Short Communication

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Effectiveness of injectable platelet-rich fibrin in conjunction with scaling and root planing as local drug delivery in the treatment of periodontitis

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ABSTRACT

Periodontitis is a multifactorial disease, characterized by the progressive destruction of periodontal supporting tissues, resulting in periodontal pocket formation. Scaling and root planing (SRP) is not frequently resolute at repairing disease-related defects. To enhance the regeneration, adjunctive therapeutic procedures have been added to conventional therapy. Platelets are important reservoirs of various GFs and cytokines, which are vital in wound repair and homeostasis. Therefore, this study aimed to assess the effectiveness injectable formulation of platelet rich fibrin (I-PRF) enables easier use of the platelet concentrate in a liquid state. A total of 20 periodontitis subjects were selected and divided using a split-mouth study design into control site: SRP alone and test site: SRP + I-PRF injection. Clinical parameters like-gingival index (GI), plaque index (PI), bleeding on probing (BOP), clinical attachment loss (CAL), pocket probing depth (PPD) were evaluated at baseline and 6 weeks. Statistically significant reduction in the clinical parameters observed in both the sites. But comparatively, test site showed more reduction in clinical parameters with gain in CAL when compared to control site. I-PRF when used along with SRP show therapeutic benefit in periodontal regeneration.

Keywords: Periodontitis, Injectable formulation of platelet rich fibrin, Non-surgical periodontal therapy

INTRODUCTION

Chronic periodontitis (CP) is a multifactorial disease, characterized by the progressive destruction of periodontal supporting tissues presents as an inflammation developed by disorders of the host immune response to the infections and characterized by loss of soft tissue attachment and alveolar bone resorption caused by pathogenic microorganisms resulting in pocket formation and or gingival recession which provides a favourable environment for the growth of pathogenic anaerobic microorganisms.¹

According to the global burden of disease study (GBD-2015), the total number of people affected by oral

diseases has increased from 2.5 billion in 1990 to 3.5 billion in 2015, with a rise in disability-adjusted life year by 64%.² Periodontitis is the sixth ubiquitous chronic disease affecting more than 743 million people worldwide, having undesirable impact on oral functions, self-confidence, systemic health and overall well-being of an individual. Due to its high prevalence, it is essential to constantly upgrade periodontal therapy.³

The primary goal of periodontal therapy is to control active inflammation associated with the disease and, where possible, to support the regeneration of periodontal tissue defects. Initial periodontal therapy, such as SRP, is often insufficient to fully repair disease-related periodontal defects. Periodontal wound healing

following SRP typically results in the formation of a long junctional epithelium, which is prone to breakdown and contributes to the frequent recurrence of periodontal pockets.⁷

In periodontal therapy, adjunctive therapeutic procedures like local drug delivery (LDD) has been added to conventional therapy for over three decades to enhance the process of regeneration for the treatment of localized periodontal pockets, demonstrating improvements in clinical and microbiological parameters comparable to those achieved with adjunctive systemic antibiotic.^{8,9} Platelets have revolutionized regenerative dentistry. Their ability to deliver a high concentration of growth factors (GFs) when applied locally makes them powerful tools in promoting healing of soft and hard tissue regeneration. Platelets are important reservoirs of various GFs and cytokines, which are vital in wound repair and homeostasis.⁷

The periodontal wound healing process involves a series of cell-to-cell interactions and molecular signals, primarily mediated by cytokines and GFs. These GFs play a crucial role in enhancing collagen production, promoting cell proliferation and differentiation, and stimulating the formation of new blood vessels.⁹

Platelet concentrates have evolved from the first generation, platelet-rich plasma (PRP), to the second generation, platelet-rich fibrin. PRF, developed by Choukroun et al is a fibrin matrix rich in platelets, leukocytes, and GFs, which promotes wound healing and tissue regeneration in a more sustained and natural means compared to PRP and enables a scaffold enriched with platelets and GFs, as well as leukocytes. The concentrate is generated from a blood harvest without any artificial biochemical modifications and anticoagulants. ¹⁰

Previous research has demonstrated that PRF contains a higher concentration of GFs compared to Platelet-Rich Plasma. PRF has been shown to induce greater fibroblast migration and enhance the expression of key GFs, including transforming growth factor- β 1 (TGF- β 1), platelet-derived growth factor (PDGF), and vascular endothelial growth factor (VEGF). These factors play critical roles in promoting tissue regeneration by stimulating cell proliferation, angiogenesis, and extracellular matrix remodeling, thereby contributing to improved wound healing and periodontal regeneration. ¹¹

