Original Research

Clinical and Radiographic Evaluation of β-Tricalcium Phosphate and Human Chorion Membrane With or Without Recombinant Human Platelet Derived Growth Factor BB in the treatment of Grade II Furcation Defects: A Randomized Controlled Trial

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Abstract

Background: The aim of the study was to correlate and compare clinically and radiographically the efficacy of recombinant human platelet-derived growth factor (rhPDGF) as an adjunct to β-tricalcium phosphate (β-TCP) and chorion membrane grafting versus β-TCP and chorion membrane alone in the treatment Grade II furcation defects in chronic periodontitis. **Materials and Methods:** Thirty sites (15 in each Group) with Grade II furcation defects were randomly assigned and treated as Group I (Control) furcation defect filled with β-TCP followed by placement of chorion membrane and Group II (Test) furcation defect filled with rhPDGF-BB + β-TCP followed by placement of chorion membrane. Clinical parameters (PI, GI, PPD, and RAL) and radiographic defect fill were recorded at Baseline, 1 month, 3 months, and 6 months. **Results:** Among the outcome measures, it resulted in significantly higher area under the curve, relative attachment level gain at 0–6 months ($P < 0.05$) and greater reduction in probing depth at the 3rd and the 6th month in Group II (rhPDGF + β-TCP + chorion membrane) than Group I (β-TCP + chorion membrane). **Conclusion:** Mean percentage defect fill was significantly greater in test sites as compared with control sites at 3 and 6 months ($P < 0.05$). Both groups demonstrated potential in enhancing periodontal regeneration; however, on comparison between the two groups, the results obtained by rhPDGF + β-TCP+ chorion membrane were significantly better with respect to both clinical and radiographic parameters.

Keywords: Recombinant platelet derived growth factor, Chorion membrane, Beta-tricalcium phosphate, Furcation defects, Periodontal regeneration.

Introduction

Periodontal tissues are destroyed in the course of periodontitis due to change in the immunologic responses to a triggering agent, such as bacteria in the biofilm.[1] Molar teeth with furcation involvement due to periodontitis have a greater chance of periodontal breakdown and respond less favorably to periodontal therapy than molars without furcation involvement or single-rooted teeth.[2] Multiple approaches have been used to resolve furcation defect including autografts,[3] demineralized freeze-dried bone allografts (DFDBAs),[4] bovine-derived xenografts,[5] barrier membranes,[6] and combinations of membranes and bone grafts.[7] In 1989, Lynch *et al.*[8] first discovered that platelet-derived growth factor (PDGF) promotes regeneration of periodontal tissues, including bone, cementum, and periodontal ligament. Development of recombinant human platelet derived growth factor BB (rhPDGF-BB) within the fields of periodontics and oral

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surgery gained significant momentum when pilot human histologic studies evaluating rhPDGF-BB in combination with decalcified freeze-dried bone allograft (DFDBA) for the treatment of severe periodontal intrabony and Class II furcation defects found robust periodontal regeneration.[9] The efficacy and safety of rhPDGF-BB plus β-tricalcium phosphate (β-TCP) in periodontal osseous defects were analyzed in a large multicenter trial.[10] rhPDGF-BB + β-TCP has been developed in India (Virchow Biotech), and its efficacy has been established in the treatment of periodontal intrabony defects.[11] One of the oldest biomaterials used for scaffolds is the fetal membrane. It is useful in the management of burns; creation of surgical dressings; as well as reconstruction of oral cavity, bladder and vagina; tympanoplasty; and arthroplasty.[12] It has gained importance because of its ability to reduce scarring and inflammation; enhance wound healing; and serve as a scaffold for cell proliferation and differentiation as a result of its antimicrobial properties. In addition, the chorionic membrane a fetal membrane is a biomaterial that can be easily obtained, processed, and transported.[13]

To the best of our knowledge, there are no studies in literature till date on the combination of β-TCP and rhPDGF-BB and chorion membrane in Grade II furcation defects. The purpose of the present study was to evaluate the efficacy of rhPDGF-BB combined with the alloplastic carrier β-TCP and chorion membrane and β-TCP combined with chorion membrane alone in the treatment of Grade II furcation defects in chronic periodontitis patients.

Materials and Methods

The present single blind, randomized controlled clinical, and radiographic study was carried out at a single center to evaluate the efficacy of the rhPDGF in combination with β-TCP and chorion membrane with that of β-TCP and chorion membrane alone in Grade II furcation defects in the treatment of chronic periodontitis patients.

