



## EFFICACY OF PLATELET-RICH FIBRIN WITH DEMINERALIZED FREEZE-DRIED BONE ALLOGRAFT COMPARED TO DEMINERALIZED FREEZE-DRIED BONE ALLOGRAFT ALONE IN THE TREATMENT OF GRADE II FURCATION – A SYSTEMATIC REVIEW

### Periodontology

**Dr Pandurang Gavhale\***

Third Year Post Graduate Student, Department of Periodontology, Dr G. D. Pol foundation's YMT dental college and hospital, Kharghar, Navi Mumbai \*Corresponding Author

**Dr Nupur Sah**

Professor and Guide, Department of Periodontology, Dr G. D. Pol foundation's YMT dental college and hospital, Kharghar, Navi Mumbai

**Dr Sangeeta Muglikar**

Professor and Head of Department of Periodontology, Dr G. D. Pol foundation's YMT dental college and hospital, Kharghar, Navi Mumbai

**Dr Manjiri Mirgane**

Second Year Post Graduate Student, Department of Periodontology, Dr G. D. Pol foundation's YMT dental college and hospital, Kharghar, Navi Mumbai

**Dr Khushi Muni**

First Year Post Graduate Student, Department of Periodontology, Dr G. D. Pol foundation's YMT dental college and hospital, Kharghar, Navi Mumbai

### ABSTRACT

The intricate anatomical structure of the furcation hinders access for both personal oral hygiene and professional root debridement. Research indicates that molars with furcation involvement exhibit a higher incidence of periodontal deterioration and respond less favorably to periodontal treatment. Successful regeneration at the furcation area is determined as the elimination or reduction of horizontal and vertical components of the lesion. Multiple approaches have been used to treat furcation defects, including autografts, DFDBA, bovine-derived xenografts, barrier membranes, and combinations of membranes and bone grafts. The efficacy of platelet-rich fibrin with DFDBA and DFDBA alone in the treatment of grade II furcation was assessed in this systematic review. This review was registered in PROSPERO with registration number CRD42024619612. The electronic database search was performed using PubMed, Google Scholar, and Science Direct. Three randomized clinical trials were analysed for clinical and radiographic parameters. Probing pocket depth, relative attachment loss, and defect depth were analysed. In conclusion, adding platelet-rich fibrin to DFDBA improved clinical metrics more than using DFDBA alone.

### KEYWORDS

Periodontitis, Grade Ii Furcation, Degree Ii Furcation, Treatment Of Grade Ii Furcation, Platelet-rich Fibrin, Demineralized Freeze-dried Bone Allograft, Periodontal Flap Surgery.

#### INTRODUCTION:

Periodontitis is a complex condition with multiple contributing factors, characterized by persistent inflammation of the periodontal tissues and damage that may eventually lead to tooth loss.<sup>1</sup> The goal of periodontal treatments is to halt the advancement of periodontal disease and restore lost dental structures. The process of periodontal regeneration is complex, requiring a systematic series of biological processes, including cell adhesion, migration, proliferation and differentiation.

The regenerative process is dependent on the interaction among osteoblasts, periodontal ligament cells, gingival fibroblasts, and epithelial cells. Periodontal regenerative techniques encompass guided tissue regeneration, root biomodifications and bone grafts, either individually or in combination. Untreated periodontal disease has the potential to damage the attachment apparatus and supporting structures, ultimately leading to tooth loss.<sup>2</sup>

