Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2024; Vol 23: Issue 1, https://carcinogenesis.com/

The Influence of Lyophilized Platelet-Rich Fibrin in The Treatment of Periodontal Intra-Bony Defects (A Randomized Clinical Trial)

Ibraheem Mahmoud Mwafey[1], Ahmed Mohamed Abd Al Rahman[2], Hamdy A Abol-Khair[3], Abdullah Ibrahim Abd Rabbouh Ali[4], Mahmoud Ahmed Mizar[5]

[1] Assistant Professor of Oral Medicine, Periodontology, Oral Diagnosis and Dental Radiology Department, Faculty of Dentistry, Al-Azhar University (Assiut Branch), Egypt. E-mail: ibrahimmwafey.46@azhar.edu.eg

[2] Lecturer, Department of Oral Medicine, Periodontology, Oral Diagnosis and Dental Radiology, Faculty of Dental Medicine, Al-Azhar University (Assiut Branch), Assiut, Egypt. E-mail: dentistahmed200@gmail.com

[3] Lecturer, Department of Oral Medicine, Periodontology, Diagnosis and Oral Radiology Faculty of Dentistry, Al-Azhar University, Cairo, Egypt. E-mail: hamdyabol-khair. 209@azhar.edu.eg

[4] Lecturer, Department of Oral Medicine, Periodontology, Oral Diagnosis and Dental Radiology, Faculty of Dental Medicine, Al-Azhar University (Assiut Branch), Assiut, Egypt. E-mail: Abdullahbeshrah923.el@azhar.edu.eg

[5] Lecturer, Department of Oral Medicine, Periodontology, Oral Diagnosis and Dental Radiology, Faculty of Dental Medicine, Al-Azhar University (Assiut Branch), Assiut, Egypt. E-mail: mahmoudmizar4@gmail.com

ABSTRACT

Objectives: The current research aimed to evaluate the influence of lyophilized platelet-rich fibrin (Ly-PRF) in the management of periodontal intra-bony deformities. Patients and Methods: 36 intra-bony deformities (IBD) in 36 individuals with stage III periodontitis of both genders participated in the present randomized controlled prospective clinical investigation. The participants were randomly received either OFD alone [group I (control, n=18)] or OFD with combination of Ly-PRF [group II (test, n=18)]. All patients were evaluated clinically at; baseline, 3- and 6-month utilizing plaque index (PI), gingival index (GI), probing pocket depth (PPD), and clinical attachment level (CAL). Radiographic evaluation of the marginal bone level (MBL) and defect depth (DD) was evaluated at baseline and after 6-month. Results: The two treatment regimens lead to statistically significant PPD decreases and CAL gain from baseline to 6 months; the decrease in PPD and the gain in CAL were significantly greater in group II in comparison to group I. Radiographically, the mean value of MBL for the two groups showed additional marginal bone loss at 6 months; this loss was non-significant between the groups. The mean DD for both groups displayed statistically significant decrease from baseline values to 6-month; the decrease in DD was significantly greater in group II in comparison to group- I. Conclusions: Given the constraints of this research, it may be concluded that the adjunctive utilize of Ly-PRF in the surgical management of periodontal intra-bony deformities exhibited promising results on the clinical and radiographic results regarding to the PPD decrease, CAL gain as well as DD reduction.

Keywords: *Open flap debridement, Periodontal intra-bony deformities, Lyophilized platelet-rich fibrin.*

How to Cite: Ibraheem Mahmoud Mwafey, Ahmed Mohamed Abd Al Rahman, Hamdy A Abol-Khair, Abdullah Ibrahim Abd Rabbouh Ali, Mahmoud Ahmed Mizar, (2024) The Influence of Lyophilized Platelet-Rich Fibrin in The Treatment of Periodontal Intra-Bony Defects (A Randomized Clinical Trial), *Journal of Carcinogenesis, Vol.23, No.1*, 988-996

1. INTRODUCTION

The multifactorial inflammatory condition known as periodontitis is typified by microbially associated host-mediated deleterious destruction of the teeth's investing and supporting apparatus. One of the main clinical challenges in treating periodontal disease is preventing alveolar bone loss, which is a sign of the disease's development. While alterations in the soft tissue of the pocket wall indicate the existence of the inflammatory illness, the current bone level is a result of previous pathologic events[(1)].