Subject selection

All the patients for the present study were selected from outpatient section, department of periodontics. The study design was approved by Institutional Ethical Committee. The nature and purpose of the study were explained to the patients in their native language and informed consent obtained.

Inclusion criteria

The following criteria were included in the study:

- Age group of 25–60 years
- Systemically healthy
- Presence of one site with vertical probing depth ≥5 mm
- Radiographic involvement of Grade II furcation.

Exclusion criteria

The following criteria were excluded from the study:

- Use of tobacco in any form
- Pregnant and lactating women
- Systemically compromised patients
- Patients with a history of drug intake known to affect the periodontium.

Clinical procedure and study design

After baseline examination and screening of 15 patients with untreated chronic periodontitis, 15 patients were selected and enrolled in the study. A simple randomization approach[14] using computer generated random numbers was employed to assign 30 sites (15 in each Group) with Grade II furcation defects into Group I (Control) and Group II (test) to one of the following two treatment modalities

Group I (Control) – furcation defect filled with β-TCP followed by placement of chorion membrane.

Group II (Test) – furcation defect filled with rhPDGF-BB + β-TCP followed by placement of chorion membrane.

The clinical parameters were recorded at baseline, 1 month, 3 months, and 6 months were

- Plaque index (Silness and Loe, 1964).[15]
- Gingival index (GI) (Loe and Silness,1963)[16]
- Probing pocket depth (PPD)
- Relative attachment level (RAL)
- Radiographic parameter to measure the area of defect fill was recorded at baseline, 3 and 6 months after treatment.

PPD and RAL

The PPD and RAL were measured using UNC-15 graduated periodontal probe. Measurements were done at selected sites. The reading was recorded to the nearest millimeter. Custom made occlusal acrylic stents were used to standardize the probe angulations and position. The radiographs were standardized using customized bite blocks and radiovisiography with millimeter grid and with long paralleling cone technique to evaluate the bone fill. Radiographically, the area of furcation was measured using UTHSCA software (Figure 1a and b).

Growth factor and bone graft materials

rhPDGF-BB

Growth factor material was supplied in vials by (PERIOGEN) (Figure 2a) Virchow Biotech, Madhapur, Hyderabad, India. Concentration of 0.3 mg/ml was used.

β-TCP

Alloplastic bone graft material was supplied by (Virchow Biotech, Madhapur, Hyderabad, India). The particle size of β-TCP used was 0.25–1.0 mm (Figure 2b).

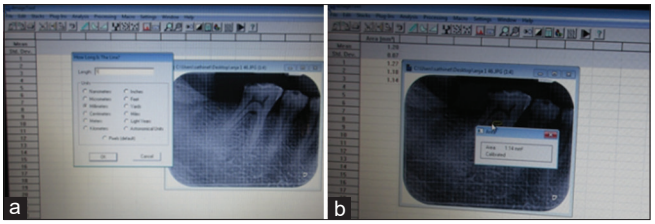

Figure 1: (a) Calibration of grid. (b) Measurement of area of radiographic furcation defect.

Chorion membrane

The barrier material used in the present study was Chorion membrane. It was procured from Tissue bank, TATA Memorial Hospital, Mumbai.

Pre-surgical therapy

After baseline examination and recording of clinical and radiographic parameters, all patients received routine oral hygiene instructions and full-mouth scaling and root debridement employing both hand instruments (Hu-Friedy, USA) and a piezoelectric ultrasonic hand piece (EMS) under local anesthesia of 2% lidocaine with 1:80,000 adrenaline until the operator achieved a hard, smooth, and calculus free root surface. Oral hygiene instructions were given to the patient.

Surgical procedure

4–6 weeks after Phase I therapy, periodontal evaluation was performed to confirm the suitability of the sites for surgery. After adequate anesthesia buccal and lingual sulcular incisions were made and mucoperiosteal flaps were reflected. Care was taken to preserve as much interproximal soft tissue as possible. Meticulous defect debridement and root planning were carried out using ultrasonic instruments, area specific, and furcation curettes. No osseous recontouring was carried-out. The furcation defects in Group I (Figure 3) were filled β-TCP and chorion membrane whereas β-TCP; chorion membrane and rhPDGF-BB were used in Group II (Figure 4). Mucoperiosteal flaps were repositioned and secured by interrupted 3–0 non-absorbable black braided silk surgical suture.

