and PPD were recorded to determine the periodontal status. The study involves 15 test sites (with PRF) and 15 control sites (without PRF).

Protocol

This study was carried in 30 sites. The selected sites were randomly allocated to test and control groups.

Before surgery, the routine oral hygiene instructions and scaling and root planing were done.

The defects were analyzed clinically and radiographically. After primary patient care, oral prophylaxis was done and patient was assessed for adequate oral hygiene maintenance.

The patient's platelet count, hemoglobin, bleeding time, clotting time, and random blood sugar were evaluated as routine investigative procedures and were found to be within the normal limits.

Platelet-rich fibrin preparation

The protocol established by Choukroun *et al*.[6] was taken as a guide for PRF preparation. Just before the surgery, the intravenous blood (by venepuncture of the antecubital vein) was collected in 10-ml sterile tubes without anticoagulant and immediately centrifuged in centrifugation machine at

3000 revolutions for 10 min. This leads to the formation of a structured fibrin clot in the middle of the tube, red corpuscles at the bottom, and platelet-poor plasma (PPP) at the top. PRF was easily separated from the red corpuscles base preserving a small-red blood cell layer using a sterile tweezer and scissor after the removal of PPP and then transferred onto a sterile container.

Surgical procedure

Extraoral antisepsis and intraoral antisepsis were performed with povidone-iodine solution and 0.2% chlorhexidine digluconate rinse, respectively. Local anesthesia was administered to the surgical sites. Each site was treated with incisions reflecting full-thickness mucoperiosteal flaps, attempting to retain all the soft tissues.

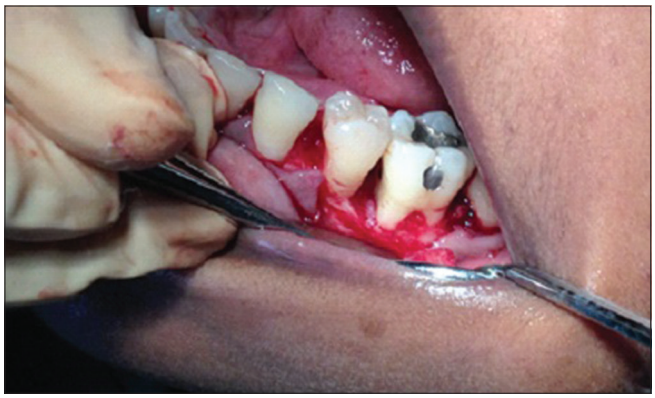

Figure 1: Full-thickness flap elevated reflecting the bony defect

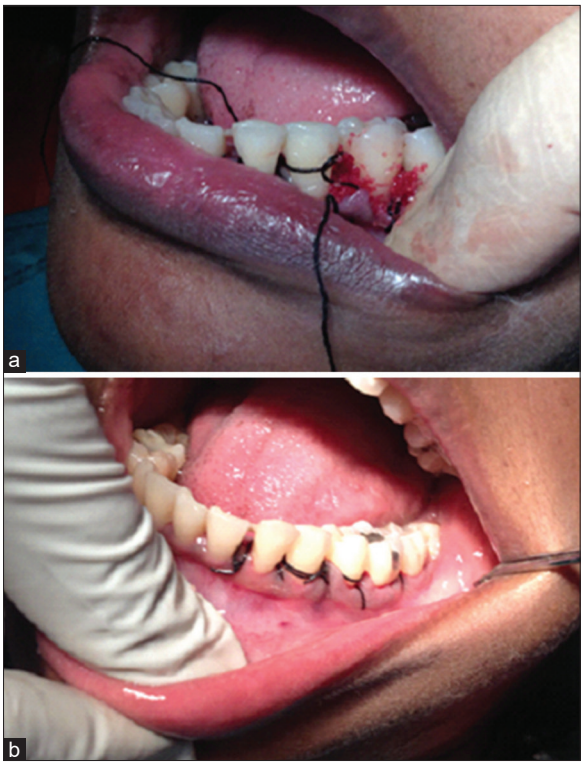

Figure 3: (a) Placement of graft with platelet-rich fibrin in the defect. (b) The flap is repositioned and the sutures placed

An intrabony defect was revealed, the exposed roots and osseous defects were completely debrided with hand instruments [Figure 1].

The experimental site defects received PRF plug derived from patient's own blood. Newly prepared PRF obtained was made into small pieces and combined with synthetic bone graft material (PG) [Figures 2 and 3a].

The control site defects received only the bone graft material (PG).

