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ORIGINAL ARTICLE

Effectiveness of Platelet-Rich Fibrin with Decalcified Freeze-Dried Bone Allograft Compared to Decalcified Freeze-Dried Bone Allograft Alone in Mandibular Grade–II Furcation Defects: A Quasi-Experimental Study

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ABSTRACT

Objective: To assess the effectiveness of platelet-rich fibrin (PRF) with decalcified freeze-dried bone allograft (DFDBA) compared to DFDBA alone in mandibular grade–II furcation defects. **Material and Methods:** A quasi-experimental study was conducted on nine patients with chronic periodontitis, each having two almost identical mandibular grade II furcation defects. Test sites (left mandibular first molars) were treated with open flap debridement (OFD), DFDBA, and PRF, whereas control sites (right mandibular first molars) received OFD and DFDBA alone. Clinical parameters (plaque index (PI), gingival index (GI), vertical clinical attachment level (VCAL) and horizontal clinical attachment level (HCAL) into the furcation defect) and radiographic measurements (mean alveolar bone defect) were done at baseline and after six months postoperatively. **Results:** The gain in relative horizontal clinical attachment level (RHCAL) in the test sites was 2.94±0.52 mm compared to 1.33±0.35 mm in control sites (p=0.01). Improvement in mean alveolar bone defect (MABD) (was 1.21±0.5 mm^2 at test sites compared to 1.15±0.7 mm^2 at control sites) probing pocket depth (PPD), recession, relative vertical attachment level (RVCAL), and percentage of bone fill was found in the test sites compared to control, which statistically insignificant. **Conclusion:** The test sites had better outcomes than control sites, which was significant for the parameter RHCAL. Therefore, combining the biological benefits of autologous PRF with DFDBA is an efficient and economical treatment modality for the management of mandibular grade II furcation defects.

Keywords: Furcation Defects; Platelet-Derived Growth Factor; Allografts; Periodontal Diseases.

Introduction

The clinical management of furcation defects is significant due to the irregular anatomy of the roots and position of the furcation, which makes the biofilm virtually inaccessible for oral hygiene measures. When appropriate parameters are addressed, the survival rate and treatment outcome of furcation has been recognized as feasible and predictable [1]. The degree of furcation involvement itself represents an important risk factor for tooth loss, next to several well-known patient-related factors such as age, gender, smoking habit, and diabetes [2].

The ultimate goal of periodontal treatment is preventing the progression of periodontal disease and the regeneration of lost structures. Periodontal regenerative procedures for grade II furcation involvement in maxillary and mandibular molars with horizontal PPD ≥3mm has been found to yield the best results [3-5]. Various controlled clinical trials have also shown periodontal regeneration with bone grafts in intrabony defects, but complete and predictable reconstruction of the periodontium still remains an elusive concept [6].

Platelet-rich fibrin (PRF), described in 2001, is a second-generation platelet concentrate with natural fibrin. It is a biological three-dimensional matrix enmeshed with platelets, cytokines, glycan chains, and structural glycoproteins, which acts as an acceptable matrix for breeding human periosteal cells, fibroblasts, and endothelial cells in tissue engineering [7]. They can be used alone or as a scaffold for other graft materials, favoring early tissue healing through the release of growth factors, chemokines, and cytokines.

Even though coronally positioned flaps, barrier membranes and biological agents have been used today in the field of periodontal regeneration, there has been an increasing interest in polypeptide growth factors [8]. Recent evidence has shown that viable growth factors in PRF, such as platelet-derived growth factors (PDGF), transforming growth factor-β(TGF-β), vascular endothelial growth factor (VEGF), and insulin-like growth factor-1(IGF-1) can induce cell proliferation of osteoblast, periodontal ligament cells, but also suppress the oral epithelial cell migration, which is a key factor in periodontal regeneration [2,7,9]. PRF is superior to other platelet concentrates as it has a greater number and variety of growth factors, which are released for a longer duration. It is cost-effective, with no additional exogenous compounds (like bovine thrombin and calcium chloride) and ease of preparation has enabled it to be a better biomimetic agent [7].

Various authors suggest the osteogenic potential of decalcified freeze-dried bone allograft (DFDBA) with strong clinical evidence for the use of DFDBA amongst bone grafts as a periodontal regenerative material [10,11].