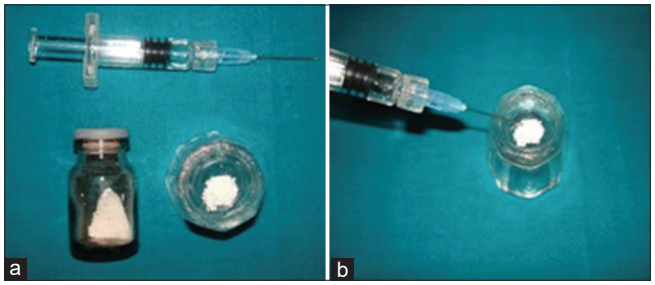

Figure 2: (a) Periogen, (b) rhPDGF-BB in gel form mixed with β-TCP

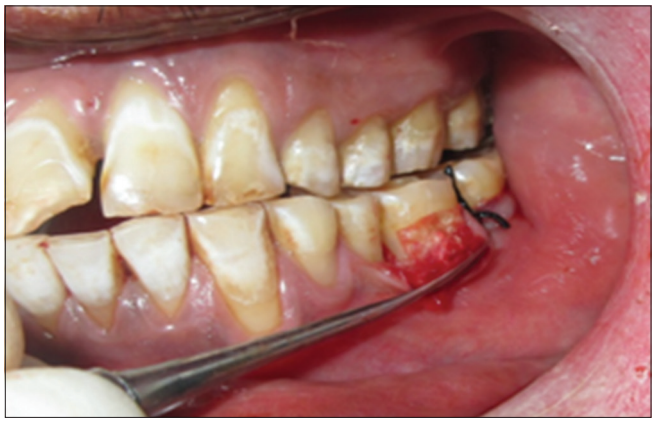

Figure 3: β-TCP and chorion membrane (Group I)

Post-surgical care

All patients were prescribed systemic antibiotic (amoxicillin 500 mg) thrice daily for 7 days and an analgesic (diclofenac sodium 50 mg) twice daily for 3 days. All patients were asked to rinse with 0.2% chlorhexidine twice daily for 2 weeks. Post-operative instructions were given to the patient.

Post-surgical procedure

Following 1 week after surgery, the periodontal dressing and sutures were removed. The area was irrigated thoroughly with 0.9% normal saline. Healing of flap was visualized and symptoms regarding discomfort, pain, swelling or any allergic reaction were asked to the patient and patients were given instructions for gentle brushing with a soft toothbrush.

Follow-up

Each patient was reinstructed for proper oral hygiene measures at 8 weeks postoperatively, and examined weekly, up to 1 month after surgery, and again. Recall appointments were made after 3- and 6-months post-surgery and at each visit, oral hygiene instructions were reinforced and scaling was done if necessary. Clinical and radiographic measurements were repeated for both the groups at 3 and 6 months postoperatively.

Post-surgical measurements of soft and hard tissue evaluation were performed 6 months after surgery. Soft tissue measurements were repeated with previously used acrylic stents. For hard tissue re-evaluation, intraoral periapical radiographs of the same study site were carried out and bone defect measurement was reassessed at 6 months.

Statistical analysis

The data were analyzed using the SPSS – software 20.00 program (SPSS Inc., Chicago, IL, USA). The intra- and inter-group comparisons of clinical parameters such as plaque index, GI were compared between Group I and Group II at various study intervals using Wilcoxon matched pairs *t*-test and Mann–Whitney U-test, respectively. The intra- and inter-group comparisons of clinical and radiographic parameters such as PPD, RAL and area of radiographic defect were compared

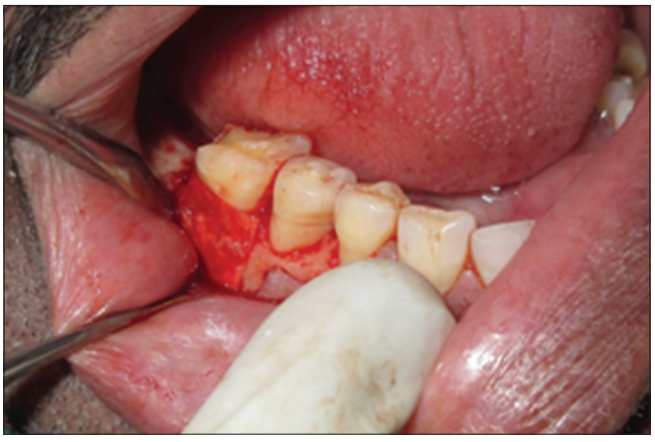

Figure 4: β-TCP, rhPDGF-BB (periogen), and chorion membrane (Group II)

between Group I and Group II at different time points using dependent and independent t test, respectively. Differences were considered as statistically significant at $P < 0.05$*.