Along with TGF- β 1, PDGF, and VEGF, PRF also exhibits higher concentrations of other key GFs such as fibroblast growth factor (FGF), insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), and platelet-derived epidermal growth factor (PDEGF). The synergistic presence of these bioactive molecules creates a biologically favorable environment that promotes tissue regeneration, cellular proliferation, angiogenesis, and wound healing. Consequently, PRF has become a widely accepted adjunct in various regenerative procedures,

including the surgical treatment of periodontal intrabony defects, furcation defect management, sinus lift procedures, and applications in tissue engineering.¹²

Since the standard form of platelet-rich fibrin is not ideal for injection due to its gel-like consistency, a injectable formulation known as I-PRF has been developed. I-PRF allows for the application of platelet concentrates in a liquid form, enabling easier handling and more versatile clinical use, especially in minimally invasive procedures. It is obtained through a low-speed centrifugation protocol and retains its liquid viscosity for approximately 15 minutes post-centrifugation, during which it can be effectively delivered to targeted sites before polymerizing into a fibrin matrix. 13,14

Initially, PRF was developed using high-speed centrifugation protocols, resulting in the formation of a fibrin clot. This clot serves as three-dimensional scaffold capable of supporting cell migration, proliferation, and differentiation, thereby promoting periodontal regeneration. The structural integrity of the fibrin matrix facilitates sustained release of GFs and provides a conducive environment for tissue repair and healing.¹⁵

The aim of this study was to determine the effects of local I-PRF application in conjunction with SRP, compared to SRP alone, on periodontal clinical parameters of CP.

METHODS

Type of study

It was a comparative study.

Study design

A total of 20 subjects; with randomized, split-mouth, controlled clinical trial recruited patients with CP aged between 30-55 years, were selected. Keeping alpha error at 5%, β error 20%, power of the study at 90%, the sample size estimated was approximately 15. For follow-up study, to avoid loss due to attrition taking 20 subjects were taken. Ethical approval was taken from the institutional ethical committee for the study.

The study was carried out on 20 patients using a split-mouth study design. Control site was SRP alone and test sites-SRP + I-PRF injection.

Each patient underwent full-mouth SRP with ultrasonic instruments. Patients with ≥5 mm periodontal pocket received I-PRF injections on test site. I-PRF was injected into periodontal pocket by using insulin syringes. Patients were recalled after 6 weeks for follow up.

Inclusion criteria

Systemically healthy subjects who are willing to participate in the study and given written consent for the

same. Subjects aged 30-55 years, both males and females who are diagnosed with CP with minimum of six teeth per quadrant; a minimum of two teeth in each quadrant with a probing depth ≥ 5 mm, BOP had to be at $\geq 40\%$ tooth sites and no involvement of furcation; good general health were included in the study.

Exclusion criteria

Subjects with systemic diseases that could influence periodontal conditions and who have undergone periodontal therapy in the past 6 months, subjects on any systemic antibiotics, anti-inflammatory, hormonal therapy or corticosteroid therapy for any other reasons which affect the periodontal status and subjects consuming tobacco in any form and pregnant and lactating women were excluded from the study.

Method of preparation of I-PRF

I-PRF was prepared by the same operator according to the protocol developed by Miron and Choukroun. 11,13 It involves collecting 5 ml of IV blood from participant using venipuncture of antecubital vein under sterile conditions. Collected blood transferred to plain sterile test tube without anticoagulant and immediately subjected to centrifugation (REMI R-8C) at 70-g force at 700 RPM for 3 min at room temperature. After centrifugation, blood separates into 2 parts: bottom layer consists of a red blood cell compartment, and the top layer is PRF plasma, which will be still in liquid consistency. Top I- PRF layer was aspirated into a 1-ml insulin syringe and maintained in liquid consistency for about 3-5 min and injected into the periodontal pocket until periodontal pocket gets filled and overflowed before it becomes a gel (Figure 1).

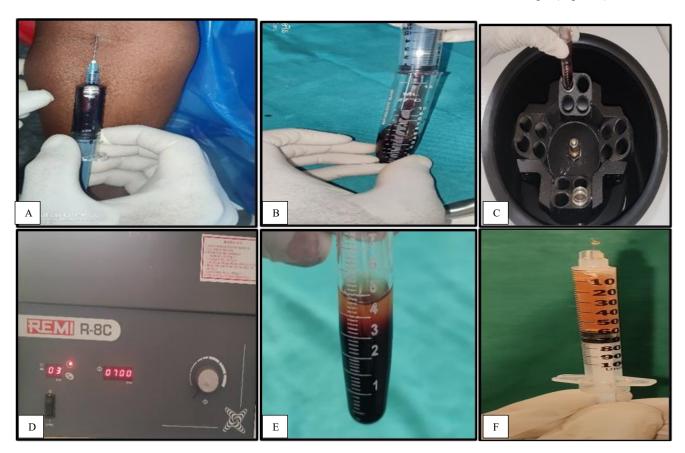


Figure 1 (A-F): A-Collecting 5 ml IV blood by venipuncture of antecubital vein under sterile conditions. B-Collected blood is transferred to a plain sterile test tube without anticoagulant. C-Immediately subjected to centrifugation. D-AT 700 rpm for 3 minutes. E-Top I-PRF layer. F-I-PRF loaded in insulin syringe.

