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Edited by Ritik Kashwani
E-mail: docritikkashwani@yahoo.com
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Comparative analysis of regenerative materials for endo-perio defects

Priyatam Maruti Karade[1], Ruchi Gulati[2,*], Kasarla Sindhu Reddy[3], Kashish Bhawar [4], Ashtha Arya[5] & Lakshmi Sadeesh[6]

[1]Department of Conservative Dentistry and Endodontics, Bharati Vidyapeeth (Deemed To Be University) Dental College and Hospital, Sangli , India; [2]Department of Periodontology & Implantology, Mansarovar Dental College, Bhopal ,Madhya Pradesh, India; [3]Department of Dentistry, Malla Reddy vishwa Vidhyapeet, Suraram ,Hyderabad, India; [4]Department of Conservative Dentistry & Endodontics, 501, Usha Nagar extension, Indore, Madhya Pradesh India; [5]Department of Conservative Dentistry and Endodontics, SGT Dental College, Hospital and Research Institute, SGT University, Gurugram, Haryana, India; [6]Department of Conservative Dentistry and Endodontics, PSM College of Dental Science and Research, Akkikavu, Kerala, India; *Corresponding author

Affiliation URL:

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Author contact:
Priyatam Maruti Karade - E-mail: priyatam.karade@bharatividyapeeth.edu
Ruchi Gulati - E-mail: gulati.drruchi@gmail.com
Kasarla Sindhu Reddy - E-mail: sindhuk2999@gmail.com
Kashish Bhawar - E-mail: kashbhawar@gmail.com
Ashtha Arya - E-mail: drashthaarya@yahoo.co.in
Lakshmi Sadeesh - E-mail: lakshmisadeesh@gmail.com

Abstract:
Endodontic-periodontal defects involve both pulpal and periodontal tissues and present challenges in achieving predictable regeneration. Therefore, it is of interest to compare the Platelet-Rich Fibrin (PRF) combined with Demineralized Freeze-Dried Bone Allograft (DFDBA) versus DFDBA alone in 100 patients with endo-perio defects. Both groups showed clinical and radiographic improvement, but PRF with DFDBA produced greater probing pocket depth reduction, clinical attachment gain, bone fill and tooth stability ($p < 0.001$). Clinical success at 12 months was higher with PRF and DFDBA than DFDBA alone (92.0% vs. 76.0%). Thus, adjunctive PRF with DFDBA improved periodontal regeneration and clinical outcomes in the management of endo-perio defects.

Keywords: Endo-perio lesions, platelet-rich fibrin (PRF), demineralized freeze-dried bone allograft (DFDBA), regenerative therapy, clinical attachment level, bone regeneration, randomized controlled trial (RCT)

Background:
Endodontic-periodontal lesions involve pathological communication between pulpal and periodontal tissues through anatomical pathways such as the apical foramen, accessory canals and dentinal tubules **[1]**. Their management requires elimination of infection and restoration of lost periodontal tissues **[2]**. These lesions may present with deep periodontal pockets, bone defects, tooth mobility and extensive attachment loss, increasing the risk of tooth loss **[3, 4]**. Treatment generally involves endodontic therapy followed by appropriate periodontal management, although regeneration remains challenging in advanced defects **[5]**. Demineralized Freeze-Dried Bone Allograft (DFDBA) has regenerative potential through its osteoconductive and osteoinductive properties but may provide variable outcomes depending on defect and patient factors **[6, 7]**. Platelet-Rich Fibrin (PRF) provides a fibrin scaffold and sustained release of growth factors that may promote angiogenesis, tissue repair and bone regeneration **[8]**. Combining PRF with bone grafts may enhance graft stability and periodontal regeneration compared with grafting alone **[9]**. However, evidence regarding optimal regenerative protocols for true endodontic-periodontal lesions remains limited **[10]**. Therefore, it is of interest to compare the clinical and radiographic effectiveness of PRF combined with DFDBA versus DFDBA alone in endodontic-periodontal defects over 12 months.