Results

Total 15 patients (nine males and six females with age ranging between 25 and 60 years) satisfying the inclusion and exclusion criteria were enrolled in the study. Total of 30 Grade II furcation defects (15 in each group) were randomized into Group I and Group II. All the participants completed 6 months study period with no loss of follow-up at recall visits.

The intragroup comparison as shown in Table 1 revealed there was a statistically significant reduction in mean PI scores from baseline to 1 month, baseline to 3 months, and baseline to 6 months at all the study intervals in both the groups ($P < 0.05$*). The intergroup comparison of mean PI scores as shown in Table 2 at baseline to 1 month, 3 months, and 6 months between Group I and Group II was not found to be statistically significant.

The intragroup comparison as shown in Table 1 revealed there was a statistically significant reduction in GI scores from baseline to 1 month, baseline to 3 months, and baseline to 6 months at all the study intervals in both the groups ($P < 0.05$*). The intergroup comparison of mean GI scores as shown in Tables 2 and 3 at baseline to 1 month, 3 months, and 6 months between Group I and Group II was not found to be statistically significant.

The intragroup comparison as shown in Table 1 revealed there was a statistically significant reduction in mean PPD scores from baseline to 1 month, baseline to 3 months, and baseline to 6 months at all the study intervals in both the groups ($P < 0.05$*). The intergroup comparison of mean PPD scores as shown in Table 2 at baseline to 1 month between Group I and Group II was not found to be statistically significant. However, there was statistically significant reduction in mean PPD scores from baseline to 3 months and baseline to 6 months (Table 3) in both Group I and Group II ($P < 0.05$*).

The intragroup comparison as shown in Table 1 revealed there was a statistically significant reduction in mean RAL scores from baseline to 1 month, baseline to 3 months, and baseline to 6 months at all the study intervals in both the groups ($P < 0.05$*). The intergroup comparison of mean RAL scores as shown in Table 2 from baseline to 1 month, baseline to 3 months, and baseline to 6 months between Group I and Group II was found to be statistically significant ($P < 0.05$*) (Table 3).

The intragroup comparison as shown in Table 4 revealed there was a statistically significant reduction in mean area of radiographic defect scores from baseline to 3 months, baseline to 6 months, and 3–6 months at all the study intervals in both the groups ($P < 0.05$*). The intergroup comparison of mean area of radiographic defect scores as shown in Table 5 from baseline to 3 months and baseline to 6 months between Group I and Group II was found to be statistically significant ($P < 0.05$*).

Discussion

Regeneration of the periodontium within the furcation defect is considered one of the most challenging aspects of periodontal therapy.[17] It has been reported that molars with periodontitis

Table 1: Intragroup comparison of Group I and Group II with respect to plaque index, gingival index scores by Wilcoxon matched pairs test and probing pocket depth and relative attachment level scores by dependent t test at different time points

Parameters	Baseline (mean±SD)			1 months (mean±SD)			3 months (mean±SD)			6 months (mean±SD)		
	Group I	Group II	*P*-value	Group I	Group II	*P*-value	Group I	Group II	*P*-value	Group I	Group II	*P*-value
Plaque index	1.10±0.33	1.04±0.27	0.0007*	0.75±0.25	0.69±0.20	0.0007*	0.50±0.18	0.44±0.11	0.0007*	0.24±0.08	0.22±0.06	0.0007*
Gingival index	1.12±0.30	1.04±0.25	0.0007*	0.73±0.24	0.69±0.21	0.0007*	0.48±0.10	0.44±0.10	0.0007*	0.24±0.05	0.22±0.07	0.0007*
PPD (mm)	6.00±1.20	6.13±0.83	0.0001*	5.67±1.11	5.53±0.74	0.0001*	4.53±1.30	3.73±0.88	0.0001*	3.73±1.33	2.53±0.74	0.0001*
RAL (mm)	6.13±1.51	6.73±1.33	0.0035*	5.67±1.45	5.67±1.45	0.0001*	4.60±1.18	4.40±1.06	0.0001*	3.73±1.33	2.60±0.91	0.0001*

P<0.005* - Significant

Table 2: Intergroup comparison of Group I and Group II with respect to plaque index, gingival index scores by Mann–Whitney U-test and probing pocket depth and relative attachment level scores by dependent *t*-test at different time points