There was no prescription for mouthwash or medications for any of the subjects, and subjects were asked to report after 6 weeks for follow-up.

Clinical examination to assess the periodontal condition

Clinical examination was performed on all the subjects using-GI (Loe and Silness), PI (Silness and Loe), BOP (Muhlemann and Son), CAL and PPD.

Statistical analysis

The data collected was analysed using Descriptive statistics with frequency, percentage, mean SD etc, Kolmogorov Smirnov test for normality, independent t test or Mann-Whitney U test for inter comparison of two groups, dependent t test or Wilcoxon matched pairs test for intra group comparison. A significance was set at 5% level of significance (p<0.05). All the participants were

clearly explained regarding need and design of study. A duly signed written informed consent was obtained from all subjects willing to participate in study.

RESULTS

The results of our study showed statistically significant reduction in the clinical parameters observed in both the sites. But comparatively, test site showed more reduction in clinical parameters with gain in CAL when compared to control site. There was no dropouts noted during the follow-up period. The comparison of GI score showed mean difference of 0.62 in control site at from baseline to 6 weeks and test site showed mean difference of 0.81 from baseline to 6 weeks (Table 1). PI score showed

mean difference of 0.43 in control site at from baseline to 6 weeks and test site showed mean difference of 0.77 from baseline to 6 weeks (Table 2). BOP score showed mean difference of 0.61 in control site at from baseline to 6 weeks and test site showed mean difference of 0.73 from baseline to 6 weeks (Table 3). PPD score showed mean difference of 2.45 in control site at from baseline to 6 weeks and test site showed mean difference of 6.20 from baseline to 6 weeks (Table 4). CAL score showed mean difference of 4.15 in control site at from baseline to 6 weeks and test site showed mean difference of 7.80 from baseline to 6 weeks (Table 5). No adverse reactions were observed during the study period for any of the interventions and none of the participants reported any discomfort with the treatment protocol.

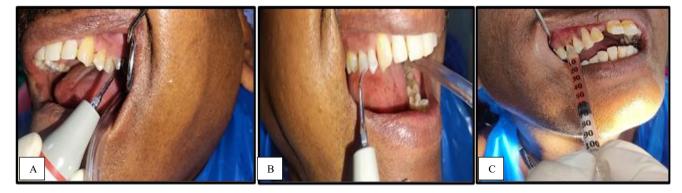


Figure 2 (A-C): LDD of I-PRF. A-Control site-SRP alone, B and C-test site-SRP along with I-PRF injection.

Table 1: Comparison of control site and test site with GI scores at baseline and 6 weeks treatment time points by Mann-Whitney U test.

Time points	Control site			Test site			7 volus	P value
	Mean	SD	Mean rank	Mean	SD	Mean rank	Z value	r value
Baseline	1.18	0.36	20.60	1.18	0.33	20.40	0.0406	0.9676
6 weeks	0.56	0.22	25.20	0.37	0.20	15.80	2.5292	0.0114*
Difference	0.62	0.31	17.50	0.81	0.39	23.50	-1.6095	0.1075

^{*}p<0.05 significant.

Table 2: Comparison of control site and test site with PI scores at baseline and 6 weeks treatment time points by Mann-Whitney U test.

Timo nointa	Control site			Test site			7 volvo	Dyalua
Time points	Mean	SD	Mean rank	Mean	SD	Mean rank	Z value	P value
Baseline	1.06	0.20	20.40	1.07	0.20	20.60	-0.0406	0.9676
6 weeks	0.64	0.19	28.40	0.30	0.17	12.60	4.2604	0.0001*
Difference	0.43	0.17	13.88	0.77	0.30	27.13	-3.5706	0.0004*

^{*}p<0.05 significant.

Table 3: Comparison of control site and test site with BOP scores at baseline and 6 weeks treatment time points by independent t test.

Time points	Control site		Test site		Tyalya	Davalus
	Mean	SD	Mean	SD	T value	P value
Baseline	0.98	0.34	1.08	0.32	-0.9599	0.3432
6 weeks	0.38	0.13	0.35	0.26	0.3868	0.7011
Difference	0.61	0.37	0.73	0.41	-1.0232	0.3127

^{*}p<0.05 significant.

