"Revitalyz: A Comprehensive Analysis of Injectable Platelet-Rich Fibrin (PRF)" – Systematic review

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ABSTRACT

BACKGROUND- Platelet-rich concentrates, namely injectable platelet-rich fibrin (i-PRF), have recently shown a potential role in the regeneration of soft and hard tissue and hence it's used as adjunct for regenerate procedures.

AIM-The aim of this systematic review is to evaluate and compare the effect of the injectable – PRF in periodontology and implantology.

OBJECTIVE- To assess the regeneration of the periodontium in patients with chronic periodontitis, pocket depth 5 mm after Phase-I therapy, furcation defects, intra-bony (1-, 2- & 3 -wall) or Gingival recession.

METHODS AND MATERIALS: Electronic bibliographic databases search of Medline, Science Direct and Google Scholar was made. Studies using i-PRF to treat periodontal intrabony defects, furcation defects, gingival recession, ridge defects, in procedures such as ridge augmentation of the maxillary or mandibular region with a follow-up period of at least 3 months were searched.

Two reviewers performed the systematic review using the PRISMA statement for reporting and the Cochrane risk-of-bias tool was used for quality assessment.

RESULT- It was found that i-PRF showed statistically significant results concerning radiographic and clinical parameters at different time intervals as compared to the control groups.

CONCLUSION- An i-PRF, provides a promising outcome, for periodontal wound healing and bone regeneration. I-PRF showed great results in intrabony defects, furcation defects, gingival recession and in periodontitis patients.

INTRODUCTION

Periodontitis is an inflammatory disease that includes the destruction of alveolar bone, root cementum, periodontal ligament and gingiva as a response to insults elicited by micro-organisms on tooth surfaces. Periodontal therapy has many primary objectives, these are gaining access to the diseased sites, achieving a reduction in pocket depth, arresting further disease progression and finally restoring the periodontal tissues that are lost due to the disease process. The main aim of the procedures is to achieve periodontal regeneration by new attachment formation. Regeneration is the reproduction or reconstitution of the lost or diseased part to restore the architecture and function of the periodontium. [1] Bone graft consists of property to increase the height of alveolar bone, jaw bone remodeling, microvascular free tissue transfer, and alveolar crest re-formation.

In recent years, To deliver high concentrations of polypeptide growth factors to periodontal surgical sites, use of autologous platelet concentrates serves as a safe and appropriate approach. PRF are different from its predecessor (PRP/PRGF) by several parameters, those are the simplicity of its preparation and its implementation in the procedure. The time and cost of preparation are both significantly lower as PRF does not necessitate the direct activation with additional factors such as bovine thrombin or extrinsic anticoagulants [2]. Because of its fibrous structure, PRF retains a larger number of cytokines and growth factors in a supportive three-dimensional fibrin scaffold for cell migration [6]. The PRF scaffold allows a continuous slow release of growth factors and cytokines over a period of 10 days, in contrast to PRP which has been shown to release the majority of its growth factors within the first day [7]. Therefore, migrating cells in near proximity to PRF scaffolds are in an environment with fibrin and growth factors throughout their entire growth cycle [8].

PRF is a surgical biological preservative prepared from centrifuging autologous blood. [9,10] Cross-linking between the fibrin fibers mechanically stabilizes the architecture of the fibrin-based scaffold. This intricate nanostructure of fibrin nanostructure shows proper biological and elastic mechanical behavior [20,21]. Injectable platelet-rich fibrin was invented in 2001 by Choukroun et al [2]. In 2014, an injectable platelet-rich fibrin (i-PRF) was developed by altering rotations and

centrifugation forces [22]. In fact, the blood centrifuged at slower centrifugation speeds in centrifugation tubes resulted in a flowable platelet rich fibrin named i-PRF. The injectable platelet-rich fibrin is injected into the skin or scalp of the face, and it remains liquid for 10 to 15 minutes before it solidifies into a clot [23].