The pattern of bone loss may be either horizontal or vertical. Deficiencies that form obliquely and leave a hollowed-out

trough in the bone together with the root are known as vertical or angular deficiencies; the base of the deficiency is situated apical to the adjacent bone. Surgical exposure is the only reliable method to determine their presence. Vertical defects increase with age, with most appearing on distal and mesial surfaces[2]. The intra-bony defect could be described as a particular osseous defect that is enclosed by one, two, or three bony walls, or a mixture of these, and has its base apical to the interdental alveolar crest. It was proposed that all other vertical bony flaws should be referred to as "infra-bony," and that just 3-wall angular flaws ought to be called "intra-bony." Intraosseous periodontal deficiencies are thought to have a high potential for regeneration.[3] However, if addressed, these abnormalities increase the likelihood of further attachment, bone loss, and advancement of the disease[4].

The primary goal of periodontal therapy is to inhibit disease activity by managing the causative and risk factors. The supreme goal is to achieve a 3D reconstruction of the lost tooth-supporting structure with tissues that have the same architecture and function as the original tissues. Several surgical methods and regeneration materials exist, including guided tissue regeneration (GTR), bone replacement grafts and substitutes, periodontal tissue engineering and biologic modifiers or combination[5].

The scientific knowledge of wound healing has grown as a result of developments in cell and molecular biology. Polypeptide growth and differentiation factors have been shown to promote wound healing and redevelopment by controlling chemotaxis, differentiated cells, cell growth, as well as matrix formation. A strategy of improving wound healing and promoting periodontal regeneration is enhancing and hastening the impact of liberated growth factors (GFs), which may speed up bone defect healing. These aims could be accomplished by activating Platelet-derived growth factors, which are ubiquitous triggers in almost all wound healing mechanisms, are released locally[6].

Over the past decade, improvements in platelet concentrate formulations have led to the introduction of PRF, which is utilized as a supraphysiological concentration of autologous growth factors with not the need for anticoagulants[7]. Numerous systematic evaluations have examined the application of PRF in periodontal bone abnormalities and shown that it greatly improves radiographic and clinical results in the treatment of IBDs when compared to OFD alone[8-10]. Despite the reported promising results of PRF in the management of periodontal IBDs, several drawbacks have been identified, including a lack of rigidity, short lifespan, rapid resorption and a tendency to compromise its ability to maintain space in the long term, especially when used as a barrier membrane. In addition, once prepared, it isn't easy to store PRF, meaning it must be used immediately[11].

Several attempts have been performed to overcome the disadvantages of fresh-PRF such as lyophilization (freeze-drying). It has been reported that lyophilization delivers considerable benefits by prolonging the stability and shelf life of sensitive medications, maintaining the biological and structural integrity of biomolecules, minimizing storage and transportation expenses without the need for refrigeration, and preserving high product quality and purity by removing water without compromising the active ingredients. This procedure entails freezing. To create a dry, resilient substance suitable for prolonged storage and transportation, initial drying (decomposition of ice) and subsequent drying (decomposition of residual unfrozen water) are used.[12]. The fundamental and biological properties of the fibrin mesh are considerably altered by lyophilization of fresh PRF. This mechanism enhances tissue repair and regeneration by promoting the attachment of cells, growth, vascular infiltration, and activation of platelets. Furthermore, by significantly lowering PRF-related leucocytes, it reduces immune system rejection and proteolytic breakdown of the created tissue[13].

Using several periodontal flap procedures with intrasulcular incision is known as open flap cleaning. Improved approach to periodontal pockets and bone deformities, sufficient root cleaning, and the encouragement of periodontal regeneration are the objectives. In addition to being utilized as a control method in clinical studies assessing regeneration therapies, OFD can be utilized for the management of IBDs[14].

Research on the utilization of Ly-PRF either by itself or in conjunction with other biologics on the treatment of periodontal IBDs is considered an innovative therapeutic modality, so the current research was performed to assess the influence of lyophilized platelet-rich fibrin on both clinical and radiographic outcomes after surgical treatment of periodontal intra-bony defects.

2. PATIENTS AND METHODS

Study setting and population

The present research was planned as a randomized, controlled and prospective clinical trial, carried out on 36 intra-bony deformities within 36 patients with third phase of periodontitis. Patients were 17 females and 19 males, ages 29 to 54. All patients were chosen from among those who visited the oral medicine and periodontology department's outpatient clinic at Al-Azhar University's Assiut branch of the Faculty of Dental Medicine.

Inclusion criteria:

1. No systemic illnesses were present in any of the individuals[15].
2. The third phase of periodontitis having clinical attachment loss (CAL) > 5 mm and probing pocket depth (PPD) ≥ 6 mm[16].
3. A 2- or 3-wall intra-bony interproximal deficiency has a width of ≥3 mm at the maximum occlusal portion and a depth of ≥3 mm.
4. A proper mouth plaque index score of less than 20% indicates good dental hygiene[17].