Complex anatomical morphology of the furcation hinders accessibility for both individual oral hygiene and professional root debridement. Studies have demonstrated that molars with furcation involvement exhibit a higher rate of periodontal breakdown and respond less favorably to periodontal therapy.<sup>3,4,5</sup> In the management of grade II furcation defects, osseous resection may be warranted when a shallow horizontal component is present without considerable vertical bone loss. Osteoplasty and ostectomy in conjunction with odontoplasty to alter furcation anatomy typically yield positive results. Bone grafts, whether utilized independently or in conjunction with barrier membranes, are extensively employed in periodontal regenerative therapy. DFDBA is commonly used allograft due to its availability, safety, and osseointegrative and osseoconductive characteristics. Demineralized bone allografts facilitate bone formation as they contain bone morphogenic proteins, including BMP 2, 4 and 7 which assist in promoting osteoinduction. It is believed that when BMPs are in their active form, they enhance the activities of platelet growth factors, which collaborate with various cell populations in the surgical site. Consequently, this leads to osteogenesis, mesenchymal cell migration, and adhesion when placed in well-vascularized bone.<sup>6</sup>

There has been a growing interest in polypeptide growth factors such as platelet-derived growth factors and TGF- $\beta$ , found in the  $\alpha$  granules of platelets, which possess the ability to regulate cell proliferation, chemotaxis, differentiation, and angiogenesis, thus facilitating wound healing.<sup>4</sup>

Over the years, two generations of platelet concentrates have evolved: platelet-rich plasma to platelet-rich fibrin with its modifications as advanced PRF, titanium PRF, injectable-PRF, PRF lysates and currently concentrated growth factor.

Platelet-rich fibrin is an autologous second-generation platelet concentrate, prepared by collecting venous blood and immediately subjecting it to a specific centrifugation protocol that facilitates natural fibrin polymerization.<sup>4,7</sup> This centrifugation process yields three distinct layers: platelet-poor plasma at the top, the PRF clot in the middle, and red blood cells at the bottom of the tube. PRF is characterized as a fibrin clot that is rich in platelets, prepared without the addition of thrombin, and contains platelets, cytokines, glycoproteins, and growth factors, which are essential for periodontal regeneration and contribute synergistically to the healing of both soft and hard tissues.<sup>3</sup> Compared to other platelet concentrates, PRF is advantageous due to its straightforward preparation, cost-effectiveness, and the absence of the need for exogenous compounds such as bovine thrombin and calcium chloride.

The viable growth factors present in PRF can stimulate the proliferation of osteoblasts and periodontal ligament cells while inhibiting the migration of oral epithelial cells, a crucial aspect of periodontal regeneration. PRF has demonstrated its efficacy in periodontal plastic surgical procedures, sinus lift operations, and various cases of multiple root coverage.<sup>4</sup>

Clinical research has indicated enhancements in clinical attachment and bone levels when DFDBA is applied to human intraosseous lesions, with histological evidence supporting the formation of new attachments through use of DFDBA.<sup>3</sup> Furthermore, PRF has been identified as a suitable scaffold for human periosteal cells in vitro, indicating its potential for applications in bone tissue engineering.

Consequently, the combination of PRF with DFDBA may improve the healing capabilities of both bone and soft tissues.

Nevertheless, there is a lack of substantial evidence concerning the application of PRF with DFDBA in the treatment of grade II furcation. Additionally, there is no consensus on its impact on the healing of soft and hard tissues following surgical procedures.

Thus, through this systematic review, the efficacy of PRF with DFDBA in the management of grade II furcation when compared to DFDBA alone is assessed through available literature.

## METHODOLOGY:

**SEARCH STRATEGY AND SELECTION CRITERIA:** A thorough search was performed on the electronic databases PubMed/Medline, Google Scholar and Science Direct, encompassing articles published from January 2000 to November 2024; thus, studies conducted over the past 25 years were included: "grade II furcation", "degree II furcation", "class II furcation", "PRF with DFDBA", "DFDBA alone" and "management of furcation" utilizing appropriate Boolean operators [AND, OR, NOT] to identify pertinent articles. Additionally, a manual search was executed in high-impact journals within the field of periodontology to incorporate further potential studies. The reference lists of both included and excluded articles were examined to identify relevant scientific papers that may have been overlooked. References in pertinent articles were manually scrutinized for additional studies. The following journals were searched for relevant literature up until November 2024: Journal of Periodontal Research, Journal of Clinical Periodontology, Journal of Periodontology, International Journal of Periodontics & Restorative Dentistry, Perio 2000, Journal of Periodontal Research, Indian Society of Periodontology and Indian Journal of Dental Research. The review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines of 2020.<sup>8</sup>