Using 3-0 nonabsorbable braided black silk surgical suture with simple interrupted sutures, the mucoperiosteal flaps

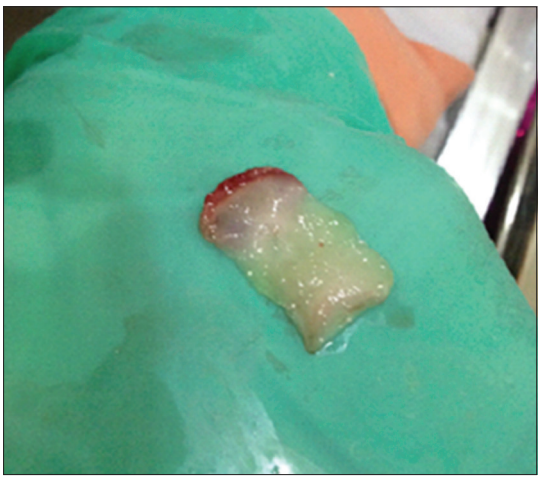

Figure 2: Blood centrifuged and the platelet-rich fibrin obtained

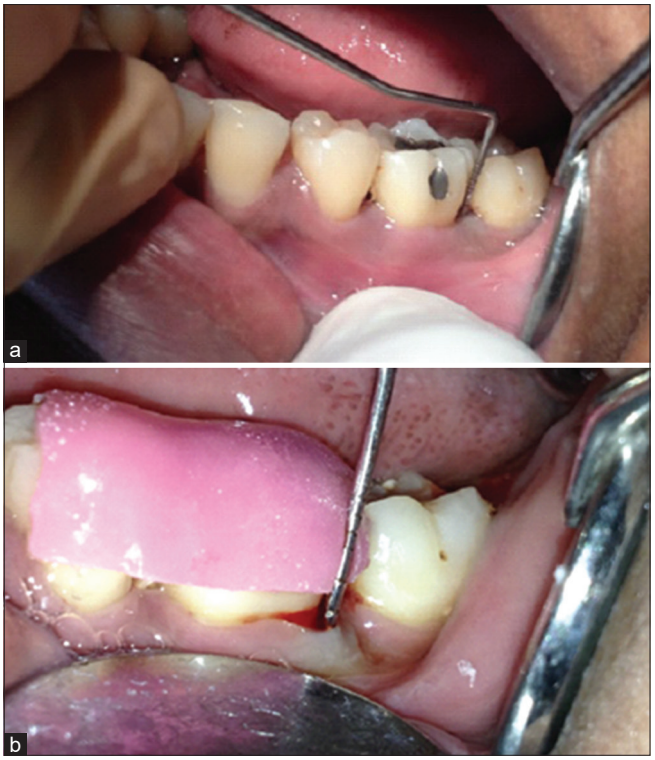

Figure 4: (a) Preoperative measurement of probing pocket depth with Williams probe. (b) Measurement of probing pocket depth with Williams probe after 6 months

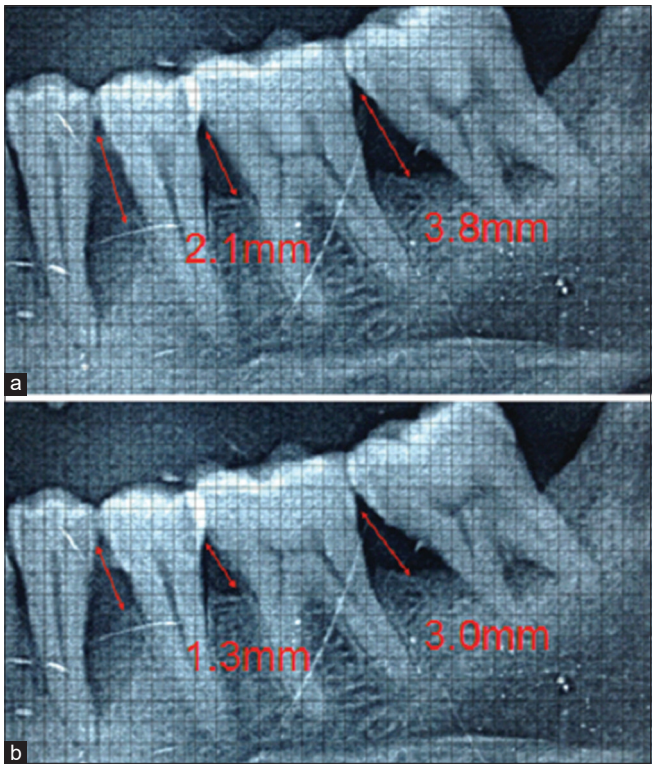

Figure 5: (a) Radiographic bone level at baseline. (b) Radiographic bone level after 6 months

were repositioned and held in place [Figure 3b]. The surgical area was secured with periodontal dressing (COE PAK).