Many studies have been conducted to evaluate the efficacy of PRF and DFDBA in the treatment of intra-bony defects and statistically significant results in probing pocket depth reduction, and clinical attachment level gain for the PRF+DFDBA group have been found [12]. Swami et al. [13] reported that PRF, along with 1% Metformin, has yielded satisfactory clinical and radiological improvements compared to PRF alone in grade II furcation defects. Also, in grade II furcation defects DFDBA along with amniotic membrane has resulted in greater volumetric changes than DFDBA alone [14]. Mehta et al. [15] reported that PRF, compared to collagen membranes and DFDBA, resulted in greater regenerative potential for grade II furcation defects. Basireddy et al. [16] analyzed the benefit of PRF and DFDBA in grade II mandibular furcation defects and found a statistically significant difference with respect to only Relative horizontal clinical attachment level gain and Gingival margin level change. Agarwal et al. [17] compared PRF+DFDBA+OFD with PRF+OFD and OFD alone and found a statistically significant decrease in horizontal and vertical furcation defect parameters.

However, similar previous studies have failed to report the total area of defect fill, which is crucial in understanding the impact of these regeneration techniques [16,17]. Also, there is no clear consensus on how

PRF will be utilized for the best possible results. This study aimed to assess the effectiveness of using PRF with DFDBA compared to DFDBA alone in mandibular grade II furcation defects for the treatment of mandibular grade II furcation defects, both clinically and radiographically.

Material and Methods

Study Design and Ethical Clearance

Quasi-experimental study (split-mouth design). Ethical clearance was obtained from the institutional ethical committee of Pushpagiri College of Dental Sciences (PCDS/IEC/S/19/12/14). An explanation about the patient diagnosis (chronic periodontitis with mandibular grade II furcation involvement), study objectives, and the treatment plan was given to the patients and thereafter, written informed consent was obtained.

Sample Size

The sample size was calculated as 18 sites (9 test sites and 9 control sites) in nine patients using an α error of 5% and the power of the test as 80% at a confidence of 95% [18].

Study Sample

Patients with chronic periodontitis were selected from the outpatient department of Periodontology, Pushpagiri College of Dental Sciences, Thiruvalla, Kerala, India, from June 2015 to June 2016.

The following inclusion criteria were established: patients diagnosed with chronic periodontitis along with two almost identical furcation defects (radiolucency in the furcation area on digital radiograph) in bilateral mandibular first molars which are asymptomatic and endodontically vital having a probing depth (PD) ≥5mm and horizontal probing depth ≥3mm were included in the study [19-21]. The diagnosis was confirmed based on clinical examination and radiological evaluation using RVG of the selected sites.

Subjects having a known history of systemic illness, those taking medications known to affect the outcome of periodontal therapy and affecting platelet count, smokers, immunocompromised individuals, and pregnant or lactating subjects were excluded from the study [20,21].

Full-mouth scaling and root planing using hand and ultrasonic instruments under local anaesthesia were carried out. Detailed instructions regarding proper oral hygiene measures were given to the study participants, which were reinforced throughout the study period.

The selected right mandibular molars were assigned to control sites (OFD+DFDBA) and left mandibular molars to test sites (OFD+ DFDBA+ PRF). The DFDBA used in the study was from the same processing batch. A schematic representation of the study is illustrated in Figure 1.

Clinical Evaluation

Clinical parameters related to the treated teeth included plaque index (PI), gingival index (GI), vertical clinical attachment level (VCAL), and horizontal clinical attachment level (HCAL) into the furcation defect, measured as a single reading at the mid-facial furcation entrance site [22]. Soft tissue measurements were performed using customized acrylic stents with a single mid-facial groove to ensure a reproducible placement of the University of North Carolina no. 15 (UNC-15) periodontal probe (Hu-Friedy Manufacturing, Chicago, USA) and Nabers probe (Hu-Friedy Manufacturing, Chicago, USA) for furcation to the nearest millimeter. These measurements were obtained just before the surgery and after 6 months of the postoperative period.

