A novel approach in the management of mandibular degree II furcation defects using bone grafts in conjunction with a biomimetic agent: A randomized controlled clinical trial

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Abstract:
Aim: Of the periodontal defects requiring regeneration, degree II furcation defects pose a substantial challenge to clinicians. This study was designed to evaluate the relative effectiveness of bone autograft (BA) and autologous platelet-rich fibrin (PRF) as against decalcified freeze-dried bone allograft (DFDBA) along with autologous PRF in the management of degree II mandibular furcation defects. Materials and Methods: Fourteen patients (11 men and 3 women; mean age: 42.36 years), with bilateral degree II buccal furcation defects in the mandibular molars, were enrolled in the study. In each patient, randomly selected sites were divided into control site (site A) which received BA with PRF membrane and test site (site B) received DFDBA + PRF mixed with graft and also as a membrane using split-mouth design. Clinical parameters including plaque index, gingival index, gingival marginal levels, probing depth, and clinical attachment level were recorded at baseline and at 3 and 6 months' postsurgery. Horizontal and vertical furcation measurements were taken prior to the surgery through sounding and after degranulation. These measurements were repeated after 6 months. Results: The mean reduction in the horizontal defect depth was 1.86 ± 0.66 mm (70.75%) in site A and 1.71 ± 0.73 mm (74.25%) in site B. The mean improvement in the vertical defect fill was 1.64 ± 0.74 mm (55.8%) in site A and 1.43 ± 1.34 mm (64.86%) in site B was achieved. Conclusion: The use of combination therapy using either BA or DFDBA in conjunction with PRF appears to be effective in treating furcations. Key words: Allograft and platelet-rich fibrin, furcation defects, guided tissue regeneration

INTRODUCTION

Of the various osseous defects that are difficult to treat, degree II furcations have posed a considerable challenge for clinicians. This difficulty can be attributed to the anatomy of the furcation. Among the various treatment modalities that have been employed for addressing furcation defects, guided tissue regeneration (GTR) has emerged as the most successful treatment for the preservation of furcation involved teeth. The use of osseous grafts in furcation therapy, along with GTR has been seen to amplify the response to treatment as compared to the use of membrane alone.

Bone autografts (BAs) are still considered as ideal materials for grafting procedures as they have conductive bone trabeculae, cells, and signaling molecules (e.g., growth factors [GFs]). Even though intraoral autografts possess ideal characteristics of graft material, their harvesting is invasive and often requires a second surgical site. Of all the graft materials currently used for regeneration, decalcified freeze-dried bone allograft (DFDBA) is popularly considered as an attractive alternative to reduce the harvesting site, while still maintaining or providing the defect with an osteoconductive matrix.

This enhanced response is achieved by the inductive effect of the graft resulting in bone restoration, concomitant with the membrane helping in better confinement of the graft and epithelial exclusion.

Bone grafts also provide the necessary structural integrity to withstand compressive forces, thereby preventing the membrane from collapsing into the defect.
effective alternative to BA. DFDBA aids in the regeneration of periodontal tissues by providing an osteoconductive surface, along with bone morphogenetic protein (BMP) such as BMP-2, -4, and -7. These BMPs help stimulation of bone formation by inducing pluripotent stem cells to get differentiated into osteoblasts. Identifying the role of GFs as key mediators in bone regeneration and soft-tissue maturation has been facilitated with improved knowledge in wound healing. One such reservoir of GFs is the α-granules of platelets. Choukroun’s platelet-rich fibrin (PRF) has opened new possibilities in wound healing and tissue regeneration. When compared to the first-generation platelet concentrates, rigid fibrin network found in PRF facilitates cytokine, and GF entrapment resulting in their sustained release. PRF promotes the healing of osseous defects through its actions by upregulating “phosphorylated extracellular signal-regulated protein kinase” and “osteoblast transcription factor-run-related transcription factor 2.” A substantial postoperative protection of the surgical site is offered when PRF is used in the form of a membrane. It can also accelerate bone formation by enhancing integration and remodeling when used along with grafted material as fragments.

Thus, the present study sought to investigate changes in furcation defect fill with the use of autogenous bone and PRF when compared to the use of DFDBA and PRF, in the management of bilateral mandibular degree II furcation defects.

