Scientific Research Publishing

Open Journal of Stomatology, 2023, 13, 106-115
https://www.scirp.org/journal/ojst
ISSN Online: 2160-8717
ISSN Print: 2160-8709

Evaluating the Benefits of Platelet Rich-Fibrin in Periodontal Regeneration: A Literature Review

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How to cite this paper: Albahar, H. and Abu-Ta'a, M. (2023) Evaluating the Benefits of Platelet Rich-Fibrin in Periodontal Regeneration: A Literature Review. *Open Journal of Stomatology*, **13**, 106-115.
https://doi.org/10.4236/ojst.2023.133008

Received: February 1, 2023
Accepted: March 14, 2023
Published: March 17, 2023

Abstract

Introduction: Platelet Rich-Fibrin (PRF) is a biological matrix derived from a patient's own blood, rich in growth factors and platelets. Its use in various periodontal and non-periodontal procedures is gaining recognition due to its potential in promoting tissue regeneration. The purpose of this review was to evaluate the benefits of using PRF in intra-bony defect regeneration, guided-bone regeneration, and sinus floor elevation. **Methods:** The study searched PubMed for manuscripts published between 2017 and 2022 to better understand the clinical and radiological effects of PRF. The manuscripts were divided into the following sections: intra-bony defect regeneration, guided-bone regeneration, and sinus floor elevation. **Results:** In intra-bony defects, PRF improved clinical and radiological parameters when compared with OFD alone, with a significant difference in wound healing at 7 days. In GBR, a CBCT evaluation shows no statistical difference between the PRF-autogenous bone complex group and the bovine bone-collagen membrane complex regarding volume change of the augmented bone with a 16% rate of bone loss following a 6-month healing period. Also, a slight increase in bone thickness has been seen when liquid PRF is used. In sinus floor elevation, results revealed no differences in graft volume between PRF group and control group at any of the evaluated time points. Although higher implant stability immediately postoperatively, higher new bone formation, the lesser amount of residual graft and earlier implant placement. **Conclusion:** Platelet Rich-Fibrin is widely accepted for use in periodontal surgery and dentistry due to its minimally invasive nature and low risk of adverse effects, with positive results in tissue regeneration. There is evidence that PRF leads to improved and faster healing, as well as cost-effective regenerative procedures compared to other treatments.

Keywords

Intra-Bony Defect, Sinus Floor Elevation, Platelet-Rich Fibrin, Guided Tissue Regeneration

1. Introduction

Regenerative therapy for periodontal tissues aims to restore function and architecture to traumatized oral tissues [1]. There are various treatment options available for this purpose, such as using a barrier membrane, application of bone-grafting materials from human, animal, or artificial sources, and the use of bioactive growth factors like BMPs and biologically active materials like Enamel Matrix protein. In recent years, Platelet Concentrates (PCs) have emerged as a promising regenerative material in the field of dentistry and periodontal surgery [2] [3].

PCs are derived from a processed blood sample, typically through centrifugation, and are classified into four categories based on their leucocyte and fibrin content, including pure platelet-rich plasma (P-PRP), leucocyte- and platelet-rich plasma (L-PRP), pure platelet-rich fibrin (P-PRF), and leucocyte- and platelet-rich fibrin (L-PRF). Platelet-rich fibrin (PRF), described by Choukroun as an improvement over plasma-rich plasma, is the latest and most advanced biologically active material in this category [4].

PRF is created through a centrifugation process that yields three distinct layers: red blood cells at the bottom, platelet-rich plasma in the middle, and platelet-poor plasma at the top [5] [6]. Platelets contain crucial growth factors like PDGF, TGFß-1, VEGF, and BMPs, which are essential for tissue regeneration and repair [7] [8]. Recently, titanium-PRF was created as a new type of PRF, as it was hypothesized that titanium tubes would activate platelets more effectively than glass tubes. PRF has been shown to enhance soft tissue healing and improve the efficacy of bone augmentation procedures when used as a supporting material [9].

This review aims to provide an updated overview of the recent advances and new articles on PRF published from 2017 to date. To the best of our knowledge, no literature review or systematic review has been conducted in this area.