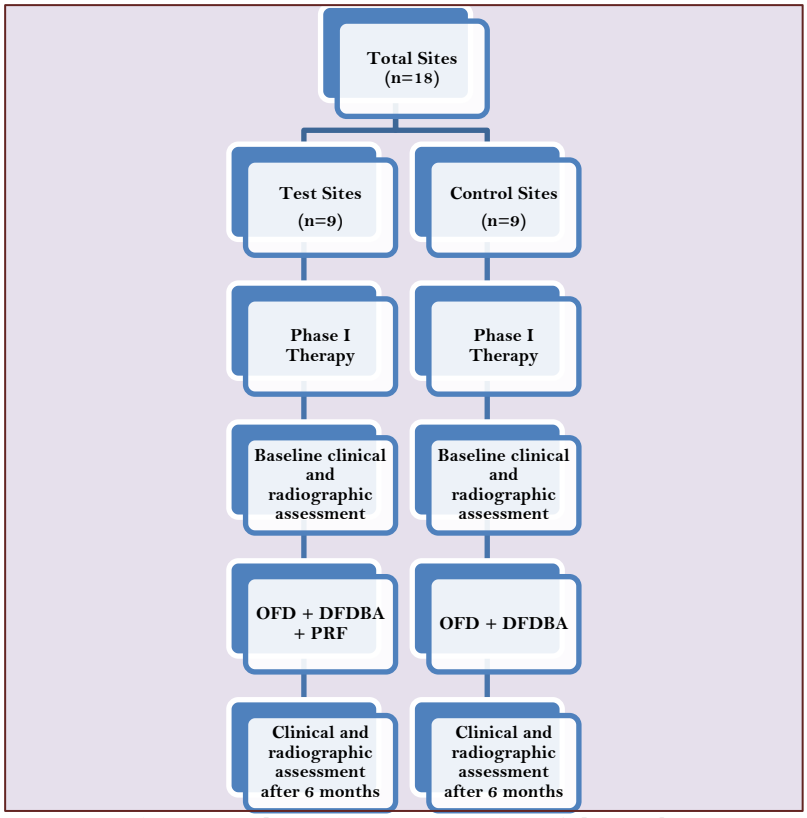
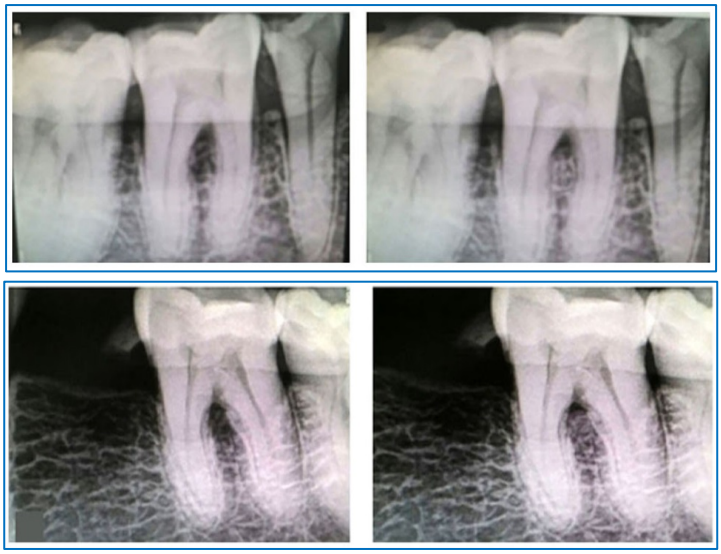


Figure 1. Schematic representation of the study.

Radiographic Evaluation

Bone defects were measured by standardized technique with the help of position indicating device (RINN XCP system, Dentsply Sirona, Gurugram, India) and digital radiovisiography (FONA S.R.L., Assago, Italy), radiographs were taken [23]. Radiographic evaluation of the defects was done at baseline and 6 months postoperatively (Figures 2A and 2B). The radiolucent area below the furcation fornix was measured by a computer-aided software program (Scion Image, Scion Corporation, Frederick, USA) [24]. All clinical and radiographic measurements were done in duplicate by the two authors (PG and AG) to avoid any bias.



(A)

(B)

Figure 2. (A) Pre-operative and post-operative radiographs at control site; (B) Pre-operative and post-operative radiographs at test site.