In a study by Wend et al [33], it was found that lower relative centrifugation force can lead to a significantly higher total cell number. Total platelet numbers were determined for whole blood and the various platelet concentrates. Similar to the previous study done by Wend et al[31], i-PRF exhibited a higher number of platelets in comparison with L-PRF and A-PRF; however, concentration of platelets in i-PRF was significantly less than those in L-PRP and pure-PRP (P-PRP) [32] In 2019, Fernández et al [33] compared the four different types of platelet concentrates (A-PRF, i-PRF, L-PRP, and P-PRP) with each other in terms of growth factors release (BMP-2, IGF-1, PDGF-BB, and VEGF). They found that during the 14-day period, the cumulative release of VEGF was demonstrated to be higher in i-PRF compared to the others. PDGF-BB exhibited a rapid release rate in i-PRF, most of which was released within the first three days of in-vitro incubation. Additionally, Varela et al [34] compared growth factor release (PDGF-AB and VEGF) of i-PRF and blood clot samples in comparison with each other over the periods of 1 hour, 8hour's, 24 hour's, 72 hour's and 240 hour's. They have found blood clot samples release more VEGF compared with i-PRF ($p < 0.05$) [30].

Methods

Development of a protocol

A protocol including all aspects of a systematic review methodology was developed prior to initiation of this review. This included definition of the focused question; a PICO (patient, intervention, comparison, outcome) question; a defined search strategy; study inclusion criteria; determination of outcome measures; screening methods, data extraction, and analysis; and data synthesis.

PICO question

A systematic search was conducted to obtain appropriate articles for critical appraisal. PICO (Population, Intervention, Comparison, and Outcome) was applied to determine and evaluate the effect of i-PRF for periodontal wound healing in Chronic periodontitis patients.

1. Population (P): Patients with Periodontitis.

2. Intervention (I): Studies evaluating i-PRF as a bone graft material in periodontal wound healing.

3. Comparison (C): Growth factors other than i-PRF.

4. Outcome (O): Patient with clinical outcome at least 3 months follow up showing, clinical attachment level (CAL) gain, probing pocket depth (PD) reduction. Radiographic evaluation of

reduction in bone defect.

5. Study Design (S): Randomized controlled clinical trials

INFORMATION SOURCES:

The search engine for the relevant articles was started from the year of origin until February 2023. Studies to be included in this systematic review were identified through electronic search of the following databases: MEDLINE (NCBI, PubMed and PMC), Scopus, Cochrane, Central Register of Controlled Trials (CCRCT), ScienceDirect, Google Scholar, EMBASE, EBSCO. Web of Science and Hand search for various journals such as Journal of Indian Society of Periodontology, Journal of Periodontology, International Journal of Oral Health Sciences, Dentistry and Medical Research, Clinical Oral Implants Research. All the articles obtained through the electronic search were thoroughly screened. Also, the reference list of all articles was searched for any additional relevant publication. The author of this trial was contacted and a copy of the existing literature trial was obtained from him through email correspondence.

SEARCH:

The keywords which were used in various combinations in the search parameters are as follows:

1. "injectable PRF", "i-PRF"

2. "Intrabony defect," "bone defect," "bony defect," "furcation defect," "gingival recession,"

"ridge preservation," "ridge augmentation," "peri-implantitis," "adjunct to implant,".

3. "i-PRF in accelerating orthodontic tooth movement"

4. "Periodontal regeneration"

5. "Adjunct to scaling and root planning,"

6. "Maxillary," "maxilla," "mandibular," "mandible."

STUDY SELECTION

The study's inclusion criteria encompass several key factors. Firstly, the study focuses on patients who are systemically healthy non-smokers and are in need of periodontal regeneration. Secondly, the research exclusively includes in vivo human studies to ensure the relevance and applicability of the findings. Furthermore, the study restricts its scope to articles published in the English language, ensuring accessibility and consistency in the literature reviewed.

Additionally, the study encompasses patients with specific periodontal conditions, such as those with probing pocket depths of 5 mm or greater after Phase-I therapy. Patients with Furcation defects, which involve bone loss in the area between the roots of multi-rooted teeth, are also included. The study incorporates patients with intra-bony defects, encompassing 1-wall, 2-wall, and 3-wall defects, which are different types of bone loss configurations.

Moreover, patients with gingival recession, a condition characterized by the exposure of the tooth roots due to gum tissue loss, are considered in the study. Patients requiring ridge augmentation procedures, which involve enhancing the volume and contours of the alveolar ridge, are also included.