2. Research Methodology

Manuscripts were searched from 2017 up to 2022 in pubmed using words (platelet rich fibrin, sinus lifting AND/OR platelet rich fibrin, sinus floor elevation AND/OR platelet rich fibrin, guided bone regeneration AND/ORplatelet rich fibrin, intra-bony defects AND/OR platelet rich fibrin, periodontal regeneration AND/OR platelet rich fibrin). Boolean terms such as AND, OR were used to combine the keywords above. A custom data extraction form was created to match the specific needs of the review. Data related to defect number, healing time, pocket reduction, CAL gain, P-value, bone fill, radiographic and histologic

evaluation were extracted. Studies including smokers, participants with systematic disease, pregnancy, poor oral hygiene patients were excluded. As a result, 21 clinical randomized clinical trial were included and divided into the following sections: intra-bony defect regeneration, GBR and sinus floor elevation.

3. Results

3.1. PRF in Intrabony Defect

One option in treatment intrabony defects once indicated is regeneration. [1] From 2017 up to date there is a 5 randomized control trial comparting PRF to OFD alone or other combination. Studies that each participant had one or more 2 - 3 walls intra-bony defects with a depth of ≥3 mm according to intraoral periapical radiographs were included. Smokers, pregnancy, lactation or poor oral hygiene were excluded. Two studies comparing the use PRF with OFD versus OFD alone in 3 wall defect sound the same result. [2] [3] An RCT utilizing PRF gel in treatment of intrabony defect, OFD + PRF group showed a mean probing depth reduction, CAL gain and percent of bone fill at end of 12 months (4.2 ± 1.32 mm, 3.60 ± 0.04 mm and 45.18% ± 7.57% respectively) in comparison to (2.4 ± 0.69 mm, 2.1 ± 0.46 mm and 21.6% ± 9.3%, respectively) in OFD alone group at end of 12 months ($p = 0.001$). At 7 days test group (PRF) showed significant wound healing at all sites and difference between test and control group at 7 days was significant ($p = 0.003$). [3] At 14 days, all sites in the test group and 9 sites in the control group showed perfect healing with 1 score thusno significant difference.

Also, for intrabony defects, a randomized control trail in 2021 comparing the A-PRF regenerative capacity to other periodontal regenerative therapies, such as PRF + OFD, GTR membrane or OFD alone in 2 - 3 walls intrabony defects. both clinical and radiographic show that PRF + OFD have the highest improvement in PD, CAL and Tissue modeling, followed by GTR and the least one is OFD alone. [2]

An interesting experiment comparing EMD + A-PRF versus EMD in treating intra bony defects. At 6 month, mean CAL gain and Gingival recession was (2.33 ± 1.58 and 3.93 ± 2.73 mm respectively) in the A-PRF + group and (2.60 ± 1.18 and 3.33 ± 1.58 mm respectively) in the EMD group ($p < 0.001$). In both groups, the CAL and GR were significant compared to baseline, but no statistically significant difference was found between the two groups. No difference between the groups was observed in term of remaining PD, CAL and GR, the results obtained with either material were similar. On the other hand, a study focused on supplementation of PRF with EMD did not show a difference between test and control (EMD only) groups. [5]

A regenerative study questioned whether PRF has an added benefit to bone and membrane in intrabony defects. [8] A fluid PRF was used in combination to bovine bone + membrane in test sites, while control sites were bovine bone +membrane. Results show that CAL gain in the test group was ≈ 0.9 mm higher

than control group at 6 months postoperatively, while at 12 and 24 months, the test group's probing depth (PD) was significantly lower than that of the control group and CAl gain difference reach 1 - 1.1 mm. Overall, GTR and BPBM-PRF complex is more effective clinically but did not show a significant difference radiographically regarding the depth of defect and vertical bone loss. Fluid PRF formula show many advantages such as more homogenous mixture, less procedure complexity, anti-inflammatory property and minimizing time of bone exposure.

Recently, a new attempt is made to enhance the PRF using Titanium tubes. [9] According to the clinical trial, either PRF or TPRF with OFD shows better results than OFD alone. However, the treatment outcomes for OFD with PRF or TPRF show no statistically significant difference (**Table 1**).

Overall, inclusion of PRF serves largely as a scaffold and may encourage tissue regeneration when introduced into the periodontal pocket especially with OFD, it helps enhancement of early soft tissue healing. PRF has a good regenerative potential in intrabony defects in term of pocket reduction and Cal gain and its best used in combination.