Exclusion criteria:

1. The last six months' worth of periodontal treatment and antibiotic use.
2. Individuals who smoke, have diabetes, are pregnant or nursing, or are alcoholics.
3. Chemotherapy and radiation treatment, which alter bone turnover, were administered to individuals having intra-bony abnormalities.
4. Individuals who have used aspirin or any other medication that might impair platelet function within the preceding three months[18].
5. One-wall deficiency, interdental craters, furcation inclusion, and Miller grade II or higher mobility.

Patient grouping and randomization

Sample size calculation

According to **Agarwal et al (2016)**[19], The sample size was determined employing the G Power statistical power analysis program (version 3.1.9.4)® with an actual power (1-β error) of 0.85 (85%) and a level of significance (α error) of 0.05 (5%) for a two-tailed hypothesis test to identify a significant variation (α error) of 1.1 ± 0.74 mm across groups, considering the alteration within CAL like the principal outcome parameter. Therefore, a sample size of 15 patients per group (30 in total) was required to detect an effect size (f)= 1.162. To account for potential participant withdrawal, the sample size was expanded by 20%, resulting in a total of n=36 (18 for each group).

Patients grouping and randomization:

The participants were divided into 2 groups randomly using a flip of a coin:
Group-1: Only open flap debridement was used to treat 18 individuals who had periodontitis with an intra-bony deficiency.
Group-2: Open flap debridement and the administration of lyophilized platelet-rich fibrin were used for treating 18 patients having periodontitis who had an intra-bony deficiency.

Presurgical periodontal preparation:

All patients received the 1st and 2nd steps (behavioral and mechanical therapy) of a pre-established stepwise therapeutic approach, depending on 2020 European Federation of Periodontology (EFP) S3 level clinical practice guidelines for the management of phase I–III periodontitis[20] aiming to motivate the patient, lower inflammation and bacterial count, treating the main causes of periodontal disease. A second assessment was conducted six weeks after the start of treatment to verify the need for periodontal surgery. Surgery was required if an interproximal location with PD > 6 mm, CAL ≥ 5 mm, and interproximal IBD of ≥ 3 mm persisted.

Preparation of Lyophilized Platelet-Rich Fibrin:

10 ml venous blood was drawn from the antecubital vein into a 10 ml conventional vacuum plain glass tube and centrifuged right away for ten minutes at 3000 rpm according to **Choukroun's** protocol[21]. The blood was divided into three layers after centrifugation. Utilizing sterilized scissors, the center layer of the tube, the new PRF clot, was removed from the bottom layer, leaving a thin coating of red blood cells. In order to create Ly-PRF, undamaged fresh PRF was frozen, kept at -80 °C for half an hour, and then freeze-dried overnight at -51 °C[22]. The specimens were stored at 4 °C after being pulverized into granules with a mortar and pestle[23].

Surgical procedure:

After administration of local anesthesia® A buccal and lingual intra-sulcular incision was performed extending to only one mesial and one distal adjacent tooth, followed by flap reflection, preserving the interproximal soft tissue possible at all sites. The defect site was thoroughly debrided of all granulation tissue without bone recontouring. Additionally, the root surface was debrided using both manual and ultrasonic tools. Finally, the deficiency was irrigated copiously using normal saline. In the group-1: Vertical internal mattress sutures were used to reposition the flap and secure it with 4-0 Polypropylene sutures (Figure. 1). In the group-2: After hydrating the Ly-PRF granules alongside a few drops of regular saline, they were applied and compressed in order to fill the IBD. The flap was then adjusted and sutured utilizing vertical internal mattress sutures and 4–0 polypropylene sutures (Figure 2).

® Artpharmadent 4% 1/100.000, ArtPharma Egypt Pharmaceuticals, 6th of October City, Cairo Governorate, Egypt)

Postoperative care;

The participants received oral and written postoperative instructions. Antibiotics (875 mg Amoxicillin/125 mg clavulanic acid)®[1] twice a day throughout one week and analgesics (ibuprofen 400 mg)®[3], three a day for 5 days, were prescribed following surgery. Additionally, chlorhexidine digluconate mouthwash (0.12%)®* was prescribed twice a day for two weeks. In the surgery regions, patients were advised not to wash or clean their teeth, until the suture removal. 2 weeks later, the suture was removed, and following one month postoperatively, all individuals were advised to return to their regular mechanical oral hygiene practices, which consisted of brushing using a soft toothbrush and flossing. Finally, the individual's follow-up appointments were arranged.