Methodology:
Study design and setting:
A prospective, parallel-arm, randomized controlled clinical trial was conducted in the Department of Periodontology in collaboration with the Department of Conservative Dentistry and Endodontics at a tertiary care teaching hospital over a period of twelve months after obtaining approval from the Institutional Ethics Committee. The study adhered to the Declaration of Helsinki and written informed consent was obtained from all participants.

Study population:
One hundred patients aged between 20 and 60 years diagnosed with endodontic-periodontal lesions requiring both root canal treatment and regenerative periodontal surgeries were recruited. Participants were randomly allocated using computer-generated block randomization.

Group: A (n=50): Conventional root canal treatment followed by regenerative surgery using Platelet-Rich Fibrin (PRF) with Demineralized Freeze-Dried Bone Allograft (DFDBA).

Group: B (n=50): Conventional root canal treatment followed by regenerative surgery using Demineralized Freeze-Dried Bone Allograft (DFDBA) alone.

Inclusion criteria:
[1] Patients aged 20–60 years.
[2] Primary endodontic lesions with secondary periodontal involvement.
[3] True combined endodontic-periodontal lesions.
[4] Probing depth ≥6 mm.
[5] Radiographic intrabony defects ≥3 mm.
[6] Teeth with adequate coronal restorability.
[7] Patients providing written informed consent.

Exclusion criteria:
[1] Smokers consuming more than ten cigarettes daily.

[2] Pregnancy or lactation.
[3] Uncontrolled diabetes mellitus.
[4] Immunocompromised patients.
[5] Aggressive periodontitis.
[6] Previous regenerative surgery at the study site.
[7] Teeth with vertical root fractures.
[8] Grade III mobility.
[9] Patients receiving antibiotics within the previous four weeks.

Sample size:
The required sample size of 100 participants was calculated considering previous clinical studies evaluating regenerative materials in periodontal intrabony defects with 80% statistical power, 95% confidence interval and 5% level of significance. Fifty participants were allocated to each treatment group.

Clinical protocol:
Following faze I periodontal therapy, all patients underwent standardized nonsurgical root canal treatment completed before regenerative surgery. For Group A, approximately 10 mL of venous blood was collected immediately before surgery and centrifuged to obtain Platelet-Rich Fibrin. After flap reflection and defect debridement, DFDBA was placed into the osseous defect and covered with PRF membrane before flap closure. For Group B, identical surgical procedures were performed except that only DFDBA was placed within the defect before flap closure. All patients received identical postoperative medications and oral hygiene instructions.

Outcome measures:
Primary outcomes:
[1] Reduction in probing pocket depth (PPD)
[2] Gain in clinical attachment level (CAL)

Secondary outcomes:
[1] Radiographic bone fill (%)
[2] Gingival recession
[3] Tooth mobility
[4] Clinical success
[5] Postoperative complications

Statistical analysis:
Data were analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as frequency and percentage. Independent t-test, paired t-test, repeated-measures ANOVA and Chi-square test were applied where appropriate. Statistical significance was established at $p<0.05$.

Results:
A total of 100 participants completed the study without loss to follow-up, with 50 patients in Group A (PRF + DFDBA) and 50 in Group B (DFDBA alone). Baseline demographic and clinical characteristics were comparable between groups ($p > 0.05$), indicating successful randomization **(Table 1).** Both groups demonstrated improvements in periodontal parameters over 12 months; however, Group A showed significantly greater probing pocket depth reduction (5.1 ± 1.0 mm vs. 3.9 ± 1.1 mm) and clinical attachment gain (5.3 ± 1.2 mm vs. 3.8 ± 1.3 mm; both $p < 0.001$) **(Table 2).** Radiographic assessment revealed significantly greater bone regeneration in Group A at 3, 6 and 12 months, reaching 79.5 ± 8.4% compared with 62.8 ± 9.2% in Group B at 12 months ($p < 0.001$) **(Table 3).** At 12 months, clinical success was higher in Group A than Group B (92.0% vs. 76.0%; $p = 0.028$), while persistent periodontal pockets and the need for additional periodontal intervention were less frequent in Group A. The difference in persistent tooth mobility was not statistically significant ($p = 0.081$) **(Table 4).** Patient-reported outcomes favored Group A, which showed significantly lower pain scores on postoperative Days 1 and 7, better early soft-tissue healing and higher patient satisfaction than Group B (all $p < 0.001$) **(Table 5).**