3.2. PRF in GBR

Through the combined effects of surface resorption and loss of bundle bone following tooth loss causes a noticeable shift in alveolar bone and results in a predictable dimensional alteration. [10] Therefore, an attempt to restore the bone resorbed is required when aiming to resort dentition using implants. [11] Low-speed centrifugation concept was introduced to increase cellular content and growth factor release, which results in liquid PRF. [12] Liquid PRF is more

Table 1. Demonstrating PPD change and clinical attachment gain in intrabony defects.

Author	Defect number	Healing time (months)	Groups	PPD reduction/change (mm)	CAL gain (mm)	P value
Patel, *et al.* 2017 [2]	26 (bilateral)	12	OFD alone PRF + OFD	2.4 ± 0.69 4.2 ± 1.32	2.1 ± 0.46 3.60 ± 0.04	PPD < 0.001 CAL < 0.001
Pham, *et al.* 2021 [1]	90	12	OFD + PRF GTR OFD alone	4.80 ± 0.71 4.63 ± 0.67 3.37 ± 1.00	5.00 ± 0.46 4.53 ± 0.57 3.37 ± 1.22	PPD < 0.001 CAL < 0.001
Csifo, *et al.* 2021 [3]	30	6	A-PRF EMD	4.67 ± 0.62 4.67 ± 0.62	2.33 ± 1.58 2.60 ± 1.18	PPD < 0.001 CAL < 0.001
Lui, *et al.* 2021 [4]	28	At 12 and 24	GTR + BPBM + PRF GTR + BPBM	NA	Buccal: 3.1 ± 0.5 Lingual: 3.1 ± 0.7 Buccal: 2.1 ± 1.1 Lingual: 2.0 ± 0.8	P < 0.05 P < 0.05
Charttejee, *et al.* 2017 [5]	90	9	OFD OFD + PRF OFD + TPRF	3.68 ± 0.72 5.46 ± 1.04 6.25 ± 1.11	4.14 ± 0.76 6.57 ± 1.47 6.74 ± 1.55	PPD < 0.001 CAL < 0.001

suitable for mixing with bone graft substitutes thus, providing greater graft integration and sufficient bone gain. [13]

A two randomized control trials were conducted. An investigation was conducted to assess how augmentation change ridge dimension using liquid PRF with simultaneous implant installation. [10] Control group was bovine bone alone while test group was bovine bone—liquid PRF. At 6 months postoperative, tested group had a slightly greater increase in augmentation thickness than control group. Although, good bone augmentation and high implant survival rate apon loading were seen in both groups. In the same study, compared to the control group, the liquid-PRF-enriched bovine-derived xenograft group showed decreased marginal bone loss.

A CBCT evaluation randomized control trial was conducted to assess augmentation volume using autogenous bone graft combined with PRF membrane versus bovine bone with collagen membrane in horizontal bone augmentation. [11] No statistical difference between the two groups regarding volume change of the augmented bone with a 16% rate of bone loss following 6 months healing period. "The multiple linear regression analysis showed that the bone resorption rate was statistical significantly influenced by region ($P = 0.01$) but not by treatment ($P = 0.66$), age ($P = 0.09$) or gender ($P = 0.06$)". Thus, anterior region showed greater rate of bone loss than premolar especially in control.

Despite the limited research, PRF serves as a good biomaterial lowering rate of resorption, reduce infection, speed up regeneration and enhancing quality and density of the residual ridge when used. Also it showed to be comparable to collagen membrane to some extent.

3.3. PRF in Sinus Floor Elevation

Due to decreased bone quality and ridge resorption brought on by sinus pneumatization following tooth loss, the posterior portion of the maxilla presents a number of difficulties for successful dental implant rehabilitation. PRF could be used in open or closed sinus elevation. A several RCTs investigated PRF role in sinus floor augmentation.

A split-mouth randomized control trial showed that there was no statistically significant difference between trans-crestal sinus floor elevation using PRF plugs in test side and blood clot in control side as a sole filling material. [14] Otherwise, Enhanced average height and bucco-palatal width at the height of the old and new sinus floor were seen in the PRF group, as well as increased bone gain in the mesial, buccal, and palatal areas more than control.