MATERIALS AND METHODS

For this study, 14 patients (11 men and 3 women; mean age: 42.36 years) scheduled for periodontal treatment were selected from the outpatient department of Periodontics and Oral Implantology of our institution. Approval was obtained from the Institutional Ethical Committee. Written informed consent was obtained from patients after explaining the treatment plan. Individuals in good systemic health with moderate-to-severe periodontitis, having at least two degree II buccal furcation defects (Hamp’s classification system) on contralateral sides of the mandibular arch, gingival marginal level (GML) above the roof of furcation defect and having adequate sites for harvesting intraoral bone were included in the study. Patients showing insufﬁcient motivation and oral hygiene maintenance (plaque index [PI] >1.5) during presurgical therapy; with teeth demonstrating greater than Grade I mobility; having teeth with periapical pathosis and caries; and smokers were not included in the study.

Clinical parameters such as PI, gingival index (GI), GMLs, probing depth (PD), and clinical attachment level (CAL) were included in the study. GML, PD, and CAL were measured from the reference point on customized acrylic stents, using UNC-15 probe (GDC, Punjab, India). All these measurements were recorded at baseline, and at 3 and 6 months. Horizontal and vertical furcation defect (VFD) measurements were taken using UNC-15 probe; for measuring the horizontal defect depth measurements a vacuum formed stent was fabricated on casts with the buccal side extending to cover the attached gingiva and a hole was made at the buccal extension of the stent approximately coinciding with the furcal entrance [Figure 1]. This hole served as a reference point. Vertical defect depths were measured from acrylic stent on the occlusal surface of teeth with a groove enabling to position probe toward furcation.

Horizontal and vertical furcation measurements were taken through sounding prior to the initial surgical procedure, which was designated as horizontal furcation defect (HFD)-(closed) and VFD (closed) [Figure 2]; these measurements were also repeated during reevaluation. Measurements taken following completion of degranulation was designated as HFD (open) and VFD (open) [Figure 3]. VFD and HFD were measured from relative reference point to the base of the defect.

Phase I therapy was administered which included oral hygiene instruction, scaling and rootplanning and occlusal corrections on all selected patients. The selected sites were divided into experimental site A (control, BA + PRF membrane) and experimental site B (test, DFDBA with PRF + PRF membrane) using split-mouth design. The sites were divided randomly (toss of a coin) into the control and test groups before the surgical procedure. At the start of the surgical procedure, PRF was prepared using the Choukroun et al., protocol. After anesthetizing the surgical site, sulcular incisions were made and mucoperiosteal flaps were elevated. The defect was debrided and root planning was carried out using area specific and Quentin furcation curettes (Gracey; Hu-Friedy, Chicago, IL, USA). For site A, autogenous bone graft was harvested from intraoral donor sites (mandibular symphysis, ramus, maxillary tuberosity, and edentulous areas) using trephines and milled with bone morselizer to obtain fine particulate bone which was then made into a cohesive mass by mixing it with the patients’ blood. It was delivered into the furcation defect with light incremental pressure using the scoop of a cuminescaler until the defect was completely filled [Figure 4]. Site B was also treated in a similar manner but the graft used was DFDBA (Tata Memorial Hospital Tissue Bank, Mumbai, India) with particle size <500 μ. This was mixed with sterile saline and was then mixed with PRF clots cut into millimeter fragments and blended to obtain a homogeneous mass [Figure 5]. The compressed PRF membrane was applied to enclose the defect area and extending at least 3 mm beyond the defect [Figure 6]. The coronally repositioned flap was adapted using a sling suture with 3-0 black silk around the tooth [Figure 7]. The operated sites were protected with periodontal dressing (Coe-pak).

Statistical analysis

The data were analyzed using Statistical Package for Social Sciences (Version 21.0, IBM SPSS, Armonk, New York, USA). Power was set at 85%. To detect mean differences of the defect fill between groups, a sample size of 14 would be sufficient. For intragroup variations, Wilcoxon–matched paired test was performed and for comparison between the two groups Mann–Whitney U-test was done. The threshold value for statistical significance was set at α = 0.05.