Table 4: Comparison of control site and test site with PPD scores at baseline and 6 weeks treatment time points by independent t test.

Time points	Control site		Test site		T value	P value
	Mean	SD	Mean	SD	1 value	r value
Baseline	10.85	2.35	10.90	2.10	-0.0710	0.9438
6 weeks	8.40	1.70	4.70	1.69	6.9084	0.0001*
Difference	2.45	1.36	6.20	2.48	-5.9263	0.0001*

^{*}p<0.05 significant.

Table 5: Comparison of control site and test site with CAL scores at baseline and 6 weeks treatment time points by independent t test.

Time points	Control sit	Control site			Taralica	Davalua
	Mean	SD	Mean	SD	T value	P value
Baseline	17.35	3.79	17.35	3.38	0.0000	1.0000
6 weeks	13.20	2.80	9.55	2.72	4.1771	0.0002*
Difference	4.15	1.66	7.80	2.44	-5.5266	0.0001*

^{*}p<0.05 significant.

DISCUSSION

The adjunctive use of LDD with SRP in periodontal pocket therapy has been extensively documented in the literature, with most evidence supporting its additional beneficial effects. 16 The rationale for employing I-PRF as a LDD vehicle for pocket therapy in the present study was based on its mesh-like fibrin architecture, which facilitates the sustained release of entrapped GFs at periodontal wound sites, with extensive biological activities. 17,18 This randomized clinical trial, employing a split-mouth design, compared the effects of SRP combined with I-PRF versus SRP alone on clinical periodontal outcomes during the initial treatment phase of CP. The results demonstrated that both treatment statistically modalities produced significant improvements in all evaluated clinical parameters six weeks after therapy initiation. At baseline, no significant differences in PPD and CAL were observed between the two groups. All participants received oral hygiene instructions and were encouraged to maintain regular home care, which may have contributed to the improvement in clinical parameters observed in both groups during the study period. Over the years, conventional periodontal therapy (SRP) has been augmented with various adjunctive approaches, most commonly through the systemic or local administration of antibiotics and antiseptics. Given the potential risks associated with their use, antibiotics and antiseptics should be prescribed only in specific cases and under optimal conditions. Although the nonsurgical application of lasers in the initial treatment of CP has gained attention in recent years, some studies suggest that their effects on PPD and CAL reduction are less pronounced than those achieved with antibiotics.19

Our research focuses on adjunctive regenerative approaches for the treatment of CP. Although a liquid, I-PRF was introduced by Choukroun et al only the fibrin membrane form of PRF has been utilized in the surgical

management of CP.10 In this study, we explored, for the first time, the application of I-PRF as a nonsurgical treatment modality for CP. Its liquid consistency offers a distinct advantage for direct application into periodontal pockets. A study by Milasin et al in their study, initial periodontal therapy combined with I-PRF resulted in significantly greater improvements in all clinical parameters like PPD and CAL compared to initial periodontal therapy alone.²⁰ The process is enabled due to the fact that after a short period of time, approximately 15 minutes, I-PRF is formed into a matrix scaffold. The scaffold has been shown to directly enhance the migration and proliferation of human gingival fibroblasts, stimulate the release of additional GFs, promote periodontal ligament cell growth, and increase osteoblast differentiation. By preventing the apical migration of junctional epithelium onto root surfaces and limiting its interference between the root and surrounding soft tissues, the scaffold facilitates the formation of new attachment on root surfaces.²¹ Dohan et al reported that PRF exhibits immunological and antibacterial properties through leukocyte degranulation and contains cytokines capable of inducing angiogenesis as well as modulating pro- and anti-inflammatory responses.²² The resulting reduction in microbial load contributes to diminished inflammation, which in turn leads to decreases in PPD, GML, and BOP values. Another study done by, Al-Rihaymee et al evaluated for platelet-rich fibrin as an adjunct to SRP, there was a significant reduction in clinical parameter like PPD with gain in CAL at 1- and 3month follow-up visits.²³

From the above observations, the use of I-PRF as an LDD system resulted in a significant reduction in all the clinical parameters like GI, PI, BOP, PPD with gain in the CAL in the test site comparative to control site with p<0.05. Thus, within the limits of this study, it can be concluded that I-PRF could be considered a potential LDD in periodontal pocket therapy.

CONCLUSION

Despite the limited sample size, the present study demonstrated that local application of I-PRF in conjunction with SRP, compared to SRP alone, significantly improved periodontal clinical parameters in the treatment of CP.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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