Patient evaluation:

1- Clinical evaluation:

The subsequent clinical criteria including plaque index[24], gingival Index[25], site-specific probing pocket depth[26] (evaluated from the gingival margin to the base of the pocket), site-specific clinical attachment level[27] (evaluated from the cementoenamel junction to the base of the pocket) were recorded using Williams' graduated periodontal probe. All parameters were estimated at the baseline, following phase I therapy, 3- and 6-month post-operatively.

2- Radiographic assessment:

The defect depth (DD) and marginal (MBL) as radiographic parameters were evaluated for all participants at baseline and 6 months post-operatively. Cone-beam computed tomography (CBCT) scanning was carried out. High-resolution images were acquired at a 12 × 8 cm. The Digital Imaging Communications in Medicine file type was then used to save every picture. Blue Sky Plan 4 software (Version 4.13.31) was used to evaluate the images after they were acquired. To the closest millimeter, the readings were rounded. The radiographs' anatomical markers were chosen using the standards established by **Schei et al. (1959)**[28], which comprise the base of the defect (BD), alveolar crest (AC), and cemento-enamel junction (CEJ). The radiography linear measures[29] (Figure 7) were calculated as following:

- Defect depth (DD): An additional line (AUX1) in the tooth axis and a secondary line (AUX2) from AC, perpendicular to AUX1, were drawn in order to calculate DD. The DD depth was determined as the distance in millimeters (mm) between the base of the deficiency and the location whereby AUX2 crossed the CEJ-BD line.
- Marginal bone level (MBL): Was determined as the distance in mm between CEJ and the location where AUX2 crossed the CEJ-BD line. The gain or loss of MBL is determined by deducting the baseline CEJ-AC from the CEJ-AC at a certain period.

Statistical analysis:

IBM® SPSS® Statistics Version 20 for Windows was used to gather, tabulate, and statistically evaluate the data. $P < 0.05$ was used as the significance criterion. For every group in every test, the mean and standard deviation values were computed. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to examine the data for normality. While the remaining data had a parametric (normal) distribution, the PI and GI data displayed a non-parametric (not-normal) distribution (scores). of non-parametric data, two groups of unrelated specimens were compared using the Whitney test. Two groups in associated specimens were compared using the Wilcoxon test. For parametric data, two groups in unrelated samples were compared using an independent sample t-test. The two groups in associated specimens were compared using a paired sample t-test.

3. RESULTS

The current randomized clinical and radiographic investigation was carried out on 36 intra-bony deficiencies in 36 patients (19 males and 17 females) with phase three periodontitis. The periodontal IBDs were randomly allocated either to group-1 (n = 18, control group) or group-2 (n = 18, test group), and no patient withdrawal. Ten males and eight females (mean age of 40.7 ± 7.83 years) made up the control group, whilst nine males and nine females (mean age of 41.63 ± 8.01 years) made up the experimental group. There were no unanticipated adverse effects (such as infection, extended hemorrhage, or surgical area exposing) recorded by individuals or clinically recognized during the healing process. (Table 1)

I. Clinical parameters:

1- Changes in the plaque index:

- A statistically significant difference in both groups at the various periods in comparison to the baseline.
- No statistically significant variation between both groups at various periods.

®[1] (Augmentin 1gm, GlaxoSmithKline Pharmaceutical Company, Fifth district, New Cairo, Egypt)
®[3] (Brufen 400 mg, Abbott International Egypt, 90th Street, Plot 76 1st Sector, 5th Settlement, New Cairo, Egypt)
®* (Orovex M.W, MACRO GROUP PHARMACEUTICALS, 83, Al Moltaka Al Arabi, Sheraton, Cairo, Egypt)

2- Changes in the gingival index:

- A statistically significant variation from the baseline across all groups at various periods.
- When comparing both groups at various intervals, there was no statistically significant variation.

3- Probing pocket depth measurements:

- A statistically significant variation was recorded in both groups at the various periods in comparison to the baseline.
- There were significant variations between both groups at 3 and 6 months after treatment.

4- Clinical attachment level measurements:

- A statistically significant variation was recorded in both groups at the various periods in comparison to the baseline.
- There were statistically significant variations between both groups at 3 and 6 months after treatment. (Table 1)

II. Radiographic parameters:

1- Marginal bone level assessment:

- A statistically significant variation was recorded in both groups at 6 months in comparison to the baseline.
- There were no statistically significant variations between both groups at 6 months after treatment; both of them showed additional bone loss.