RESULTS

A statistically significant reduction in the PI and GI was observed in both groups at various time intervals [P ≤ 0.001; Table 1]. Mean PD reduction and gain in CAL were observed in both groups at various time intervals which were found to be statistically significant [P < 0.001; Tables 2 and 3].
Mean gain in GMLs at site A and B, respectively, was $0.64 \pm 0.5$ mm (87.87%) and $0.43 \pm 0.94$ mm (91.63%) at 3 months, $0.79 \pm 0.43$ mm (85.26%) and $0.5 \pm 0.94$ mm (90.27%) at 6 months. These values were found to be statistically highly significant [$P < 0.00001$; Table 4].
The mean change in the horizontal defect depth reflected as defect fill was 1.86 ± 0.66 mm (70.75%) and 1.71 ± 0.73 mm (74.25%) in site A and site B, respectively [Table 5]. The mean change in the vertical defect fill was 1.64 ± 0.74 mm (55.8%) and 1.43 ± 1.34 mm (64.86%) in site A and site B, respectively [Table 6]. Statistically significant ($P < 0.0001$) difference was observed in both groups with respect to defect fill at 6 months [Figures 8-11].

No significant difference was observed between the two groups for any of the clinical parameters at various time intervals. Mean change in horizontal and vertical defect measurements using open and closed methods at baseline was also found to be nonsignificant in both the groups ($P > 0.05$; Table 7).

**DISCUSSION**

The main objective in the management of furcation defects is to prevent further loss of periodontal tissue and also to enable the patient to effectively maintain the region – this can be best achieved by regeneration of lost tissue. This study was designed to evaluate the relative efficacy of PRF with DFDBA and PRF with BA and to evaluate whether DFDBA can act as a substitute for BA in treating furcations when used in conjunction with PRF. Measuring furcations for their assessment has posed...
In order to overcome these drawbacks, this study made use of a customized stent as described by Laxman et al. to provide a fixed reference point for measuring the horizontal component of the furcation; this reference point served to evaluate changes in presurgically and postsurgically measurements.

Table 1: Comparison of mean site plaque and gingival index scores at experimental site A and site B at baseline, 3 months, and 6 months

| Groups                  | Mean±SD         | Reduction from baseline to 3 months | Reduction from baseline to 6 months | Reduction from 3-6 months |
|-------------------------|-----------------|------------------------------------|------------------------------------|--------------------------|
| PI                      |                 | Baseline 3 months                  | Baseline to 6 months               | 3-6 months               |
| Experimental site A     | 0.23±0.12       | 0.09±0.27                          | 0.001*                             | 0.001*                   |
| P                       | 0.18±0.21       | 0.11±0.16                          | 0.11±0.23                          |
| Experimental site B     | 0.32±0.19       | 0.09±0.23                          | 0.002*                             | 0.001*                   |
| P                       | 0.23±0.18       | 0.13±0.21                          | 0.11±0.23                          |
| GI                      |                 | 0.09±0.23                          | 0.11±0.23                          | 0.02±0.15                |
| Experimental site A     | 0.14±0.21       | 0.04±0.19                          | 0.001*                             | 0.001*                   |
| P                       | 0.05±0.11       | 0.04±0.09                          | 0.02±0.15                          |
| Experimental site B     | 0.1±0.16        | 0.05±0.11                          | 0.001*                             | 0.001*                   |
| P                       | 0.05±0.11       | 0.05±0.2                           | 0.02±0.15                          |

*P≤0.05 significant. SD – Standard deviation; PI – Plaque index; GI – Gingival index; SD – Standard deviation; P – Probability value

Table 2: Comparison of experimental site A and site B mean probing pocket depth scores (mm) at baseline, 3 months, and 6 months

| Groups                  | Mean±SD         | Reduction from baseline to 3 months | Reduction from baseline to 6 months | Reduction from 3-6 months |
|-------------------------|-----------------|------------------------------------|------------------------------------|--------------------------|
|                         |                 | Baseline 3 months                  | Baseline to 6 months               | 3-6 months               |
| Experimental site A     | 4±0.78          | 1.5±0.52                           | 1.79±0.58                          | 0.29±0.61                |
| P                       | 2.5±1.09        | 2.21±0.7                           | 1.93±0.47                          |
| Experimental site B     | 3.86±0.86       | 1.71±0.61                          | 1.93±0.62                          | 0.21±0.58                |
| P                       | 2.14±0.95       | 1.93±0.47                          | 88.4                               |
| Percentage of change in A | 62.5           | 0.001*                             | 0.001*                             | 0.001*                   |
| P                       |                 | 55.4                               | 90.19                              |
| Percentage of change in B | 54.4           | 0.002*                             | 0.001*                             | 0.001*                   |
| P                       |                 | 0.33                               | 0.53                               | 0.75                     |

*P≤0.05 significant. mm – Millimeters; SD – Standard deviation; P – Probability value