Parameters	Baseline (mean±SD)			1 months (mean±SD)			3 months (mean±SD)			6 months (mean±SD)		
	Group I	Group II	*P*-value	Group I	Group II	*P*-value	Group I	Group II	*P*-value	Group I	Group II	*P*-value
Plaque index	1.10±0.33	1.04±0.27	0.5476	0.75±0.25	0.69±0.20	0.6041	0.50±0.18	0.44±0.11	0.5755	0.24±0.08	0.22±0.06	0.4807
Gingival index	1.12±0.30	1.04±0.25	0.3952	0.73±0.24	0.69±0.21	0.6187	0.48±0.10	0.44±0.10	0.3952	0.24±0.05	0.22±0.07	0.4068
PPD (mm)	6.00±1.20	6.13±0.83	0.7257	5.67±1.11	5.53±0.74	0.7025	4.53±1.30	3.73±0.88	0.0500*	3.73±1.33	2.53±0.74	0.0051*
RAL (mm)	6.13±1.51	6.73±1.33	0.2578	5.67±1.45	5.67 ±1.45	1.0000	4.60±1.18	4.40±1.06	0.6290	3.73±1.33	2.60±0.91	0.0112*

P<0.005* - Significant

Table 3: Clinical changes of plaque index, gingival index probing pocket depth, and relative attachment level at various time intervals (in mm)

Parameters and groups	Baseline to 1 month			Baseline to 3 months			Baseline to 6 months		
	I	II	*P*-value	I	II	*P*-value	I	II	*P*-value
	Mean±SD			Mean±SD			Mean±SD		
Plaque index	0.35±0.23	0.35±0.22	0.9174	0.61±0.27	0.60±0.25	0.8519	0.86±0.30	0.82±0.27	0.6632
Gingival index	0.38±0.21	0.35±0.21	0.5203	0.64±0.23	0.60±0.20	0.4553	0.87±0.28	0.82±0.24	0.5476
Probing pocket depth	0.33±0.49	0.60±0.51	0.1534	1.47±0.52	2.40±0.74	0.0004*	2.27±0.59	3.60±0.51	0.0001*
RAL (mm)	0.47±0.52	1.07±0.46	0.0022*	1.53±0.92	2.33±0.62	0.0090*	2.40±0.91	4.13±1.06	0.0001*

P<0.005* - Significant

Table 4: Intragroup comparison of Group I and Group II with respect to area of radiographic defect (sq mm) by dependent *t*-test at different time points

Groups	Time points	Mean ± SD	Mean Diff.	SD Diff.	% Of change	Paired t	*P*-value
	Baseline	3.03±1.56					
	3 months	2.54±1.34	0.49	0.33	16.13	5.7771	0.0001*
	Baseline	3.03±1.56					
Group I	6 months	2.01±1.11	1.02	0.65	33.58	6.0232	0.0001*
	3 months	2.54±1.34					
	6 months	2.01±1.11	0.53	0.41	20.80	5.0184	0.0001*
	Baseline	3.09±1.51					
	3 months	1.89±0.97	1.19	0.65	38.68	7.1508	0.0001*
	Baseline	3.09±1.51					
Group II	6 months	0.90±0.37	2.18	1.20	70.73	7.0719	0.0001*
	3 months	1.89±0.97					
	6 months	0.90±0.37	0.99	0.66	52.27	5.7823	0.0001*

P<0.005* - Significant

Table 5: Intergroup comparison of Group I and Group II with respect to area of radiographic defect (sq mm) at different time points by independent *t*-test

Variable	Groups	Mean±SD	SE	t-value	*P*-value
	Group I	3.03±1.56	0.40	-0.1081	0.9147
Baseline	Group II	3.09±1.51	0.39		
	Group I	2.54±1.34	0.35	1.5097	0.1423
3 months	Group II	1.89±0.97	0.25		
	Group I	2.01±1.11	0.29	3.6766	0.0010*
6 months	Group II	0.90±0.37	0.09		
Baseline to 3 months	Group I	0.49±0.33	0.08	-3.7729	0.0008*
	Group II	1.19±0.65	0.17		
Baseline to 6 months	Group I	1.02±0.65	0.17	-3.3181	0.0025*
	Group II	2.18±1.20	0.31		

P<0.005* - Significant

involving furcation are having a higher rate of periodontal breakdown and furcation involved molars have respond less favorably to different periodontal therapies than molars without furcation involvement or single-rooted teeth. This can be explained by the complex anatomy of the furcation that impedes adequate accessibility for individual oral hygiene and inadequate professional root debridement in the molar region.[18] Clinically, successful regeneration at furcation sites is determined as the elimination or reduction of the horizontal and vertical components of the lesion (i.e. gain of clinical attachment level and bone fill), but conclusive evidence of true regeneration can only be achieved by histological means.[19]