Furthermore, an anothersplit mouth randomized clinical trial in which two stage Maxillary sinuses on both sides of the mouth were randomly assigned to either the test group (DBBM + L-PRF) or the control group (DBBM). On the test side, a mixture of L-PRF membranes and DBBM was used (0.25 - 1 mm). 0.5 g of DBBM was added into each membrane fragment of L-PRF (4 - 5 mL). The sinus cavity was gently compressed with the transplant materials. Results re-

vealed that no differences in graft volume between test and control group at any of the evaluated time points. Higher implant stability immediately postoperatively, higher new bone formation, lesser amount of residual graft and earlier implant placement at 4 months in test sites than control group at 8 months. [15] Another split mouth RCT comparing DBBM + PRF and DBBM show that both methods of maxillary sinus augmentation were successful, and after six months of healing, the addition of L-PRF to DBBM had no effect on the amount of regenerated bone or the degree to which the graft had been assimilated into the new bone, as determined by histological and histomorphometric evaluation. [16] An overall survival rate 100% in both groups of both studies.

In a study to radiographically evaluate the benefit of PRF versus saline after hydraulic transcrestal sinus elevation, PRF showed superior results as a filler material compared to saline demonstrating higher bone gain [17].

Two studies were compared PRF to allogenic bone graft. [14] [18] First study aims to compare PRF filling versus allogenic graft in terms of implant stability. In contrast, second study investigated a balloon lifting technique with addition of T-PRF in tested and allogenic graft in control. Results show that allogenic graft is better in term of RG bone density, height and volume while implant survival show no statistical difference and comparable new bone formation. [18] Also T-PRF was investigated with beta tricalcium phosphate graft and show no statistical difference in terms of new bone, residual graft and soft tissue thus, no added benefit to beta tricalcium phosphate. [19]

A recent RCT in 2022, investigating xenograft in a wide sinus alone or in combination with autogenous or PRF. Histologic evaluation show that xenograft + autogenous is better in term of new bone formation and modelling than xenograft + PRF and xenograft alone. Otherwise, xenograft plus PRF show less residual graft and more amount connective tissue. [20]

The main advantage from addition of L-PRF to the maxillary sinus resulted in accelerate bone graft maturation, allowing for earlier implantation following sinus augmentation.

4. Discussion

The present literature review focused on the added benefit of using platelet-rich-fibrin with intra-bony defect regeneration, guided-bone-regeneration and sinus floor elevation. In intra-bony defects, PRF improved clinical and radiological parameters when compared with OFD alone, with a significant difference in wound healing at 7 days. These findings are comparable to another clinical study by Chandardas *et al.* in 2016 on pocket reduction and radiographic bone fill. [21] However, the included studies in this review did not measure gingival recession. In GBR, a CBCT evaluation shows no statistical difference between PRF-autogenous bone complex group and bovine bone–collagen membrane complex regarding volume change of the augmented bone with a 16% rate of bone loss following a 6-month healing period. Also, a slight increase in bone thickness has been seen when liquid PRF is used. In sinus floor elevation, results

revealed no differences in graft volume between PRF group and control group at any of the evaluated time points. Although higher implant stability immediately postoperatively, higher new bone formation, the lesser amount of residual graft and earlier implant placement. Also, these results were confirmed in a clinical trial done by Kanayama *et al.* in bone gain when using PRF as a sole graft material. [22]

Overall, the result fits the theory that there is an added benefit of using PRF in regenerative attempts, and its clinical importance revealed that PRF created a better result, faster healing, slower growth factors release, and less time and cost.

Also, PRF has been shown to be safe and effective when used alone or in conjunction with other biomaterials. It could be beneficial in intrabony defects, GBR and sinus floor elevation. Thus, it is widely accepted and intended for use in oral surgery and dentistry as it is minimally invasive treatment with low risk and good results. Combination therapy using PRF and bone grafts yielded the best results in terms of bone regeneration.

The strength of this literature review is that it provides a comprehensive, up-to-date overview of PRF aimed at demonstrating the effectiveness of PRF regenerative potential in intrabony defect, guided bone regeneration and sinus lifting. The present review included studies that have not been included in other reviews.

The limitation of this review includes the poor quality of some included studies and the limited number of included studies. This review is a literature review that did not meet the standards and the strength of a systematic review. Therefore the results of this literature review cannot be generalized. Further work should conduct high quality, up-to-date systematic review with meta-analysis.

5. Conclusion

Platelet-rich-fibrin is widely accepted and intended for use in periodontal surgery and dentistry as it is a minimally invasive treatment with low risk and good results. PRF-included therapy yielded the best results in terms of tissue Regeneration. There is evidence that PRF help to perform a comparative result and even better, faster healing and less cost regenerative procedures. Further studies are required.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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