## INCLUSION CRITERIA:

1. Randomized controlled trials that assessed the effectiveness of PRF with DFDBA in treating grade II furcation,
2. Studies employing PRF with DFDBA in the test group and DFDBA alone in the control group for the treatment of grade II furcation,
3. Studies that reported outcomes in terms of relative attachment level, pocket depth, and radiographic bone fill,
4. Studies that included at least eight cases treated for grade II furcation with a follow-up period of at least 6 months,
5. Studies involving human subjects, studies published in open-access journals, articles that reported outcomes in terms of mean and standard deviation, and studies published exclusively in the English language were included in the review.

## EXCLUSION CRITERIA:

1. Case reports, case series, animal model studies, in vitro studies,
2. Studies conducted before January 2000,
3. Studies that used other agents influencing the outcome measures,
4. Studies comparing PRF with any other material, commentaries, and interviews
5. Unpublished research was excluded from review.

**DATA EXTRACTION:** The information collected includes details about the author, the year of publication, the design of the study, the size of the sample, characteristics of the defects, the age of the patients, relative attachment level, pocket depth, and the radiographic bone fill.

**QUALITY ASSESSMENT OF INCLUDED STUDIES:** The methodological quality of the clinical trials or randomized controlled trials that were included was evaluated using the Cochrane Collaboration risk of bias (ROB) - 2 tool, which examines its various domains in the Review Manager (RevMan) 5.4 software.<sup>9</sup>

**RISK OF BIAS IN INDIVIDUAL STUDIES:** This evaluation was performed utilizing the recommended methodology for assessing the risk of bias in studies incorporated in Cochrane reviews, Higgins (2011), employing the tool RevMan 5.4. The risk of bias in the studies included is illustrated in the graph. The studies incorporated Basireddy A, Prathypaty SK, Yendluri DB et al, (2019)<sup>11</sup> & Ittycheria PG,

Veliyaveetil TG, George Ak et al, (2023)<sup>3</sup>, exhibited a low risk of bias, whereas Desai KN, Thakkar RR, Patel J, Gupta E et al (2024)<sup>10</sup> presented an unclear risk of bias. The risk of bias in individual studies is depicted in Graph no. 1, while the summary of the risk of bias across studies is represented in Graph no 2. The quality assessment of the studies included, utilizing the Cochrane risk of bias tool for RCT, is displayed in Table no 2.

## RESULTS:

**STUDY SELECTION:** A total of 64 articles were discovered through an electronic search, while four additional articles were found via a manual search and evaluated for eligibility. In total, 68 articles were screened, with seven identified as duplicates. Consequently, 61 articles were assessed for eligibility, resulting in the exclusion of 58 articles that did not satisfy the inclusion criteria. Three studies<sup>3,10,11</sup> were ultimately included in the review, as depicted in Figure no 1.

**STUDY CHARACTERISTICS:** Data from three studies were analyzed; of these, two studies employed a randomized controlled trial design, while one utilized a quasi-experimental design. The studies were conducted in Gujarat, Kerala, and Telangana, India.<sup>3,10,11</sup> Assessments were made from baseline through a duration of six months. Primary outcomes were evaluated based on periodontal clinical parameters (probing depth and relative attachment loss), while secondary outcomes were assessed through radiographic parameters. The characteristics of the studies are presented in Table 1.