In the treatment of mandibular Class II furcations, many comparative studies using diverse materials and therapies have been performed. While some reports demonstrated significant clinical attachment and bone gains, other studies did not show a significant clinical improvement. Several non-surgical and surgical therapies have been suggested and attempted for managing furcation defects, but the results have been largely unpredictable.[20] Hence, not a single regenerative material is considered as the gold standard in the treatment of furcation defects.[21]

Various treatment modalities such as guided tissue regeneration (GTR), root surface conditioning, and the use of enamel matrix derivative or platelet-rich plasma, and platelet-rich fibrin (PRF), have been proposed and implemented to promote and/or sustain periodontal regeneration.[22] There is a large body of evidence using cells in animal models demonstrating the effectiveness of growth factors in periodontal regeneration and bone augmentation.[23] Howell *et al*.[24] were the first to report utilization of growth factors in the treatment of human infrabony and furcation defects.

Current therapy for periodontal defects usually focuses on the use of alloplastic materials such as β-TCP. β-TCP resulted in improvements of clinical outcomes such as PPD reduction and CAL gain, but histological evaluation has demonstrated that β-TCP may not be capable to form new connective tissue, cementum, and bone. However, the osteoconductive nature of β-TCP makes it a good scaffold for GFs, and recent histological findings[22,25] suggest that the combination of rhPDGF can support regeneration in intraosseous periodontal defects.

In the present study, after the placement of rhPDGF-BB with β-TCP plus chorion membrane or β-TCP plus chorion membrane alone, there were no adverse effects. This is in accordance with Maroo and Murthy[26] who have used the same graft material in infrabony defects. However, in a multicenter

trial by Jayakumar *et al*.,[11] minor adverse effects such as pain and tooth mobility were observed in 16% of the test (rhPDGF-BB+β-TCP) group and 36% of control (β-TCP) group.

To the best of our knowledge, this is the first study to explore the efficacy of rhPDGF-BB+ β-TCP exclusively in Grade II furcations. Hence, direct comparisons could not be made with similar studies. Within the limitations of the study, the following parameters were compared.

In this study, the mean GI in Group I reduced from 1.12 ± 0.30 at baseline to 0.24 ± 0.05 at the end of 6 months and in Group II baseline it was 1.04 ± 0.25 which reduced to 0.22 ± 0.07 at the end of 6 months. Intragroup comparison of GI from baseline to 1 month, 3 months, and 6 months in both the groups has shown improvement and they were statistically significant ($P < 0.05$*) but intergroup comparison they were not significant. This was in accordance with Maroo and Murthy[26] who have used similar graft in intraosseous defects. Mansouri *et al*.[27] reported a significant improvement in GI at 6 months using bovine porous bone mineral (BPBM) and BPBM + plasma rich in growth factor (PRGF). This may be because of more inflammation at baseline in their study (GI is 1.61 ± 0.22) as compared to the present study.

In this study, the mean plaque index (PI) in Group I was 1.10 ± 0.33 at baseline which reduced to 0.24 ± 0.08 at the end of 6 months, in Group II it was 1.04 ± 0.27 at baseline which reduced to 0.22 ± 0.06 at the end of 6 months. There was statistically significant improvement of the mean plaque index in intragroup comparison. There was improvement in indices from baseline to 1, 3, and 6 months in both the groups. Intergroup comparison was not statistically significant on. This finding is similar with the studies of Maroo and Murthy[26] using similar graft as the present study and Mansouri *et al*.[27] using BPBM and BPBM+PRGF. This may be attributed to the good plaque maintenance by the patients as well as routine supragingival scaling at recall visits at 1 month, 3 months, and 6 months.

In the present study, the mean PPD in Group I was 6.00 ± 1.20 mm at baseline which reduced to 3.73 ± 1.33 mm at the end of 6 months and in Group II mean PPD at baseline was 6.13 ± 0.83 mm which reduced to 2.53 ± 0.74 mm at the end of 6 months. Intragroup comparison showed that there was a statistically significant reduction in PPD scores from baseline to 1 month, baseline to 3 months, and baseline to 6 months at all the study intervals in both the groups ($P < 0.05$*). However, intergroup comparison was a statistically significant reduction in mean PPD scores from baseline to 3 months and baseline to 6 months between Group I and Group II ($P < 0.05$*). And higher reduction in mean PPD scores was noticed in Group II (test group).