Lastly, the study mandates a minimum follow-up period of 3 months to ensure an adequate assessment of the treatment outcomes. This duration allows for an evaluation of the long-term effectiveness and stability of the periodontal regeneration interventions employed. By employing these inclusion criteria, the study aims to gather comprehensive and relevant data regarding periodontal regeneration in a specific patient population, excluded studies were animal studies and invitro studies.

TABLE – 1 STUDY CHARACTERISTICS

REFERENCE NO.	AUTHOR AND YEAR	YEAR	GEOGRAPHIC AREA	TYPE OF STUDY	Comparative Group	# iPRF Protocol	FOLLOW UP	PERIODONTAL REGENERATION	OUTCOME
35	Lydia N. Melek 2017	2017	Egypt	A randomized clinical trial	Group I (study group): Ridge augmentation was performed using Genesis bone graft combined with injectable platelet–rich fibrin Group II (control group): Ridge augmentation was performed using Genesis	700 RPM and 3 min	Baseline, 6 months	Ridge defect	Bone Gain

					bone graft only.				
31	izol Serhat İzol 2019	2019	Turkey	A randomized clinical trial.	control group- free gingival graft (FGG) Test group – i-PRF and FGG	700 RPM and 3 min	Baseline and 3months	Recession	Gain in recession
39	Onur Ucak Turer 2019	2019	Turkey	A randomized clinical trial	control group - free gingival graft (FGG) experiment group- free gingival graft and injected with I-PRF as a root surface biomodification agent (FGG+I-PRF).	700 RPM and 3 min	Baseline, 6 months	Recession	Gain in recession
40	Eldrida D'sa 2021	2021	India	A randomized clinical trial.	Group I: 18 intrabony defects were treated using Open flap debride	700 RPM and 3 min	Baseline, 3months, 6 months, 9 months	Intrabony defects	Gain in bone fill

					ment alone. Group II: 21 intrabony defects were treated using Open flap debridement + i-PRF (sticky bone). Group III: 18 intrabony defects were treated using Open flap debridement + autologous PRF				
41	Laxmikanta Patra 2022	2022	India	A randomized clinical trial.	control group-vestibular incision subperiosteal tunnel access test group-vestibular incision subperiosteal tunnel access using	700 RPM and 3 min	Baseline, 3months, 6months	Recession	Gain in recession

					collagen membrane with i-PRF				
42	Nair.P 2022	2022	India	A randomized clinical trial.	Control group- Open flap debridement with the nano-hydroxyapatite. Test group- Open flap debridement with sticky bone (i-PRF + nano-hydroxyapatite)	700 RPM and 3 min	Baseline, 3 months, 6 months and 9 months	Grade II furcation	Gain in bone fill
43	Jayasheela Mallappa 2022	2022	India	A randomized clinical trial.	Group A- APRF + i PRF + nHA Group B- nHA alone	700 RPM and 3 min	Baseline, 6 months	3 walled intrabony defect	Gain in bone fill
44	Ahmed Elbarbary 2022	2022	Egypt	A randomized clinical trial.	Test group- xenograft along with i-PRF. Control group- xenograf	700 RPM and 3 min	Baseline, 6 months	Stage III intrabony defect	Gain in bone fill

					t as bone fill				
45	MM Alshoiby 2023	2023	Egypt	A randomized clinical trial.	Test group- i-PRF+ deminera lized freeze-dried bone allograft. Control group-deminera lized freeze-dried bone allograft alone.	700 RPM and 3 min	Baseline, 3, 6 and 9 months follow up.	Stage III periodontitis .	Gain in bone fill

Outcome measure determination

The main objective of this study was to assess the regenerative or reparative potential of Injectable Platelet-Rich Fibrin (PRF) in various clinical applications within the field of dentistry. Different primary outcomes were considered depending on the specific clinical indication being investigated.

In studies focusing on intrabony defect regeneration, the primary outcomes measured were probing pocket depth (PPD) and clinical attachment levels (CAL). For studies addressing gingival recessions, the primary outcome was the calculation of root coverage as a percentage. Studies examining the use of PRF for furcation defect regeneration utilized CAL gains as the primary outcome measure. Lastly, in studies exploring bone regeneration, the primary outcomes were the dimensional changes and density of hard tissues, which were compared for evaluation.