Table 1: Baseline demographic and clinical characteristics (n=100)

Variable	Group A (PRF+DFDBA) (n=50)	Group B (DFDBA) (n=50)	p-value
Age (years), mean ± SD	41.8 ± 8.6	42.3 ± 9.1	0.781
Male, n (%)	28 (56.0)	26 (52.0)	0.689
Female, n (%)	22 (44.0)	24 (48.0)	0.689
Mean PPD (mm)	8.2 ± 1.0	8.1 ± 1.2	0.644
Mean CAL (mm)	9.3 ± 1.4	9.2 ± 1.3	0.752
Mean defect depth (mm)	6.5 ± 1.2	6.4 ± 1.3	0.691
Tooth mobility	1.8 ± 0.5	1.7 ± 0.6	0.537

Table 2: Comparison of clinical periodontal parameters

Parameter	Group A	Group B	p-value
Baseline PPD (mm)	8.2 ± 1.0	8.1 ± 1.2	0.644
12-month PPD (mm)	3.1 ± 0.8	4.2 ± 1.0	<0.001
Mean PPD reduction (mm)	5.1 ± 1.0	3.9 ± 1.1	<0.001
Baseline CAL (mm)	9.3 ± 1.4	9.2 ± 1.3	0.752
12-month CAL (mm)	4.0 ± 1.1	5.4 ± 1.2	<0.001
Mean CAL gain (mm)	5.3 ± 1.2	3.8 ± 1.3	<0.001

Table 3: Radiographic bone regeneration

Follow-up	Group A (%)	Group B (%)	p-value
Baseline	0	0	–
3 Months	34.6 ± 8.2	24.8 ± 7.9	<0.001

6 Months	58.2 ± 9.6	43.1 ± 8.8	<0.001
12 Months	79.5 ± 8.4	62.8 ± 9.2	<0.001

Table 4: Clinical treatment outcomes at 12 months

Outcome	Group A (n=50)	Group B (n=50)	p-value
Clinical success	46 (92.0%)	38 (76.0%)	0.028
Persistent periodontal pocket	3 (6.0%)	9 (18.0%)	0.049
Persistent mobility	2 (4.0%)	7 (14.0%)	0.081
Additional periodontal intervention	2 (4.0%)	8 (16.0%)	0.046

Table 5: Patient-reported postoperative outcomes

Parameter	Group A	Group B	p-value
VAS pain score (Day 1)	2.6 ± 1.0	4.1 ± 1.3	<0.001
VAS pain score (Day 7)	0.6 ± 0.5	1.2 ± 0.7	<0.001
Early soft tissue healing index	4.7 ± 0.5	3.9 ± 0.6	<0.001
Patient satisfaction score (10-point scale)	9.2 ± 0.8	8.1 ± 1.0	<0.001

Discussion:

The management of endodontic-periodontal lesions remains a significant clinical challenge because successful treatment requires elimination of infection while achieving regeneration of the periodontal attachment apparatus. The present randomized controlled clinical trial demonstrated that both regenerative protocols resulted in significant clinical and radiographic improvement after 12 months; however, the combination of Platelet-Rich Fibrin (PRF) with Demineralized Freeze-Dried Bone Allograft (DFDBA) produced significantly greater probing pocket depth reduction, clinical attachment gain, radiographic bone fill and clinical success than DFDBA alone. These findings suggest that the addition of PRF enhances the regenerative potential of conventional bone grafting by creating a biologically favorable environment for periodontal wound healing. One of the principal findings of this study was the significantly greater reduction in probing pocket depth observed in the PRF group. Reduction in periodontal pocket depth is considered an important indicator of successful periodontal regeneration because it reflects resolution of inflammation and re-establishment of periodontal support. Similar findings were reported by Pullishery *et al.* (2024), **[11]** who demonstrated through a systematic review and meta-analysis that injectable platelet-rich fibrin significantly improved probing pocket depth reduction and clinical attachment gain compared with conventional regenerative procedures. They suggested that the fibrin matrix provides prolonged release of growth factors that stimulate fibroblast proliferation and connective tissue maturation, thereby enhancing periodontal healing. The greater reduction in pocket depth observed in the present investigation may therefore be attributed to the sustained biological activity of PRF during the early phases of wound healing. Another important outcome of the present study was the significantly greater gain in clinical attachment level among patients treated with PRF and DFDBA. Restoration of clinical attachment represents true periodontal regeneration rather than simple repair and remains one of the most reliable indicators of treatment success. Comparable observations were reported by Silva *et al.* (2024) **[12]** in a network meta-analysis of randomized clinical trials evaluating regenerative therapies for periodontal intrabony defects. Their analysis concluded that PRF used in combination with bone grafts produced significantly greater attachment gain than bone grafts alone, emphasizing the synergistic effect of autologous platelet concentrates and osteoconductive graft materials. The findings of the present study support this concept and indicate that combining PRF with DFDBA enhances periodontal attachment regeneration in endo-perio lesions. Radiographic evaluation also demonstrated significantly greater bone regeneration in the PRF group throughout the twelve-month follow-up period. The enhanced radiographic defect fill observed in the present study is in agreement with the systematic review by Sarika *et al.* (2021), **[13]** who concluded that PRF significantly increases bone regeneration when used as an adjunct to regenerative periodontal surgery. The authors proposed that the fibrin scaffold serves as a three-dimensional matrix that facilitates migration of osteogenic cells while continuously releasing platelet-derived growth factor, transforming growth factor-β and vascular endothelial growth factor, thereby promoting angiogenesis and new bone formation. Similar biological mechanisms may explain the significantly greater percentage of bone fill observed in the present investigation. Improved tooth stability and higher overall clinical success were additional findings favoring the combined regenerative approach. Reduction in tooth mobility generally reflects successful regeneration of alveolar bone and periodontal ligament support. These findings correspond with those reported by Tsuchida *et al.* (2024), **[14]** who evaluated the role of PRF in periodontal regenerative procedures and demonstrated significant improvements in clinical attachment, radiographic bone fill and tooth prognosis compared with conventional regenerative therapy. Their systematic review suggested that PRF improves graft stability and enhances early wound healing, resulting in superior clinical outcomes. The biological advantages observed in the present study may be explained by the unique composition of PRF. Unlike conventional biomaterials that primarily provide structural support, PRF functions as an autologous fibrin scaffold containing platelets, leukocytes, cytokines and multiple growth factors. Miron *et al.* (2022), **[15]** explained that PRF gradually releases platelet-derived growth factor, transforming growth factor-β, vascular endothelial growth factor, insulin-like growth factor and epidermal growth factor over several days, thereby stimulating angiogenesis, collagen synthesis, fibroblast proliferation and osteoblastic

differentiation **[16, 17]**. These biological effects accelerate soft tissue healing while simultaneously promoting regeneration of periodontal ligament and alveolar bone. Such mechanisms likely contributed to the superior clinical and radiographic outcomes observed in the PRF-treated group. Overall, the findings of the present randomized controlled clinical trial demonstrate that the adjunctive use of PRF with DFDBA provides superior periodontal regeneration compared with DFDBA alone **[18, 19]**. While the results are encouraging, further multicenter randomized clinical trials with larger sample sizes, longer follow-up periods and direct comparisons with other contemporary regenerative biomaterials are required to establish standardized evidence-based treatment protocols for the management of endodontic-periodontal defects.

Conclusion:

PRF combined with DFDBA produced greater clinical and radiographic improvement than DFDBA alone in endodontic-periodontal defects. The combined treatment improved probing pocket depth, clinical attachment, bone fill and tooth stability over 12 months. Larger multicenter trials with longer follow-up are needed to confirm its long-term regenerative benefits.

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