PRF Preparation

A standard protocol of PRF preparation was followed as proposed by Choukron et al. [25]. From the antecubital vein, 10 ml of blood was drawn just before the surgery. The collected blood was immediately centrifuged at 3,000 rpm for 10 minutes, which resulted in three layers: (1) Top most layer consisted of acellular platelet-poor plasma (PPP) as a supernatant; (2) PRF clot in the middle layer; and (3) RBCs at the bottom.

The platelet-poor plasma (PPP) was removed from the centrifugation tube. PRF was separated from the red corpuscles, which were present at the base level, using sterile tweezers and scissors. After that, it was transferred to a sterile dappen dish.

Surgical Protocol

Intraoral and extraoral antiseptics were applied, and local anesthesia was given at the required site. A crevicular incision was made using a No. 15 blade and a full thickness flap was reflected to expose the furcation defect. Meticulous defect debridement was done using a furcation curette (Buccal-Lingual Quetin Furcation Curette, Hu-Friedy Manufacturing, Chicago, USA).

Following OFD, DFDBA (Rocky Mountain tissue bank allograft-cortical particulate, Rocky Mountain Tissue Bank, Aurora, USA) was placed in the control sites. For test sites, following OFD, the obtained PRF was divided into two parts: one part was mixed with DFDBA and placed at the defect site following which the second part of PRF was trimmed and placed over the defect as a membrane [26]. Using 3-0 nonabsorbable braided black silk surgical suture, mucoperiosteal flaps were repositioned and sutured. Non-eugenol periodontal dressing (Coe-Pak) was also placed.

Post-Operative Care

After the surgical procedure, the patients were prescribed suitable antibiotics: Amoxicillin 500mg t.i.d; and NSAIDs (a combination of Ibuprofen 400 mg and Paracetamol 325 mg t.i.d). Chlorhexidine Digluconate 0.2% mouthwash to rinse twice daily was also prescribed for two weeks. Periodontal dressings and sutures were removed two weeks after surgery. Oral hygiene instructions were again reinforced.

Recall Protocol

All the study participants were recalled after 6 months of the post-operative period. All the clinical and radiographic parameters were recorded.

Data Analysis

The statistical analysis of data was done using the statistical package SPSS Version 17 (IBM SPSS Statistics for Windows, Armonk, NY, USA). Clinical parameters with continuous data were presented as mean, standard deviation and range. The data on outcome variables were tested for normality using the Shapiro-Wilk test. Since the data was found to significantly deviate from a normal distribution, non-parametric tests were used for analysis. Differences in the measurements between test and control sites were analyzed using Wilcoxon signed rank test for statistical significance. The changes after 6 months, as compared to baseline data in both groups, were tested using Friedman test. A p-value less than 0.05% was considered statistically significant.

Results

The mean age of the participants was 55.78±6.1years, ranging from 40-65 years. The materials used in the study were well-tolerated as no postoperative infection cases were reported. Healing of all the sites was also uneventful during the study.

The maintenance of oral hygiene was satisfactory in all the patients. The mean gingival index (GI) of the study group at baseline was 2.20±0.7 and at 6 months was 0.20±0.4 (p=0.007). The mean reduction from baseline to 6 months was 1.99±0.3. The mean Plaque index (PI) of the study group at baseline was 2.78±0.6 and at 6 months was 0.67±0.5 (p=0.006). The mean reduction from baseline to 6 months was 2.11±0.1. Gingival index and plaque scores showed a statistically significant reduction in the study sample from baseline to six months.

The mean reduction from baseline to 6 months in control and test groups was 1.33±0.3 and 2.94±0.5, respectively, and was found to be statistically ($p<0.05$). The mean reduction in RHCAL was also more in the test group than in the control group. Here the reduction was statistically significant between the two groups (p=0.011). Table 1 describes the intragroup comparisons in the test and control sites between baseline and 6 months.

Table 1. Intragroup comparison of clinical and radiographic parameters for both the groups at baseline and after six months.