Table 3: Comparison of experimental site A and site B clinical attachment level - midfacial (mm) scores at baseline, 3 months, and 6 months

| Groups                  | Mean±SD         | Reduction from baseline to 3 months | Reduction from baseline to 6 months | Reduction from 3-6 months |
|-------------------------|-----------------|------------------------------------|------------------------------------|--------------------------|
|                         |                 | Baseline 3 months                  | Baseline to 6 months               | 3-6 months               |
| Experimental site A     | 4.5±1.02        | 1.43±0.65                          | 1.93±0.73                          | 0.5±0.62                 |
| P                       | 3.07±1.21       | 2.57±1.22                          | 1.93±0.73                          | 0.14±0.36                |
| Experimental site B     | 4.21±0.97       | 1.79±0.7                           | 1.93±0.73                          | 83.71                    |
| P                       | 2.43±1.02       | 2.29±0.73                          | 57.11                              |
| Percentage of change in A | 0.001*         | 0.001*                             | 0.001*                             | 0.001*                   |
| P                       |                 | 57.11                              | 94.24                              |
| Percentage of change in B | 0.002*         | 0.001*                             | 0.001*                             | 0.001*                   |
| P                       |                 | 0.17                               | 1                                  | 0.05*                    |

*P≤0.05 significant. mm – Millimeters; SD – Standard deviation; P – Probability value

Table 4: Comparison of experimental site A and site B mean gingival marginal level scores (mm) at baseline, 3 months, and 6 months

| Groups                  | Mean±SD         | Reduction from baseline to 3 months | Reduction from baseline to 6 months | Reduction from 3-6 months |
|-------------------------|-----------------|------------------------------------|------------------------------------|--------------------------|
|                         |                 | Baseline 3 months                  | Baseline to 6 months               | 3-6 months               |
| Experimental site A     | 5.36±0.5        | 0.64±0.5                           | 0.79±0.43                          | 0.14±0.36                |
| P                       | 4.71±0.47       | 4.57±0.51                          | 4.64±1.01                          |
| Experimental site B     | 5.14±1.03       | 0.43±0.94                          | 0.5±0.94                           | 0.07±0.27                |
| P                       | 4.71±0.91       | 4.64±1.01                          | 87.87                              |
| Percentage of change in A | 0.0001*        | 0.0001*                            | 0.0001*                            | 98.51                    |
| P                       |                 | 90.27                              | 98.51                              |
| Percentage of change in B | 0.00001*       | 0.00001*                           | 0.00001*                           | 0.00001*                 |
| P                       |                 | 0.46                               | 0.31                               | 0.56                     |

*P≤0.05 significant. mm – Millimeters; SD – Standard deviation; P – Probability value

In order to overcome these drawbacks, this study made use of a customized stent as described by Laxman et al. to provide a fixed reference point for measuring the horizontal component of the furcation; this reference point served to evaluate changes in presurgically and postsurgically measurements.
Table 5: Comparison of experimental site A and site B mean horizontal change in furcation defect measurements scores (mm) at baseline and 6 months

| Groups          | Baseline, mean±SD | 6 months, mean±SD | Reduction from baseline-6 months | Percentage of change |
|-----------------|-------------------|-------------------|----------------------------------|----------------------|
|                 | Mean±SD           | Mean±SD           | Mean±SD                          | Percentage of change |
|                 |                   |                   |                                 |                      |
| Experimental site A | 6.36±0.71         | 4.5±0.96          | 1.86±0.66                        | 70.75                |
| Experimental site B | 6.64±0.47         | 4.93±0.45         | 1.71±0.73                        | 74.25                |
| P (inter group)  | 0.33              | 0.38              | 0.59                             |                      |

*P≤0.05 significant. mm – Millimeters; SD – Standard deviation; P – Probability value

Table 6: Comparison of experimental site A and site B mean vertical change in furcation defect measurements mm) at baseline and 6 months

| Groups          | Baseline, mean±SD | 6 months, mean±SD | Reduction from baseline-6 months | Percentage of change |
|-----------------|-------------------|-------------------|----------------------------------|----------------------|
|                 | Mean±SD           | Mean±SD           | Mean±SD                          | Percentage of change |
|                 |                   |                   |                                 |                      |
| Experimental site A | 3.71±0.29         | 2.07±0.72         | 1.64±0.74                        | 55.8                 |
| Experimental site B | 4.07±0.84         | 2.64±0.74         | 1.43±1.34                        | 64.8                 |
| P (inter group)  | 0.29              | 0.09              | 0.61                             |                      |