PPD reduction is not only a desirable outcome of periodontal regenerative procedures but may also be the most important parameter in patient care for the clinician because it directly impacts one's ability to instrument a treated area during maintenance appointments. Wallace *et al*.[28] observed a PPD reduction of 1.5 mm using expanded polytetrafluoroethylene (ePTFE) at 6 months. Luepke *et al*.[29] reported PPD reduction of 1.37 ± 0.95 mm using resorbable GTR.

Kanoriya *et al*.[30] reported a PPD reduction of 1.73 ± 0.96 mm using cellulose membrane (resorbable GTR) at 6 months. It is a well-known fact that GTR is consistently effective in the treatment of furcation defects. It is observed that PPD reductions in the test group of present study were superior to those of the above-mentioned studies. PPD reduction could be due to good plaque maintenance by the patients and supragingival scaling during recall visits. The improvement in soft-tissue parameters also reflects PDGF's chemotactic effect on periodontal ligament osteoblasts, fibroblasts, and cementoblasts.

Scott *et al*.[31] reported a PPD reduction of 0.3 ± 1.6 mm at 6 months using ePTFE. Eickholz *et al*.[32] observed PPD reduction of 0.5 ± 1.73 mm and 0.54 ± 1.10 mm at 12 months using polylactide and polydioxanon barriers. In the present study, rhPDGF-BB plus β-TCP plus chorion membrane demonstrated better PPD reduction (2.53 ± 0.74) than the barriers alone.

The RAL in the present study in Group I was 6.13 ± 1.51 mm at baseline, which reduced to 3.73 ± 1.33 mm at the end of 6 months and in Group II it was 6.73 ± 1.33 mm at baseline which reduced to 2.60 ± 0.91 mm at the end of 6 months. Intragroup comparison of RAL scores has shown statistically significant reduction from baseline to 1 month, baseline to 3 months, and baseline to 6 months at all the study intervals ($P < 0.05$*). The intergroup comparison of mean RAL scores from baseline to 1 month, baseline to 3 months, and baseline to 6 months between Group I and Group II was also found to be statistically significant ($P < 0.05$*) (Table 3). Better reductions in mean RAL scores were observed in Group II (test group).

Luepke *et al*.[29] in their 6-month re-entry study observed CAL gain of 1.83 ± 1.36 mm using resorbable barrier and DFDBA. Mansouri *et al*.[27] reported CAL gain of 1.57 ± 0.96 mm, 1.65 ± 1.24 mm using BPBM and BPBM+PRGF. In the present study, the mean CAL gain was 4.13 ± 0.42 mm at the end of 6 months in the test group which showed better improvement compared to the above studies which is due to the enhanced action of use of growth factor, that is, rhPDGF-BB.

Nevins *et al*.[10] reported a CAL gain of 3.2 ± 2.17 mm at 9 months using rhPDGF-BB in combination with DFDBA. Kanoriya *et al*.[30] and Pradeep *et al*.[31] proclaimed CAL gain of 2.33 ± 0.49 mm, 2.87 ± 0.85 mm, 3.39 ± 0.49 mm, and 3.31 ± 0.52 mm, respectively, at 9 months using PRF.

The RAL gain at 6 and 9 months in the test and control groups of the present study surpasses the attachment gain achieved in the above-mentioned studies. This enhanced attachment gain in the present study is attributed to the presence of β-TCP. Although β-TCP does not form new connective tissue, it provides a scaffold for new bone formation and also facilitates

the stabilization of the blood clot. As β-TCP is porous, it entraps growth factors such as rhPDGF within its micropores, thereby prolonging their action.

Jayakumar *et al*.[11] and Maroo and Murthy[26] reported a statistically significant PPD reduction and CAL gain at 6 months on intergroup comparison using the same graft material as the present study in intraosseous defects. Jayakumar *et al*.,[11] in addition, to the placement of graft material has also carried out tetracycline root conditioning, and to render the root surface more conducive for effective growth factor utilization. However, in the present study, no root conditioning was done. The conditioned root surface may have also served as additional slow-release delivery system of PDGF-BB, thereby enhancing periodontal regeneration.

In the present study, it was also observed that buccal furcation defects had more attachment gain than that of lingual furcations. Yet, a comparison could not be made as the proportion of buccal and lingual furcations were not equal. Pontoriero *et al*.[32] likewise found attachment level improvement by 4.1 mm in buccal defects and 2.9 mm in lingual furcation with ePTFE alone.