By considering these different primary outcomes across various clinical indications, this study aimed to provide a comprehensive assessment of the regenerative and reparative effects of PRF in dentistry. Tables 1–4 for the various clinical studies accordingly.

Data extraction and analysis

The data extraction process involved gathering several key details from the selected studies. These included general characteristics such as authors and year of publication, as well as specific

REFERENCE NO.	Author Years	Study design, Duration	Number of participants, Drop outs	Comparison group	result	Summary
35	Lydia N. Melek 2017	A randomized clinical trial. Baseline, 6 months	14 Patients, 00 Patient drop out.	Group I (study group): Ridge augmentation was performed using Genesis bone graft combined with injectable platelet–rich fibrin Group II (control group): Ridge augmentation was performed using Genesis bone graft only.	Control group v/s Study group • Width of alveolar ridge; Baseline- 3.1±0.5 3.1±0.6 After 3 months- 6.7a ±0.6 5.2a ±0.8 After 6 months 4.5ab±0.6 6.0ab±0.5 • Density of bone Baseline- 1223.4±3.9 1247.5±157.4 After 3 months- 1300.6a ±4.2 1264.8a ±161.0 After 6 months 1353.1ab±4.0 1595.2ab±167.1 • Height of labial plate of bone Baseline- 10.0±0.5 13.8±0.8 After 3 months- 13.7a ±0.5 15.9a ±1.3 After 6 months 14.6ab±0.5 18.1ab±0.8	Favorable to test ($p<0.01$) Not significant ($p>0.05$) Favorable to test ($p<0.05$) Not significant ($p>0.05$)
31	Bozan Serhat İzol 2019	A randomized clinical trial. Baseline and 3months	40 Patients, 00 Patient drop out.	control group-free gingival graft (FGG) Test group – i-PRF and FGG	Control group v/s Test group Baseline 4.1±1.07 mm 4.7±1.49 mm After 3 months 3.5±1.05mm 3.9±0.78mm	Favorable to test ($p<0.01$) Not significant ($p>0.05$) Favorable to test ($p<0.05$)

						Not significant (p>0.05)
39	Onur Ucak Turer 2019	A randomized clinical trial. Baseline, 6 months	72 Patients, 07 Patient drop out.	control group - free gingival graft (FGG) experiment group- free gingival graft and injected with I-PRF as a root surface biomodification agent (FGG+I-PRF).	Control group v/s test group Mean root coverage- 83.16±18.48% 88.35 ± 15.64% Baseline – 4.1±1.07 mm 4.7±1.49 mm After 3 months- 3.9±0.78 mm 3.5±1.05 mm	Favorable to test (p<0.01) Not significant (p>0.05) Favorable to test (p<0.05) Not significant (p>0.05)
40	Eldrida D'sa et al 2021	A randomized clinical trial. Baseline, 3months, 6 months, 9 months	Seventeen participants with 57 intrabony defect sites. 00 Patient drop out.	Group I: 18 intrabony defects were treated using Open flap debridement alone. Group II: 21 intrabony defects were treated using Open flap debridement + i-PRF (sticky bone). Group III: 18 intrabony defects were treated using Open flap debridement + autologous PRF	Group I v/s Group II v/s Group III • Probing depth Baseline 7.94±2.21 mm v/s 7.90±1.84 mm v/s 8.83±1.86 mm After 3 months 7.06±1.92 mm v/s 5.29±1.74 mm v/s 5.56±1.34 mm • Relative attachment level. Baseline 5.72±2.42 mm v/s 5.86±1.98 mm v/s 6.00±1.88 mm After 3 months 4.22±1.96 mm v/s 2.29±1.01 mm v/s 3.06±1.11 mm • Bone fill percentage 15.96% ± 13.91%	Favorable to test (p<0.01) Not significant (p>0.05) Favorable to test (p<0.05) Not significant (p>0.05)