**QUALITATIVE ASSESSMENT AND ANALYSIS:** Desai KN, Thakkar RR, Patel J, Gupta E, et al (2024)<sup>10</sup> conducted a clinical trial involving 20 healthy individuals with grade II furcation involvement on both sides of their mouths. The participants were divided into two groups: a test group that received DFDBA combined with PRF and a control group that received DFDBA alone. The test group exhibited statistically significant differences when compared to the control group at 3 and 6 months in terms of probing depth, residual horizontal clinical attachment level, and residual vertical clinical attachment level. No statistically significant difference was observed in the mean gingival marginal level between baseline and 6 months in the test group, and the mean depth of bone abnormalities decreased in both groups. Ittycheria P, Veliyaveetil T, George A et al (2023)<sup>3</sup> conducted a study involving 9 individuals diagnosed with chronic periodontitis, each exhibiting grade II furcation bilaterally. Baseline clinical and radiographic measurements were recorded and subsequently compared with those taken after a six-month follow-up period. This study indicated a reduction in the relative horizontal clinical attachment level from the beginning of the study to the six-month mark in favor of the test group. The intergroup comparison revealed a more significant decrease in probing depth, recession, gain in relative vertical clinical attachment level, mean alveolar bone defect, and percentage of bone fill in the test group; however, these results were not statistically significant. All other parameters, including probing pocket depth, changes in recession, relative vertical attachment level, bone fill, and defect depth, did not reach statistical significance. The gingival index and plaque index scores demonstrated a statistically significant reduction from baseline to six months.

Basireddy A, Prathypaty SK, Yendluri DB et al in (2019)<sup>11</sup> conducted a clinical trial with random assignment involving 14 individuals with 28 instances of bilateral mandibular furcation defects at degree II. The test group exhibited statistically significant differences in the intragroup comparison of probing depth, relative horizontal attachment level, relative vertical attachment level, gingival marginal level, vertical defect depth, and horizontal defect depth when compared to the control group. At baseline, the parameters of both the test and control groups did not show any statistically significant differences. The intragroup comparison of clinical and radiographic parameters at baseline and after 6 months in the test group revealed statistically significant differences in mean PD, RVCAL, and HDD. The comparison between groups regarding the mean change in PD, RVCAL, the percentage change in VDD, and HDD did not yield statistically significant results. Conversely, the mean change in RHCAL and GML exhibited statistically significant differences. The characteristics of the studies included are presented in Table no.1

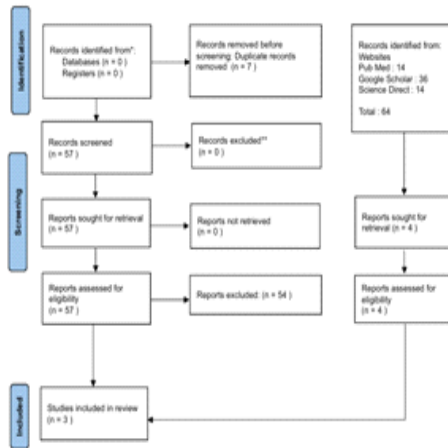
## DISCUSSION:

PRF is a second-generation, autogenous concentrated blood product that forms a fibrin matrix consisting of molecular and cellular components that facilitate optimal enhancement. Additionally, PRF

promotes the production of osteoprotegerin, which stimulates osteoblast proliferation and functions as an osteoconductive and osteoinductive material, thereby initiating bone regeneration.<sup>12,13</sup> It possesses a dense fibrin matrix, resulting in a delayed and prolonged release of growth

In studies conducted by **Choukroun & Dohan et al., (2006)**<sup>7</sup> there was considerable gains in RAL, LBG, and % BF could be attributed to the use of DBM, which preserves the space for tissue development to occur and the osteoconductive nature of the graft which functions as a scaffold for the creation of mineralized tissue. During the demineralization process, bone