2- Defect depth assessment:

- A statistically significant difference was recorded in both groups at 6 months in comparison to the baseline; both groups displayed a reduction in the defect depth.
- There was a statistically significant variation in group-2 in comparison with group-1 at 6 months following treatment; the Iy-PRF group displayed higher defect depth reduction. (Table 1)
-

Table (1): Baseline characteristics, clinical and radiographic parameters for both groups at different evaluation intervals.

Parameters	Group I (OFD) (n =18)	Group II (OFD +Ly-PRF) (n =18)	*P*- value
	Mean ± SD	Mean ± SD	
Baseline characteristics			
Age [(mean ± SD) years]	40.7±7.83	41.63±8.01	0.523
Gender [n (%)]	Male: 10 (55.56%)	Male:9 (50%)	0.475
	Female: 8 (44.44%)	Female:9(50%)	
PI scores			
Baseline	0.85 ± 0.16	0.82 ± 0.19	0.617 ns
After 3 months	0.49 ± 0.21	0.44 ± 0.24	0.334 ns
After 6 months	0.97 ± 0.14	0.76 ± 0.16	0.532 ns
GI scores			
Baseline	0.89 ± 0.13	0.86 ± 0.15	0.593 ns
After 3 months	0.58 ± 0.14	0.51 ± 0.11	0.321 ns
After 6 months	0.95 ± 0.16	0.86 ± 0.13	0.563 ns
PPD (mm)			
Baseline	8.7 ± 0.73	8.5 ± 0.84	0.781 ns
After 3 months	5.9 ± 0.82	4.7 ± 1.13	0.03 s
After 6 months	5.12 ± 0.95	4.3 ± 0.62	0.04 s
CAL (mm)			
Baseline	7.9 ±1.38	8.1 ± 1.01	0.812 ns
After 3 months	5.6 ±1.26	4.9 ± 0.94	0.031s
After 6 months	5.3 ±1.34	4.4 ±1.28	0.027 s

MBL (mm)			
Baseline	3.45 ± 0.39	3.47 ± 0.25	0.837 ns
After 6 months	3.52 ±0.31	3.51 ±0.35	0.797 ns
DD (mm)			
Baseline	4.58 ± 0.13	4.56 ± 0.15	0.582 ns
After 6 months	3.76 ± 0.17	2.88 ± 0.61	< 0.031 s

S: significant p value < 0.05, HS: highly significant p-value <0.01, NS: non-significant p-value ≥0.05.

4. DISCUSSION

In addition to continuously delivering numerous essential growth/differentiation factors into the wound site, platelet-rich fibrin, a second-generation platelet concentrate, proved its capacity to improve periodontal wound healing incidents through offering 3-D fibrin scaffolds for cellular migration, adhesion, and differentiation[30, 31]. In spite of these relevant results of PRF, several drawbacks have been identified, among them a lack of rigidity, short lifespan, rapid resorption and a tendency to compromise its ability to maintain space in the long term, especially when used as a barrier membrane. In addition, once prepared, it isn't easy to store PRF, meaning it must be used immediately[11].

Compared to fresh PRF, the lyophilized PRF is more stable for storage and has a greater porous structure, which may eventually result in sustained growth factor release and improved osteogenic potential[22]. Ly-PRF exhibits remarkable osteogenic power via improving bone cell differentiation and mineralization, serving as a biomimetic scaffold for several growth-promoting release factors such as Platelet-derived growth factor, Transforming growth factor-β, and vascular endothelial growth factor[32].

In the current investigation, the 2018 classification system of periodontitis framework was used in selecting the patients because it offers an additional individualized method to periodontal diagnosis and management by taking into account both the patients' present state of disease and any future risk[16]. In addition, a parallel design was selected in order to prevent the "carry-across" impact reported by the split-mouth design[33]. Besides, all patients suffering from any systemic diseases, pregnant or lactating females, smokers, and alcoholic individuals were excluded to confirm the accuracy of the results that might be affected[15].

The current study's findings revealed no significant difference between the two groups' PI and GI ratings at various periods with respect to plaque accumulation and gingival inflammation. This result is related to the outcomes of the patient education about the nature of the periodontal disease and the patient's adherence to the oral hygiene program, as reported by **Echeverria et al (2018)**[34] in their conclusion, which stated that in addition to reducing plaque and bleeding during probing, maintaining periodontal health adherence may slows down or halts the development of the disease.