					63.39% ± 16.52% 56.46% ± 9.26%	
41	Laxmikanta Patra 2022	A randomized clinical trial. Baseline, 3months, 6 months	13 Patients, 00 Patient drop out.	control group-vestibular incision subperiosteal tunnel access test group-vestibular incision subperiosteal tunnel access using collagen membrane with i-PRF	Test group v/s control group • Plaque index Baseline 0.625 ± 0.151 0.625 ± 0.154 After 1 months 0.865 ± 0.134 0.835 ± 0.172 After 3 months 0.6 ± 0.133 0.545 ± 0.139 After 6 months 0.54 ± 0.127 0.56 ± 0.134 • Gingival index Baseline 0.625 ± 0.164 0.625 ± 0.65 After 1 month 0.89 ± 0.141 0.89 ± 0.18 After 3 months 0.545 ± 0.119 0.575 ± 0.155 After 6 months 0.51 ± 0.149 0.51 ± 0.137 • Probing depth Baseline 1.75 ± 0.444 mm 2.05 ± 0.6 mm After 1 month 2.65 ± 0.489 mm 2.8 ± 0.83 mm After 3 months 2.05 ± 0.489 mm	Favorable to test ($p<0.01$) Not significant ($p>0.05$) Favorable to test ($p<0.05$) Not significant ($p>0.05$)

					2.1 ± 0.3 mm After 6 months 1.75 ± 0.444 mm 1.95 ± 0.223 mm • Recession depth Baseline 2.7 ± 0.86 mm 2.9 ± 0.71 mm After 1 month 0.25 ± 0.4 mm 0.5 ± 0.51 mm After 3 months 0.5 ± 0.5 mm 0.95 ± 0.51 mm After 6 months 0.9 ± 0.64 mm 1.3 ± 0.57mm • Recession width Baseline 3.5 ± 0.6 mm 3.7 ± 0.73 mm After 1 month 0.5 ± 0.8 mm 1 ± 1.02 mm After 3 months 1 ± 1.02 mm 1.85 ± 0.85 mm After 6 months 1.65 ± 1.03 mm 2.55 ± 0.75 mm	
42	Nair.P et al 2022	A randomized clinical trial. Baseline, 3 months, 6 months and 9 months.	32 Patients. 02 Patients drop out.	Control group- Open flap debridement with the nano-hydroxyapatite.	Test group v/s control group • Vertical probing depth	Favorable to test ($p<0.01$) Not significant ($p>0.05$)

				Test group- Open flap debridement with sticky bone (i-PRF + nano-hydroxyapatite)	Baseline 3.50 ± 0.54mm v/s 3.33 ± 0.81mm After 3 months 3.16 ± 0.75mm v/s 3.00 ± 1.09mm After 6 months 1.16 ±0.40mm v/s 2.50 ±0.83mm • Clinical attachment level Baseline 5.16±0.75mm v/s 3.83±1.83mm After 3 months 3.16±0.98mm v/s 3.16±1.32mm After 6 months 1.00±0.00mm v/s 2.33±0.81mm • Bone fill Baseline 2.91±0.88mmv/s 3.40±1.39mm After 9 months 5.68±1.10mm v/s 3.98±1.40mm	Favorable to test ($p<0.05$) Not significant ($p>0.05$)
43	Jayasheela Mallappa et al 2022	A randomized clinical trial. Baseline and 6 months	28 sites from 20 chronic periodontitis patients. 00 Patient drop out.	Group A- APRF + i PRF + nHA Group B- nHA alone	Group A v/s Group B • Probing pocket depth Baseline 7.1 ± 1.38 v/s 6.5 ± 0.74	Favorable to test ($p<0.01$) Not significant ($p>0.05$) Favorable to test ($p<0.05$)

					At 6 months 3.6 ± 0.74 v/s 4.3 ± 0.82 • Relative attachment level Baseline 9.8±1.72mm v/s 10±1.93mm At 6 months 6.5±1.34mm v/s 7.9±2.10mm • Bone fill Baseline 8.3±1.19mm v/s 8.4±1.46 At 6 months 5.0±0.85mm v/s 6.2±1.34mm	Not significant (p>0.05)
44	Ahmed Elbarbary et al 2022	A randomized clinical trial. Baseline and 6 months	24 Patients. 00 patient Drop out.	Test group-xenograft along with i-PRF. Control group-xenograft as bone fill	Test group v/s control • Probing depth Baseline 6.6 ±1.1 v/s 7.8±1.8 At 6 months 2.4 ±0.9 v/s 4.5±1.4 • Clinical attachment level Baseline 6.8±1.1 v/s 8±2 At 6 months 3.0±0.8 v/s 5.1±1.9	Favorable to test (p<0.01) Not significant (p>0.05) Favorable to test (p<0.05) Not significant (p>0.05)