Postoperative care

The patients were prescribed with preferable antibiotics and analgesics along with chlorhexidine digluconate rinses (0.2%) twice daily for 2 weeks. After 10 days, periodontal dressing and sutures were removed with saline irrigation. The patients were trained for gentle brushing with a soft toothbrush. Reevaluation was done weekly for up to 1 month after surgery and then at 3 and 6 months. The RBL was measured. The values were compared with pre-operative measurements [Figures 4a, b and 5a, b].

Statistical analysis

Mean values were obtained by assessing the differences between preoperative and postoperative values of each site which were presented as mean ± standard error (SE) differences between the mean values were assessed by Student's *t*-test. $P < 0.05$ is considered to be statistically significant.

Results

A total of 30 sites having moderate-to-severe periodontal osseous defects (test site, $n = 15$ and control site, $n = 15$ sites) completed the 6-month follow-up period. In all cases, the patient revealed acceptable oral hygiene maintenance with a good compliance during the course of observation period. The healing was uneventful, with no signs of infections and/or complications indicating the biocompatibility of both grafting modalities.

Digital radiographic reevaluations were performed at 6-month postoperatively. The radiographic analysis of the defect revealed significant bone formation at the end of 6 months.

Tables 1 and 2 depict the results of the study as comparison of clinical and radiological parameters between the test and control sites at 6 months.

The defect characteristics between preoperative and postoperative of the test and control sites showed that the mean and SE of PPD (in mm) in test site were 3.93 ± 0.23 and in control site was 2.00 ± 0.24.

CAL was found to be in test site as 4.93 ± 0.34 and in control site as 2.60 ± 0.29.

The mean and SE of RDL (mm) in test site were 1.24 ± 0.04 and 0.79 ± 0.07 at control site, respectively.

The mean PPD was very significantly reduced in the test sites as compared to the control sites ($P < 0.001$).

Similarly, mean CAL was also significantly reduced in the test sites as compared to the control sites ($P < 0.001$).

A further radiographic evaluation revealed that the mean radiographic defect fill (RDL) was significantly higher in test sites.

Discussion

Periodontal disease is a pathological inflammatory condition of the periodontal tissues characterized by chronic inflammation and manifested as loss of connective tissue attachment with destruction of periodontal tissues including bone. The primary objective of the periodontal therapy is to regenerate the lost periodontal tissues.

Although various graft materials have given successful clinical outcome, no single graft material is regarded as accurate therapy for intrabony defects.

After periodontal surgery, during wound healing the epithelial cells, cells from the gingival connective tissue, alveolar bone cells, and periodontal ligament cells are repopulated the wound area and form structures typical of the periodontal tissue.

The fibrin formation and the accumulation of platelets in the wound healing area initiates the release of growth factors from the platelets into the surrounding tissues through molecular signals that are principally transmitted by cytokines.[16] Evidence from the literature proved that the existence of growth factors and cytokines in the platelets plays a pivotal role during inflammation and wound healing.[17]

Fibrin, fibronectin, and vitronectin, which are secreted by platelets serve like adhesion molecules for effective

cell migration as well as matrix for the connective tissue.[5] These biological properties make the use of platelets as therapeutic tool to accelerate the tissue repair and periodontal wound healing. Thus, the healing after periodontal therapy can also get augmented by platelet concentrates.

Choukroun *et al*. in 2001 introduced PRF which is considered as the second-generation platelet concentrate[6] which constitutes 97% of platelets and >50% of leukocytes in a specific three-dimensional distribution. In PRF, cytokines, glycanic chains, and structural glycoproteins are enmeshed within a slowly polymerized fibrin network.[18] The steady prolonged release of autologous growth factors such as platelet-derived growth factor and transforming growth factor-beta and superior induction of osteoblastic differentiation and proliferation by PRF when compared to PRP was demonstrated by He *et al*.[19] in their *in vitro* study.

PRF is superior to other platelet concentrates such as PRP that the wound healing and regeneration is rapid and enhanced. Other properties such as easy and cheap method of preparation without any chemical modification and its elastic and flexible properties make PRF as a comfortable alternate graft material for comprehensive periodontal therapy. In addition, PRF technique does not require a second surgical site opening as seen in autogenous graft procedure. When compare to PRP, PRF has supportive role in the immune system. Since PRF is prepared from patient's own blood, it also avoids the risk of disease transmission. Thus, PRF has emerged as one of the promising regenerative materials in the field of periodontics.[20]

Bioactive glass, when used as a bone regenerative material, is considered to be a second-best graft material when compared to autograft. This has been used successfully in various clinical applications as sole or with combination of other regenerative materials. As soon as PG interacts with blood, a natural process begins which leads to a new layer of calcium phosphate that is favorable for the recruitment and proliferation of osteoblasts and new bone formation. Adding PRF with this could enhance rapid healing and bone augmentation by its probable dense fibrin network and rich growth factors.