Significant clinical indicators of effective periodontal regeneration treatment include a decrease in PPD and an increase in CAL. The current research found a reduction in the PPD and gain in CAL at 3 and 6 months following therapy in comparison to the baseline scores in the two studied groups, but the Ly-PRF group displayed a greater decrease in PPD and CAL gain values in relation to the OFD group. These positive outcomes in the Ly-PRF group should be due to a sustained growth factor design that may prolong the release of a chemotactic gradient for recruitment of stem cells which in turn underwent differentiation and encourage regeneration-based healing[22]. Similar findings were reported by **Thorat et al (2011)**[35] they concluded that there was a more significant decrease in PPD and more CAL gain at sites treated with PRF than the open flap debridement alone. Also, **Ustaoglu and colleagues (2020)**[36] found that the titanium-PRF group showed a further decrease in PPD depth and an increase in CAL gain compared to the OFD alone group. Contrary to these findings, **Sharma et al (2011)**[37] found that, after a nine-month follow-up, areas treated with OFD showed comparable CAL increase to those treated with PRF or platelet-rich plasma.

Regarding the marginal bone level, the result of the current research found further marginal bone loss in both study groups, but this loss was not significant. These findings are agreed with the results of **Piemontese et al (2008)**[38] and **Agarwal et al (2016)**[19] but the amount of loss is a little bit greater in the current research. On the other hand, the outcomes of **Pham (2021)**[39] reported that the OFD+PRF showed marginal bone gain by a mean value of (1.07 ± 0.52 mm) while the OFD group showed marginal bone loss by a mean value of (-0.37 ± 0.62 mm) at the 6-month evaluation period. This conflict is attributed to differences in methodology; the present study utilized CBCT scanning rather than conventional intra-oral radiography used by these authors.

With reference to the reduction in the defect depth as a major radiographic outcome the current trial reported promising

changes in the defect depth; the group I showed a change from (4.58 ± 0.13 mm) to (3.76 ± 0.17 mm) at baseline and 6 months correspondingly, while the group II presented a change from (4.56 ± 0.15 mm) to (2.88 ± 0.61 mm) at baseline and 6 months respectively, this changes were significant between the group the endpoint. Such outcome in line with **Chatterjee et al (2017)**[40] who demonstrated that the titanium-PRF group showed more reduction in the defect depth, followed by the Leukocyte-PRF group and finally the OFD group was least at 6 months. Additionally, **Ajwani et al (2015)**[41] concluded that in comparison to OFD alone, the combined application of PRF with OFD greatly enhances defect fill. Similar findings were also reported by **Thorat and his coworkers (2017)**[42] but with greater values of defect depth reduction, these authors reported that the mean defect depth reduction value was 1.67mm in the OFD group, while in the PRF group, the mean reduction value was 3.09 mm. This may be justified by the longer follow-up period, which was 12 months.

The variations in both study groups' clinical and radiographic outcomes are in accordance with a systematic review's conclusion that management of IBDs utilizing certain biomaterials or biologicals is more effective than utilizing OFDs[43]. The present study outcomes confirm Ly-PRF's beneficial role in treating periodontal intra-bony deficiencies.

5. CONCLUSIONS

According to outcomes of the current investigation, it was concluded that, compared to OFD alone, Ly-PRF's supplemental use in the regenerative management of periodontal intra-osseous deficiencies presents a promising result in term of both the clinical and radiographic outcomes.
Further studies with extended follow-up periods and bigger sample sizes are recommended to secure the reliability of the results.