					• bone defect Baseline 8.5 ± 0.9 v/s 9±0.7 At 6 months 5.9±1.2 v/s 7±1.4	
45	MM Alshoiby 2023	A randomized controlled clinical trial. Baseline, 3, 6 and 9 months follow up.	20 sites in 20 patients. 00 patient drop out.	Test group- i-PRF+ demineralized freeze-dried bone allograft. Control group- demineralized freeze-dried bone allograft alone.	Test group v/s control group. • Probing pocket depth Baseline 6.70±0.95 6.50±1.08 At 3 months 4.20±0.42a 4.10±0.57a At 6 months 3.80±0.79b 3.80±0.79b At 9 months 3.20±0.63a 3.70±1.16c • Clinical attachment level Baseline 5.80±0.92 6.50±2.32 At 3 months 3.60±0.97 4.00±1.41 At 6 months 3.30±0.67 3.80±1.55	Favorable to test ($p<0.01$) Not significant ($p>0.05$) Favorable to test ($p<0.05$) Not significant ($p>0.05$)

					At 9 months 3.40±0.97 4.00±2.26 • Bone fill percentage At 6months 27.83±12.67 25.52±9.42 At 9 months 41.64±10.43 41.35±10.64	

information related to the defect type, number of patients, healing period, treatment groups, primary outcome measurements, and significant values.

Considering the extensive scope of the study and the numerous treatment procedures involving injectable Platelet-Rich Fibrin (PRF) that were compared, a meta-analysis was not conducted due to feasibility constraints. Instead, a systematic approach was adopted to present the data, providing an organized overview of all studies that fulfilled the search criteria.

Subsequently, data was meticulously extracted from the collection of articles and presented in separate tables to facilitate analysis and comparison. The findings were then discussed in accordance with the extracted data, enabling a comprehensive understanding of the outcomes across the included studies. By employing this structured approach, the study ensured a thorough examination of the relevant information, allowing for a detailed exploration of the findings and their implications in a clear and organized manner.

RESULTS

SEARCH AND SELECTION RESULTS

Out of 1177 studies searched, only nine studies met the inclusion criteria with a quality assessment tool, which were published in the English language. Search was done through electronic databases MEDLINE (NCBI, PubMed and PMC), Scopus, Cochrane, Central Register of Controlled Trials (CCRCT), ScienceDirect, Google Scholar, EMBASE, EBSCO. with the help of several keywords such as i-PRF, periodontal defects, intra bony defects, furcation defect, gingival recession, Chronic Periodontitis. Web of Science and Hand search for various journals such as Journal of Indian Society of Periodontology, Journal of Periodontology, International Journal of Oral Health Sciences, Dentistry and Medical Research, Clinical Oral Implants Research was also carried out.

TABLE -2 RESULTS

Nine randomized clinical trials were conducted, with patient numbers ranging from 14 to 72 and participants' mean age ranging from 25 to 55 years. Three studies utilized standardized periapical radiographs and clinical parameters for evaluation.

Lydia N et al. (2017)[35] studied 14 patients with ridge defects, randomly assigning them to two groups. Ridge augmentation using Genesis bone graft combined with injectable platelet-rich fibrin was performed in the study group, while the control group received Genesis bone graft alone. Radiographic parameters were assessed at baseline and after 6 months. İzol BS et al. (2019) [31]divided 40 patients with gingival recession into two groups. The control group received free gingival graft (FGG), while the test group received a combination of i-PRF and FGG. Root coverage was assessed at baseline and after 3 months.

Ucak Turer O et al. (2019) [39]assessed PD, CAL, RW, RD, and CRC in 72 patients with gingival recession. The control group received FGG, and the experimental group received FGG with injected i-PRF as a biomodification agent. Assessments were conducted at baseline and after 6 months. Eldrida D'sa et al. (2021)[40] examined 17 patients with intrabony defects, dividing them into three treatment groups. Open flap debridement alone, open flap debridement with i-PRF (sticky bone), or open flap debridement with autologous PRF were performed. Clinical parameters and radiographic bone fill were assessed at multiple time points.