**Figure no. 1: Flow chart of literature search results and study selection.**



factors from leukocytes and platelets. Platelet-rich fibrin acts as a source of transforming growth factor  $\beta$ , platelet-derived growth factor, insulin-like growth factor 1, epidermal growth factor, and vascular endothelial growth factor. The presence of leukocytes in platelet concentrates imparts an antimicrobial effect on the wound. The primary advantages of PRF include its positive biological effects, low cost, and ease of preparation.<sup>19</sup> In the research conducted by **Piemontese M et al. (2007)**<sup>12</sup> a total of sixty interproximal intrabony osseous defects were treated, divided into a test group of 30 intrabony osseous defects (PRP+DFDBA) and a control group of 30 intrabony osseous defects (DFDBA+saline). Compared to baseline, the results after 12 months indicated that both treatment modalities led to significant changes in all clinical parameters i.e. gingival index, bleeding on probing, probing depth, clinical attachment level and gingival recession; and radiographic parameters (hard tissue fill and bone depth reduction). However, the test group exhibited statistically significantly greater changes compared to the control group in probing depth reduction mm versus clinical attachment gain. This improvement is attributed to the synergistic effect of the two substances. The superior probing depth reduction observed in platelet-rich fibrin-treated areas may be related to the increased amounts of polypeptide growth factors, which may have facilitated soft tissue healing.<sup>3</sup>

**Table 1: Characteristics of included studies.**

Sr no.	Aut hors (Year)	Type of study	Rand om sequence generation	Allo cation conceal ment	Blinding of partici pants	Blindi ng of Outco me	Incomp lete outcom e data	Selecti ve report ing
1.	Desai KN, Thakkar RR, Patel J, Gupta E et al 2024 <sup>10</sup>	RCT	Unclear risk bias	Unclear risk bias	Unclear risk bias	Unclear risk bias	Unclear risk bias	Unclear risk bias
2.	Ittycheria PG, Veliyaveetil TG, George Ak et al 2023 <sup>3</sup>	Experimental study (Split mouth design)	Low risk bias	Low risk bias	Unclear risk bias	High risk bias	Unclear risk bias	High risk bias
3.	Basireddy A, Prathypaty SK, Yendluri DB et al 2019 <sup>11</sup>	RCT	Low risk bias	Low risk bias	Low risk bias	High risk bias	High risk bias	High risk bias

**Table 2: Quality assessment of the studies included using Cochrane Risk of bias tool RCT**

Author, years of study	Country	Study design	Sample size	Intervention / Comparator	Parameters assessed	Follow up (in months)	Conclusion
Desai KN, Thakkar RR, Patel J, Gupta E et al 2024 <sup>10</sup>	Gujarat (India)	Randomized clinical trial	20	Test group (DFDBA + platelet-rich fibrin [PRF]) vs Control group (DFDBA)	Probing depth (PD), residual horizontal clinical attachment level (RHCAL), and residual vertical clinical attachment level (RVCAL), and mean gingival marginal level (GML), Bone defect depth by using RVG with grid.	3 months 6 months	In intergroup comparison mean gingival marginal level (GML) was found no statistically significant difference in the test group as compared to control group.  Intergroup comparison of bone defect depth at 6 month was found statistically significant difference in the test group as compared to control group i.e. p =0.01 (p≤ 0.05).  The test group showed statistically significant difference over the control group at 3 months, 6 months in probing depth (PD), residual horizontal clinical attachment level (RHCAL), and residual vertical clinical attachment level (RVCAL).  Between baseline and 6 months, the mean depth of bone abnormalities reduced in both groups.
Ittycheria P, Veliyaveetil T, George A 2023 <sup>3</sup>	Kerala (India)	Quasi-Experimental study (Split mouth design)	09 (18 sites)	Test group (OFD + DFDBA + platelet-rich fibrin [PRF]) vs Control group (OFD + DFDBA)	PPD, Recession, relative vertical clinical attachment level (RVCAL), relative horizontal clinical attachment level (RHCAL), Alveolar bone depth ABD by using image analysis software - Scion image, scion corporation)	6 months	Gingival index, plaque index, mean reduction in RHCAL at baseline to six months showed a statistically significant difference (p<0.05).  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.