REFERENCES

1. **Tsoromokos N, Parinussa S, Claessen F, Moin D, Loos B**. Estimation of alveolar bone loss in periodontitis using machine learning. international dental journal. 2022;72:621-7.
2. **Cavalla F, Biguetti CC, Garlet TP, Trombone AP, Garlet GP.** Inflammatory pathways of bone resorption in periodontitis. InPathogenesis of Periodontal Diseases: Biological Concepts for Clinicians 2017;27: 59-85.
3. **Sculean A, Nikolidakis D, Nikou G, Ivanovic A, Chapple I, Stavropoulos A**. Biomaterials for promoting periodontal regeneration in human intrabony defects: a systematic review. Periodontology 2000. 2015;68:182-216.
4. **Barbato L, Selvaggi F, Kalemaj Z, Buti J, Bendinelli E, Marca M, et al.** Clinical efficacy of minimally invasive surgical (MIS) and non-surgical (MINST) treatments of periodontal intra-bony defect. A systematic review and network meta-analysis of RCT's. Clinical oral investigations. 2020;24:1125-35.
5. **Najeeb S, Khurshid Z, Agwan MA, Ansari SA, Zafar MS, Matinlinna JP.** Regenerative potential of platelet rich fibrin (PRF) for curing intrabony periodontal defects: a systematic review of clinical studies. Tissue engineering and regenerative medicine. 2017;14(6):735-42..
6. **Cho , Kim K, Lee Y, Ku Y, Seol Y**. Periodontal wound healing and tissue regeneration: a narrative review. Pharmaceuticals. 2021;14:1-17.
7. **Dohan D, Choukroun J, Diss A, Dohan S, Dohan A, Mouhyi J, et al.** Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part II: platelet-related biologic features. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:45-50.
8. **Miron R, Moraschini V, Fujioka-Kobayashi M, Zhang Y, Kawase T, Cosgarea R, et al.** Use of platelet-rich fibrin for the treatment of periodontal intrabony defects: a systematic review and meta-analysis. Clinical oral investigations. 2021;25:2461-78.
9. **Theodosaki A, Filippou S, Kazantzidis G, Doufexi A**. Effectiveness of platelet rich fibrin alone or in combination with bone grafts in the treatment of infrabony defects: systematic review and metanalysis. Health Sciences Review. 2022;5:1-12.
10. **Li A, Yang H, Zhang J, Chen S, Wang H, Gao Y.** Additive effectiveness of autologous platelet-rich fibrin in the treatment of intrabony defects: A PRISMA-compliant meta-analysis. Medicine. 2019;98(11):14759.
11. **Borie E, Olivi D, Orsi I, Garlet K, Weber B, Beltran V, et al.** Platelet-rich fibrin application in dentistry: a literature review. Int J Clin Exp Med. 2015;8:7922-9.
12. **Wang Z, Li L, Ren G, Duan X, Guo J, Liu W, et al.** A comprehensive review on stability of therapeutic proteins treated by freeze-drying: induced stresses and stabilization mechanisms involved in processing. Drying Technology. 2022;40:3373-88.
13. **Moradian H, Rafiee A, Ayatollahi M.** Design and fabrication of a novel transplant combined with human bone marrow mesenchymal stem cells and platelet-rich fibrin: new horizons for periodontal tissue regeneration after dental trauma. Iranian journal of pharmaceutical research. 2017;16(4):1370.