Parameters	Control Group		p-value	Test Group		p-value#
	Baseline (mm) Mean ± SD	6 Months (mm) Mean ± SD		Baseline (mm) Mean ± SD	6 Months (mm) Mean ± SD	
PPD	4.78 ± 0.667	2.33 ± 0.707	0.001*	4.56 ± 0.527	2.23 ± 0.18	0.001*
REC	3.67 ± 0.500	2.22 ± 0.441	0.001*	3.78 ± 0.441	2.78 ± 0.667	0.001*
RHCAL	5.33 ± 1.118	2.389 ± 0.600	0.010*	4.44 ± 1.130	3.11 ± 0.782	0.010*
RVCAL	8.44 ± 0.882	4.44 ± 1.014	0.006*	8.22 ± 0.667	5.11 ± 1.167	0.007*
ABD	2.13 ±1.243	0.92 ± 0.736	0.008*	2.08 ± 1.117	0.93 ± 0.447	0.008*

PPD: Probing Pocket Depth; REC: Recession; RHCAL: Relative Horizontal Clinical Attachment; RVCAL: Relative Vertical Clinical Attachment; ABD: Alveolar Bone Defect; #Intergroup comparison by Friedman test; *Statistically significant.

There was comparatively greater reduction in probing pocket depth (PPD), recession and gain in relative vertical attachment level (RVCAL), mean alveolar bone defect (MABD) and percentage of bone fill in the test site, but the results were not statistically significant. A comparison between the test and control sites at baseline and at 6th month is given in Table 2.

Table 2. Comparison of clinical and radiographic parameters in control and test group.

Parameters	Test Group Mean ± SD	Control Group Mean ± SD	p-value#
PPD change (mm)	2.45±0.18	2.23±0.71	1.000
Rec change (mm)	1.45±0.06	1.00±0.27	0.564
RHCAL (mm)	2.94±0.52	1.33±0.35	0.011*
RVCAL (mm)	4.00±0.13	3.11±0.50	0.059
Bone Fill (mm^2)	1.21±0.51	1.15±0.67	0.373
Bone Defect Fill (%)	58.76±10.84	50.84± 21.33	0.313

PPD: Probing Pocket Depth, Rec: Recession; RHCAL: Relative Horizontal Clinical Attachment Level; RVCAL: Relative Vertical Clinical Attachment Level; #Wilcoxon Signed Ranks Test for inter-group comparison; *Statistically significant.

Discussion

Our study assessed the effectiveness of PRF with DFDBA in comparison with DFDBA alone for the treatment of mandibular grade II furcation defects, both clinically and radiographically. In our study, test sites presented greater pocket depth reduction. The results are in concordance with other studies, which demonstrated

a significant reduction in probing depth from baseline to 6 months [18,27,28]. The mean change in recession in test sites was 1.45±0.06 mm and in control sites was 1.00±0.2 mm, respectively, but the difference in PPD and recession between the sites was statistically not significant. As the fibrin matrix has been found to have mechanical properties and biological functions like fibrin glue, it might maintain the flap in a high and stable position, enhancing neo-angiogenesis, reduced necrosis and shrinkage of the flap. Therefore guaranteed maximal root coverage [29]. The reduction in gingival recession achieved in our study was better as compared to the study done by Chadwick et al. [27], where the mean reduction in PRF and DFDBA groups were 1.06±1.2 mm and 0.84±0.9 mm, respectively. The results showed gingival margin was maintained without much recession due to the placement of the PRF membrane slightly hanging over the edge of the gingival collar, as proposed by Del Corso et al. [29].

The gingival and plaque indices showed significant improvement from baseline to six months in the study group. The patients in the study sample exhibited good oral hygiene maintenance during the entire study period, which might be due to repeated reinforcement of oral hygiene instructions. According to Machtei and Schallhorn [8], optimal plaque control has been considered to be a crucial factor in the regenerative outcome.

A gain in clinical attachment is an important clinical outcome of a periodontal regenerative procedure. The RHCAL measured using Naber's probe, as suggested by Eickholz [30] showed a gain of 2.94±0.5 mm and 1.33±0.4 mm in the test and control sites, respectively, and was found to be statistically significant ($p<0.05$).

The test sites presented with a greater RVCAL gain than the control sites, but were statistically not significant. The mean gain in RVCAL agrees with other studies by Pradeep et al. [19] (4.57±2.9 mm), Sharma and Pradeep [31] (3.31±1.7 mm), and Bowers et al. [32] (1.33 mm) with the combined use of polytetrafluoroethylene and DFDBA. This may be because both the test and control sites have grade II furcation in which the interproximal bone height is coronal to the entrance of the furcation defect; hence there is a greater tendency to gain in RVCAL following any regenerative procedures.