Basireddy A, Prathyapaty SK, Yenduri DB et al 2019 <sup>11</sup>	Telanga (India)	Randomized clinical trial	14 (28 sites)	Test group (DFDB A + PRF) vs Control group (DF DBA alone)	PD (Probing depth), RVCAL – (Relative vertical clinical attachment level), RHCAL – (Relative horizontal clinical attachment level), GML – (Gingival margin level), VDD – Vertical defect depth, HDD – Horizontal defect depth by using cone beam computed tomography (CBCT).	1 week, 2 week, 1 months, 3 months, 6 months	The intragroup comparison of PD, RVCAL, RHCAL, VDD, HDD at baseline and 6 months in the test group showed statistically significant difference.  There was no statistically significant difference in mean GML from baseline to 6 months in the test group.  The intergroup comparison showed no statistically significant difference in the mean change of PD, RVCAL, % change in VDD and HDD.
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attachment level. The exclusion of some pertinent studies may have been influenced by unpublished data and language restrictions. Therefore, it is essential to conduct more multicenter RCTs with larger sample sizes, extended follow-up durations, and standardized protocols to mitigate heterogeneities order to determine the optimal regenerative potential of various types of platelet-rich fibrin in conjunction with DFDBA.

**CONCLUSION:**

This systematic review aimed to assess and evaluate the efficacy of PRF combined with DFDBA compared to DFDBA alone in managing grade II furcation. Qualitative analysis of the included RCTs revealed improvements in periodontal clinical indicators such as probing pocket depth, RHCAL, and RVCAL. Further clinical studies with larger sample sizes and extended follow-up periods should be conducted to assess the secondary outcomes described, thereby obtaining overall high-quality evidence. In conclusion, the addition of PRF to DFDBA resulted in significantly greater improvements in clinical metrics compared to the use of DFDBA alone.

**IMPLICATIONS FOR FUTURE RESEARCH:**

1. Future studies should assess regenerative potential through histological evaluation.
2. To achieve predictable regenerative outcomes in treating furcation defects, it is crucial to evaluate and, if possible, control adverse systemic and local factors (such as diabetes, smoking, oral hygiene, vitality, and tooth mobility).
3. Patient-centered outcomes should be considered when evaluating the risk/benefit ratio.
4. Long-term follow-up is necessary to assess tooth survival rates and to inform the therapeutic prognosis for teeth with furcation defects.

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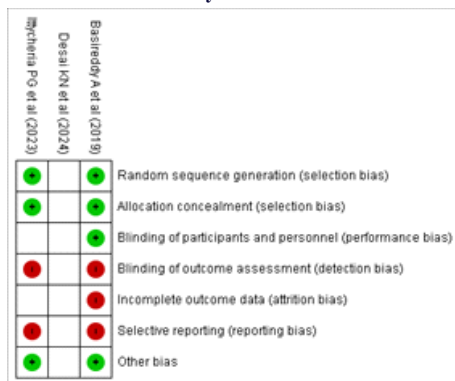
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**Graph 1: Risk of bias in individual studies.**



**Graph 2: Risk of bias summary across studies.**



morphogenetic protein, which is found in DBM, is released. DFDBA contains bone morphogenic proteins, including BMP 2, 4 and 7, which help to promote osteoinduction. It is thought that when BMPs are in their active (osteoinductive) state, they improve the platelet growth factor activities, which work along with the different cell populations in the surgical wound.<sup>14</sup> As a result, there is osteogenesis, mesenchymal cell migration and adhesion when placed in well-vascularized bone. Overall, a difference could be observed in the evaluated clinical parameters in the randomized clinical trials included. Improvements in periodontal clinical indicators such as PPD, RHCAL, and RVCAL were found by qualitative analysis.

**LIMITATIONS:**

There are some limitations for this systematic review. The search process led to the inclusion of only three articles, the number of which was very small. This systematic review has certain limitations. The search process resulted in the inclusion of only three articles, which is a notably small number. To conduct a precise evaluation of clinical and radiographical improvements, the follow-up period for RCTs should have exceeded one year to adequately assess probing depth and