14. **Graziani F, Gennai S, Cei S, Cairo F, Baggiani A, Miccoli M, et al.** Clinical performance of access flap surgery in the treatment of the intrabony defect. A systematic review and meta-analysis of randomized clinical trials. J Clin Periodontol. 2012;39:145-56.
15. **American Dental A**. General guidelines for referring dental patients. Revised June. 2007;55:87-9.
16. **Tonetti M, Greenwell H, Kornman K**. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. Journal of periodontology. 2018;89:159-72.
17. **O'Leary T, Drake R, Naylor J**. The plaque control record. J Periodontol. 1972;43:38-40.
18. **Sezgin Y, Uraz A, Taner I, Çulhaoglu R**. Effects of platelet-rich fibrin on healing of intra-bony defects treated with anorganic bovine bone mineral. Braz Oral Res. 2017;31:1-11.
19. **Agarwal A, Gupta N, Jain A**. Platelet rich fibrin combined with decalcified freeze-dried bone allograft for the treatment of human intrabony periodontal defects: a randomized split mouth clinical trail. Acta Odontol Scand. 2016;74:36-43.
20. **Sanz M, Herrera D, Kebschull M, Chapple I, Jepsen S, Beglundh T, et al.** Treatment of stage I-III periodontitis-The EFP S3 level clinical practice guideline. J Clin Periodontol. 2020;47:4-60.
21. **Dohan D, Choukroun J, Diss A, Dohan S, Dohan A, Mouhyi J, et al.** Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:37-44.
22. **Ngah N, Dias G, Tong D, Mohd-Noor S, Ratnayake J, Cooper P, et al.** Lyophilised Platelet-Rich Fibrin: Physical and Biological Characterisation. Molecules. 2021;26:1-14.
23. **Xu F, Zou D, Dai T, Xu H, An R, Liu Y, et al.** Effects of incorporation of granule-lyophilised platelet-rich fibrin into polyvinyl alcohol hydrogel on wound healing. Sci Rep. 2018;8:1-10.
24. **Silness J, Loe H**. PERIODONTAL DISEASE IN PREGNANCY. II. CORRELATION BETWEEN ORAL HYGIENE AND PERIODONTAL CONDTION. Acta Odontol Scand. 1964;22:121-35.
25. **Loe H**. The Gingival Index, the Plaque Index and the Retention Index Systems. J Periodontol. 1967;38:610-6.
26. **Polson A, Caton J, Yeaple R, Zander H**. Histological determination of probe tip penetration into gingival sulcus of humans using an electronic pressure-sensitive probe. J Clin Periodontol. 1980;7:479-88.
27. **Ramfjord S**. The Periodontal Disease Index (PDI). J Periodontol. 1967;38:602-10.
28. **Schei O, Waerhaug J, Lovdal A, Arno A**. Alveolar bone loss as related to oral hygiene and age. The Journal of periodontology. 1959;30:7-16.
29. **Gorski B, Jalowski S, Gorska R, Zaremba M**. Treatment of intrabony defects with modified perforated membranes in aggressive periodontitis: a 12-month randomized controlled trial. Clinical Oral Investigations. 2018;22:2819-28.
30. **Dohan D, Choukroun J, Diss A, Dohan S, Dohan A, Mouhyi J, et al.** Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part II: platelet-related biologic features. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2006;101:45-50.
31. **El Bagdadi K, Kubesch A, Yu X, Al-Maawi S, Orlowska A, Dias A, et al.** Reduction of relative centrifugal forces increases growth factor release within solid platelet-rich-fibrin (PRF)-based matrices: a proof of concept of LSCC (low speed centrifugation concept). European Journal of Trauma and Emergency Surgery. 2019;45:467-79.
32. **Li Q, Reed DA, Min L, Gopinathan G, Li S, Dangaria S, et al.** Lyophilized platelet-rich fibrin (PRF) promotes craniofacial bone regeneration through Runx2. Int J Mol Sci. 2014;15:8509-25.
33. **Yusri S, Elfana A, Elbattawy W, Fawzy K**. Effect of locally delivered adjunctive antibiotics during surgical periodontal therapy: a systematic review and meta-analysis. Clinical oral investigations. 2021;25:5127-38.
34. **Echeverria J, Echeverria A, Caffesse R**. Adherence to supportive periodontal treatment. Periodontology 2000. 2019;79:200-9.
35. **Thorat M, Pradeep A, Pallavi B**. Clinical effect of autologous platelet-rich fibrin in the treatment of intra-bony defects: a controlled clinical trial. J Clin Periodontol. 2011;38:925-32.
36. **Ustaoglu G, Ugur Z, Ozelci F**. Comparison of GTR, T-PRF and open-flap debridement in the treatment of intrabony defects with endo-perio lesions: a randomized controlled trial. Med Oral Patol Oral Cir Bucal. 2020;25:117-23.
37. **Sharma A, Pradeep A**. Treatment of 3-wall intrabony defects in patients with chronic periodontitis with autologous platelet-rich fibrin: a randomized controlled clinical trial. J Periodontol. 2011;82:1705-12.
38. **Piemontese M, Aspriello S, Rubini C, Ferrante L, Procaccini M**. Treatment of periodontal intrabony defects with demineralized freeze-dried bone allograft in combination with platelet-rich plasma: A comparative clinical trial. Journal of periodontology. 2008;79:802-10.
39. **Pham T**. Intrabony defect treatment with platelet-rich fibrin, guided tissue regeneration and open-flap debridement: a randomized controlled trial. Journal of Evidence Based Dental Practice. 2021;21:1-27.
40. **Chatterjee A, Pradeep A, Garg V, Yajamanya S, Ali M, Priya V.** Treatment of periodontal intrabony defects using autologous platelet-rich fibrin and titanium platelet-rich fibrin: a randomized, clinical, comparative study. J Investig Clin Dent. 2017;8:1-6.

41. **Ajwani H, Shetty S, Gopalakrishnan D, Kathariya R, Kulloli A, Dolas R, et al.** Comparative evaluation of platelet-rich fibrin biomaterial and open flap debridement in the treatment of two and three wall intrabony defects. Journal of international oral health: JIOH. 2015;7:32-7.
42. **Thorat M, Baghele O**. Adjunctive Effect of Autologous Platelet-Rich Fibrin in the Treatment of Intrabony Defects in Localized Aggressive Periodontitis Patients: A Randomized Controlled Split-Mouth Clinical Trial. International Journal of Periodontics & Restorative Dentistry. 2017;37:302-9.
43. **Tavelli L, Chen C, Barootchi S, Kim D**. Efficacy of biologics for the treatment of periodontal infrabony defects: an American Academy of Periodontology best evidence systematic review and network meta-analysis. Journal of Periodontology. 2022;93:1803-26.