Patra L et al. (2022) [41]evaluated 13 patients with chronic periodontitis, dividing them into control and test groups. Different procedures were performed, with the test group receiving additional collagen membrane and i-PRF. Clinical parameters were assessed at baseline, 3 months, and 6 months. Nair UP et al. (2022) [42]examined 32 patients with furcation defects, dividing them into control and test groups. Open flap debridement with nano-hydroxyapatite or sticky bone (i-PRF + nano-hydroxyapatite) was performed. Clinical parameters and bone area fill were recorded at multiple time points.

Mallappa.J (2022)[43] evaluated 20 patients with intrabony defects and chronic periodontitis. Group A received a combination of APRF, i-PRF, and nano-hydroxyapatite, while Group B received nano-hydroxyapatite alone. Clinical parameters and radiographic defect fill were assessed at baseline and after 6 months. Elbarbary.A (2022) [44]studied 24 patients with chronic periodontitis, dividing them into a test and control group. The test group received xenograft with i-PRF, while the control group received xenograft alone. Probing depth, clinical attachment level, bone defect depth, and bone density were assessed at baseline and after 6 months. MM Alshoiby (2023) [45]evaluated 20 patients divided into test and control groups. The test group received i-PRF and demineralized freeze-dried bone allograft, while the control group received only the allograft. Probing pocket depth, clinical attachment level, and bone area fill were assessed using clinical measurements and radiographs at multiple time points.

DISCUSSION

Injectable platelet-rich fibrin (I-PRF) is an advanced form of PRF that differs from traditional PRF by omitting the formation of a PRF membrane and utilizing a slower liquid-based centrifugation process. I-PRF is injected into affected soft tissues, mucous membranes, or skin, making it a promising treatment option for tissue regeneration.

In this systematic review, randomized clinical studies exploring the use of PRF in dentistry were examined. The focus was on evaluating the current literature regarding the clinical applications of i-PRF in wound healing, tissue regeneration, and repair. The analysis compared the efficacy of i-PRF to conventional treatments such as open flap debridement (OFD) for intrabony and furcation defects, as well as other bone grafts commonly used in these procedures.

Lydia N's study (2017) [35]assessed the efficacy of i-PRF combined with bone graft in treating ridge defects. It found that i-PRF regulates proinflammatory cytokines, MMPs, and MMP inhibitors during early wound healing, leading to favorable wound healing processes. Histological analysis showed good integration of the epithelial layer with the recipient sites when i-PRF was used. Guiha et al. (2001) demonstrated that the group treated with i-PRF and connective tissue grafts had deeper rete pegs compared to the group treated with connective tissue grafts alone at the 6-month biopsy.

The presence of well-developed rete pegs in the keratinized epithelial layer provides mechanical resistance to external irritation. The test group in the current study exhibited increased keratinized tissue height and greater reduction in recession depth, which can be attributed to the improved resistance and rapid angiogenesis facilitated by i-PRF, leading to enhanced tissue proliferation and healing at the surgical site.

İzol BS (2019) [31] and Ucak Turer O (2019)[39] utilized i-PRF in conjunction with free gingival grafts for treating recession defects. Eldrida D'sa (2021) [40] employed i-PRF as a sticky bone during open flap debridement for managing intrabony defects. Patra L et al. (2022) [41]utilized i-PRF along with vestibular incision subperiosteal tunnel access (VISTA) and collagen membrane for managing recession defects.

Nair UP et al. (2022) [42]performed phase I therapy followed by open flap debridement using i-PRF for removing diseased tissue. They utilized a combination of nano-hydroxyapatite bone graft mixed with i-PRF for the treatment. Mallappa.J (2022) [43]combined i-PRF with A-PRF and nHA to create a PRF block for intrabony defect treatment. Elbarbary.A (2022) [44]packed i-PRF along with xenograft into intrabony defects. MM Alshoiby (2023) [45]used i-PRF along with demineralized freeze-dried bone allograft. Importantly, none of these studies reported any adverse effects associated with i-PRF. This systematic review is aimed to find the efficacy of i-PRF as compared to other growth factor in the periodontal wound healing, which includes intrabony defect, gingival recession, furcation, ridge defects and many more.