Similar to previous studies, radiographic measurement of the defect was carried out using a computer-aided software program [19,26,33,34]. A definite increase in radiopacity was observed in the furcation areas after six months in both test and control sites. The mean defect fill in the test and control site were 1.21±0.5 mm^2 and 1.15±0.7 mm^2, respectively. The percentage of defect fill achieved in test and control sites were 58.8% and 10.8%, respectively but was not statistically significant ($p>0.05$). A bone fill percentage of 50.8% and 28.66% was reported by Sharma and Pradeep [31] and Thorat et al. [26], respectively in the PRF group. Pradeep et al. [19] reported a percentage bone fill of 61.9% when hydroxyapatite graft+PRF+1.2% gel Rosuvastatin was used for the management of mandibular grade II furcation defect. Shah and Kolte [35] also reported DFDBA along with human chorion membrane showed better results as compared to DFDBA alone in the management of grade II furcation defects both clinically and using CBCT.

Agarwal et al. compared OFD+PRF+DFDBA, OFD+PRF and OFD alone and significant improvements in probing depth, CAL and horizontal and vertical bone fill were found in OFD+PRF+DFDBA, OFD+PRF as compared to OFD group alone [17]. Basireddy et al. [16] compared PRF and DFDBA with DFDBA alone and found significant difference in gingival margin level and RHCAL. Similarly, the results of our study yielded greater clinical and radiographic improvements in test sites compared with the control sites, only RHCAL was found to be statistically significant.

In the present study, the combination of PRF with DFDBA demonstrated better results in all clinical and radiographic parameters. This result may be attributed to the beneficial effects of PRF. A portion of the PRF obtained was mixed with the DFDBA, as PRF fragments serve as a biological connector between bone particles.

Moreover, it has been associated with the gradual release of cytokines ensuring self-regulation of inflammatory and infectious phenomena within the grafted material [18].

Similar to previous studies, the study period was of six months [28]. This ensured maximum patient compliance for the study to evaluate effective radiographic changes. Long-term studies are more expensive and the risk of loss to follow-up is higher.

In this study, we utilized digital radiographs instead of CBCT even though it is known to be accurate in the diagnosis of furcation involvement [36,37]. CBCT is known to have shortcomings in capturing thin areas of bone and assessment of periodontal ligament space [38,39]. Also, the image quality of CBCT might be affected as it is prone to display artifacts [36]. The radiation dose for intraoral periapical radiograph is only 0.65µ SV, whereas even for CBCT, small FOV (Field of View) is 45µ SV [40]. Long-term radiation hazard due to CBCT is not known [41]. As per the recent best evidence consensus statement by the American Academy of Periodontology, further research is needed to substantiate the use of CBCT to assess radiographic changes following periodontal regenerative procedures [42]. The ALARA principle (As Low as Reasonably Achievable) for CBCT has not been advised as the standard of care for periodontal procedures [41]. The high cost as compared to digital radiographs is a major deterrent to advise this diagnostic modality for assessment of periodontal regeneration [41].

Future long-term studies with larger sample sizes can be carried out to assess the long-term prognosis following this treatment modality. Also, histomorphometric analysis of grade II furcation defects treated with PRF and DFDBA could go a long way in assessing whether there is true periodontal regeneration with this technique.

Conclusion

Our study showed significant improvements in the furcation defects after 6 months compared to baseline levels clinically and radiographically in both the test and control sites. The clinical and radiographic parameters had improved more in test sites than in control sites, though a significant difference was found only for RHCAL. PRF along with DFDBA has been shown to be an effective treatment option for mandibular grade II furcation defects. Utilization of PRF in periodontal regeneration procedures would be less demanding and more worthwhile both for the patient and the dentist.

Authors' Contributions

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All authors declare that they contributed to critical review of intellectual content and approval of the final version to be published.

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None.

Conflict of Interest

The authors declare no conflicts of interest.

Acknowledgements

The data used to support the findings of this study can be made available upon request to the corresponding author.

Data Availability

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