The primary objective of the present study was to compare the results of β-TCP plus chorion membrane with that of β-TCP +chorion membrane+ rhPDGF-BB. Thus, for the evaluation of the main outcome, variables such as PPD and clinical attachment levels were considered. Change in the clinical parameters following regenerative therapy is the most commonly used clinical outcome variable.[33] Clinical attachment gain in the test group was found to be higher than control group at the end of the study and was statistically significant ($P < 0.05$*). The improved clinical parameters in the test group can be attributed to the usage of rhPDGF-BB which stimulates periodontal regeneration by functioning as a periodontal tissue engineering material, recruiting cells such as osteoblasts, cementoblasts, periodontal ligament cells, and endothelial cells into the graft to improve the regenerative outcome. β-TCP acts as a scaffold to physically fill the periodontal defect and prevents soft-tissue from collapsing into the defect, and it performs as a carrier for rhPDGF-BB.

Mean area of radiographic defect scores (sq mm) for Group I at baseline was 3.03 ± 1.56 mm^2 reduced to 2.01 ± 1.11 mm^2 at end of 6 months. In Group II at baseline, it was 3.09 ± 1.51 mm^2 which reduced to 0.90 ± 0.37 mm^2 at the end of 6 months. There was a statistically significant reduction in mean area of radiographic defect scores from baseline to 3 months, baseline to 6 months and 3–6 months at all the study intervals in both the groups ($P < 0.05$*). The intergroup comparison of mean area of radiographic defect scores from baseline to 3 months and baseline to 6 months between Group I and Group II was also found to be statistically significant ($P < 0.05$*). rhPDGF-BB has the ability to enhance the directed migration of osteoblasts coronally and into the defect. This chemotactic action toward periodontal ligament osteoblasts (in addition to the osteoconductive action of β-TCP) is responsible for the increased bone fill seen in the test site as opposed to the control site, in which the osteoconductive action of the β-TCP alloplast alone contributed to bone fill. β-TCP is absorbed over 6–8 months and thus did not obscure the bone fill in the radiograph. Further, because both the controls and test groups included β-TCP, any increase in radiopacity that might be caused by residual β-TCP would presumably be similar in both groups.

In the present study, favorable results were reported with both the treatment modalities. A question arises whether the initial beneficial effects in clinical and radiographic parameters observed with rhPDGF-BB + β-TCP at 3 and 6 months are transient or sustained. McGuire *et al*.[34] reported that CAL gain and % BF observed at 6 months were maintained even at 18- and 24-months post-surgery. However, the investigation of occurrence of true periodontal regeneration can be performed only with histological studies, and the biologically plausible benefit of the association cannot be evaluated through clinical and radiographic evaluation. Although histologic evaluation is the only way to confirm periodontal regeneration, because of ethical considerations and patient management limitations, no histologic evidence was obtained in the present study to establish proof of periodontal regeneration.

It is also noteworthy that radiographic assessment of alveolar bone fill often underestimates actual bone fill measured clinically (i.e. at surgical re-entry). Thus, the current study results, which demonstrate a gain in radiographic bone fill, may actually underestimate the amount gained. To overcome this scenario, cone beam computed tomography (CBCT) also known as digital volume tomography can be employed to shed some light on the 3-dimensional view of the furcations and also obtain volumetric bone fill. Surgical and CBCT measurements have been shown to be equivalent about 82–84% of the time, and very rarely overestimates and underestimates, which makes CBCT measurements a reliable alternative to surgical measurements.[35]

The drawbacks in the present study are (1) limited sample size used for the comparison of rhPDGF-BB + β-TCP + chorion membrane and β-TCP + chorion membrane alone, (2) the follow-up time, and (3) radiographic assessment which gives only a two-dimensional interpretation of complex furcation anatomy. The strength of the present study is its novelty where in two groups' rhPDGF-BB + β-TCP + chorion membrane and β-TCP + chorion membrane alone are compared where both the materials improve the regeneration potential.

Further long-term multicenter randomized controlled studies with a larger sample are required to prove the efficacy of rhPDGF-BB + β-TCP + chorion membrane in the treatment of Grade II furcations. Future studies could also benefit by using advanced imaging techniques like CBCT to assess the bone fill which could have been underestimated in the present study. Within the limitations of the present study, it could be said that both the treatment modalities were successful in showing promising results in the treatment of Grade II furcation defects in chronic periodontitis patients.

Conclusion

Within the limitations of the study, it can be concluded that treatment with rhPDGF + β-TCP + chorion membrane resulted in a significantly greater PPD reduction, RAL gain, and defect fill, in comparison with β-TCP + chorion membrane. Based on the results of the present study rhPDGF-BB used as an adjunct to β-TCP and chorion membrane, can provide a new direction in the management of furcation defects.

Conflicts of Interest

The authors declare they have no potential conflict of interests regarding this article.

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