In various studies, i-PRF was compared to different treatments in dental procedures. Lydia N (2017) [35] compared i-PRF with Genesis bone graft in ridge augmentation and found significant

improvements in alveolar bone width and density. İzol BS 2019 [31] and Ucak Turer O 2019 [39]compared i-PRF with free gingival graft in managing gingival recession. Eldrida D'sa 2021 [40]used open flap debridement alone as one control group, while another group received open flap debridement with A-PRF in treating intrabony defects. Nair UP et al 2022 [42]used open flap debridement with nano-hydroxyapatite as a control group in furcation defect management. Mallappa.J 2022 [43]used nano-hydroxyapatite, Elbarbary.A 2022 [44] used xenograft, and MM Alshoiby 2023 [45] used demineralized freeze-dried bone allograft as control groups in treating intrabony defects. The studies showed varying effects of i-PRF on alveolar ridge width, bone density, and height. In vitro studies have shown the potential of i-PRF in promoting bone regeneration. Combining i-PRF with stem cells and other growth factors can enhance bone regeneration. The time-dependent flowability of i-PRF allows it to easily fill defects and maintain its shape. Combining i-PRF with other biomaterials can further enhance its resistance against forces. Lyophilization has been proposed as a method to overcome the time limitation of PRF application.

In some cases, it may not be necessary to obtain blood during each visit for the preparation of I-PRF. By using freeze-dried I-PRF, blood can be collected once and stored for future use, making regenerative therapies more convenient, especially for children. Autologous platelet concentrates, rich in growth factors, are highly beneficial in regenerative procedures. However, certain conditions such as bleeding disorders, sepsis, and trauma can hinder the use of patient blood. In such cases, exploring mechanisms like decellularization can facilitate the use of allogeneic or xenogeneic applications of I-PRF. Decellularized tissues have reduced immunogenicity and retain essential protein structures and growth factors.

The results of the studies showed significant differences in alveolar bone width and density between the control and study groups. The use of injectable PRF with its high growth factor content contributed to more favorable and predictable bone formation at the grafted site. However, there was no significant difference in the height of the labial plate of bone between the two groups.

İzol BS 2019 [31]evaluated recession coverage and found a significant difference in root surface coverage between the FGG+I-PRF group and the control group. Ucak Turer O 2019[39] assessed various parameters and observed that the addition of I-PRF to the treatment showed improvements in increasing keratinized tissue height and decreasing recession depth.

Eldrida D'sa 2021 [40] examined plaque index, gingival index, probing pocket depth, relative attachment level, and bone fill. The PRF and PRF+HA groups showed significantly greater mean bone fill compared to the control group. Additionally, the PRF+HA group exhibited a higher percentage of bone fill compared to the PRF group. There were no significant differences in probing pocket depth between different groups at 3 months.

These findings demonstrate the positive effects of I-PRF in various regenerative procedures, including recession coverage, root coverage, and bone fill.

The mean defect depth reduction scores showed that Group II had a higher reduction compared to Group I and Group III. There was a significant difference between the groups at the 9-month period. Group II and Group III showed better results in all parameters compared to Group I. The defect depth reduction at 9 months was 41.59% for OFD, 72.75% for i-PRF, and 62.11% for PRF.

Patra L et al 2022 [41] assessed various parameters and found that the test group showed significant reduction in recession depth compared to the control group at 3 and 6 months. The test group also exhibited higher root coverage percentages at different time points compared to the control group. The minimally invasive VISTA technique, collagen membrane, and injectable form of platelet-rich fibrin were effective in treating gingival recessions.

Nair UP et al 2022 [42]evaluated different parameters and observed significant improvement in clinical parameters and radiographic bone fill in both groups. The test group, where i-PRF with a nano-HA bone graft was used, showed better results compared to the control group in terms of bone area fill.

Mallappa.J 2022 [43]assessed various parameters and found that the test group had significantly higher reduction in probing pocket depth and greater gain in relative attachment level compared to the control group at 6 months. The test group also demonstrated higher bone volume gain compared to the control group.

Elbarbary.A 2022 [44]and MM Alshoiby 2023 [45]assessed similar parameters and both studies showed significant reduction in probing depth, gain in clinical attachment level, and improvement in bone density in each group separately. The test group showed better results compared to the control group in terms of probing depth reduction and clinical attachment level gain.

Overall, these studies indicate the positive effects of i-PRF in various clinical parameters related to periodontal and bone regeneration

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