Choukroun *et al*. demonstrated the effect of PRF on bone allograft in sinus lift procedure, and histologically proved a reduced healing time to 4 months with the addition of PRF to bone graft[21] and thus proving fast healing and osteogenic ability of PRF.

The observations of the present study are similar with Choukroun's above-mentioned study, and the recently reported comparative studies involving the combination therapy of PRF with commercially available bone grafts.[19,20-24]

The current study was carried out as a single-centered randomized clinical trial to evaluate clinically and radiographically, the effectiveness of bioactive glass alone and the combination of bioactive glass and PRF in treating intrabony periodontal defects.

The previous studies using PRF as a complex scaffold along with synthetic bone graft material in various bone defects has proven the excellent biocompatibility and rapid wound healing properties of PRF.[25,26]

Use of PRF as membrane to cover the defect has also given postoperative clinical observation of as minimal recession and good bone fill of the defects which proved a good maintenance of defect boundary by the membrane.

Our study shows statistically highly significant RDL in the test site, and significantly reduced mean PPD and mean CAL over the test sites at 6-month interval.

The mean RDL were 1.24 ± 0.04 mm and 0.79 ± 0.07 mm respectively over the test and control sites. The mean PPD over the test sites were 3.93 ± 0.23 mm and in control sites 2.00 ± 0.24 mm.The mean CAL was found to be 4.93 ± 0.34 mm over the test sites and in control sites it was 2.60 ± 0.29 mm [Tables 1 and 2].

These similar biological effects were repeatedly reported by studies of Pradeep *et al*., Inchingolo *et al.*, Ranganathan and Chandran, and Naqvi *et al*.[19,23,24,27]

Li *et al*.[28] in their study reported the benefits of PRF in enhancing the alveolar bone augmentation was possibly facilitated by the fibrin-mediated effect of PRF on

Table 1: Comparison of clinical and radiological parameters between test and control sites at 6 months

Clinical parameters	Sites	Mean±SE
PPD (mm)	Control	2.00±0.24†
	Test	3.93±0.23†
CAL (mm)	Control	2.60±0.29†
	Test	4.93±0.34†
RDL (mm)	Control	0.79±0.07†
	Test	1.24±0.04†

SE: Standard error; PPD: Probing pocket depth; CAL: Clinical attachment level; RDL: Radiographic defect fill

Table 2: Comparison of clinical parameters between test and control sites at 6 months

Clinical parameters	Sites	Mean (mm)	SE	*t*	Significance
PPD (mm)	Control	2.00	0.24	5.85	S*
	Test	3.93	0.23		
CAL (mm)	Control	2.60	0.29	5.18	S*
	Test	4.93	0.34		
RDL (mm)	Control	0.79	0.07	5.34	S*
	Test	1.24	0.04		

*S Statistically significant at $P<0.001$; SE: Standard error; PPD: Probing pocket depth; CAL: Clinical attachment level; RDL: Radiographic defect fill

RUNX2 expression, osteoblast differentiation, and matrix mineralization and also by the alkaline phosphatase activity – stimulating effect of fibrin.

According to Chang *et al*.,[29] PRF promotes the expression of phosphorylated extracellular signal-regulated protein kinase (P-ERK) and stimulates the osteoprotegerin (OPG) which causes proliferation of osteoblasts and potential bone formation.

Careful patient selection and protocol standardization for PRF also influences the outcome of the results. In this study, the inclusion of only younger patients who are nonsmokers and nondiabetics might also an added value to the significant outcome of the study.

This study results demonstrated the use of combined synthetic bone graft material (PG) and PRF gave a favorable clinical outcome.

Conclusion

The growth factors and cytokines are two potential factors for regulation and management of the wound healing. PRF could be considered as natural fibrin-based biomaterial with inherent source of these two factors which is completely physiologic in nature. These aspects make use of PRF as effectively applied graft/membrane for regenerative periodontal procedure. The combination of PRF and bone graft can be successfully used in the treatment of periodontal intrabony defects with significantly improved clinical outcomes. This combination technique also assurances the added advantage of rapid and early bone formation. However, the confirmatory histological evaluation and larger randomized controlled clinical trials are required to provide definitive evidence of efficacy of this combination therapy. The additive effects of these materials on postoperative pain perception and other clinical symptoms would be of future research interests. Since PRF has to be prepared freshly, a standardized protocol technique for storage, larger amount of PRF preparation for the application in complex, and larger defects have to be explored further for reproducible outcomes.

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Conflicts of interest

There are no conflicts of interest.

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