*P≤0.05 significant. mm – Millimeters; SD – Standard deviation; P – Probability value

Table 7: Comparison of changes in horizontal and vertical defect measurements (mm) using open and closed methods at baseline

| Groups          | Parameters                   | Mean±SD | Mean difference | SD difference | P     |
|-----------------|------------------------------|---------|-----------------|---------------|-------|
|                 | Vertical furcation defect closed | 3.71±0.29 | 0               | 0.39          | 0.99  |
| Experimental site A | Vertical furcation defect open         | 3.71±1.23 |                 |               |       |
|                 | Horizontal furcation defect sounding | 6.35±0.71 | 0              | 0.36          | 0.7   |
|                 | Horizontal furcation defect open      | 6.5±0.66 | 0.14            | 0.53          | 0.66  |
| Experimental site B | Horizontal furcation defect closed     | 6.64±0.47 | 0              | 0.58          | 0.81  |
|                 | Horizontal furcation defect open      | 6.85±0.73 | 0              | 0.58          | 0.81  |
|                 | Vertical furcation defect closed      | 4.07±0.84 | 0              | 0.53          | 0.66  |
|                 | Vertical furcation defect open        | 3.92±1.76 | 0              | 0.53          | 0.66  |

P≤0.05 significant. mm – Millimeters; SD – Standard deviation; P – Probability value

over time. The evaluation of hard tissue changes using bone sounding was found to be reliable by Zybutz et al. (2000) and Suh et al. (2002). In the present study, the comparison between bone sounding measurements before flap reflection and open bone level measurements after flap reflection at baseline showed no statistically significant difference, suggesting that transgingival probing can be used as a reliable method to assess changes in furcation measurement without the need for re-entry. Despite the lack of significant differences in pocket depth reduction and CAL gain between groups, the results obtained in this study were not commensurate to earlier studies which achieved more favorable results with the use of combination therapy for treating furcation defects.[22,24-27] This can be attributed to the presence of shallower pocket depths at baseline in this study – 4 mm and 3.8 mm in Group A and B, respectively, when compared to the reference studies.

Gingival recession is one of the factors that influence the final outcome of periodontal regeneration. It often results in reduced regenerative capacity.[28,29] A mean gain in the gingival margin levels of about 0.64 mm (87%) and 0.79 mm (85%) in Group A and 0.43 mm (91%) and 0.5 mm (90%) in Group B was found at 3 and 6 months, respectively. Gupta et al. (2014) reported a significant improvement in the recession height of 2.17 ± 0.35 mm, with mean root coverage of 97.22% and Arora et al. reported root coverage of about 88% when PRF was used to treat gingival recession.[30,31]

A recent study by Mehta et al. showed no significant difference with the use of either collagen or PRF along with DFDBA in treating furcations.[32] These results were similar to the results obtained in this study where in PRF was used as a membrane to cover the furcation defect.

The most important outcome for studies assessing the effectiveness of regenerative procedures in Class II furcations include improvement in furcation status (reduction into Class I or total closure) through horizontal bone fill.[1,33] None of the experimental groups exhibited complete furcation fill. The mean positive change in the horizontal defect fill in this study was 1.86 ± 0.66 mm (70.75%) for Group A and 1.71 ± 0.73 mm (74.25%) for Group B. The results from this study demonstrated slightly lesser horizontal defect fill when compared to the results from the previous studies by Luepke and Mellonig,[32] which employed a biodegradable barrier with DFDBA demonstrating a horizontal bone fill of 2.10 mm at 6 months. Maragos et al. made use of calcium sulfate as a graft/barrier material mixed with DFDBA.
Variation in the results of this study in comparison to studies which made use of combination therapy by employing different materials in the management of furcation can probably be due to a different level of prognostic factors such as variations in defect morphology,[37] a differing surgical procedure along with the use of different barrier material and grafts. In addition, these studies have measured horizontal defect depth using different reference points, further alienating comparisons among studies. The absence of statistical significance for defect fills between the two groups suggests that DFDBA can serve as a substitute for BA when used in conjunction with PRF.

**CONCLUSION**

This study demonstrated that the use of PRF as a membrane, along with DFDBA, can serve as a cost-effective and less invasive combination, when compared to PRF with BA. However, long-term, randomized, controlled clinical trials with histological and densitometric evaluations will be needed to know the clinical efficacy of PRF along with DFDBA, and if it can be considered an alternative to BA in treating osseous defects.

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**Conflicts of interest**
There are no conflicts of interest.

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