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Assessment of effectiveness of platelet rich fibrin in comparison to open flap debridement in the treatment of three walled intrabony defects in stage II and stage III periodontitis: A clinical study

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ABSTRACT

Background: Platelet Rich Fibrin, (PRF) a new generation Platelet concentrate, provisioned with simplified preparation and agglomeration of various growth factors has been used for regeneration of periodontal intrabony defects. The goal of this study was to evaluate and compare the effectiveness of Platelet Rich Fibrin with Open Flap Debridement (OFD) in the treatment of three walled bony defects in stage II and stage III Periodontitis. *Method*: In a split-mouth study design, fifty interproximal intrabony defects in 25 healthy patients diagnosed with Stage II and Stage III Periodontitis were randomly assigned to Open Flap Debridement group (Group I) or Platelet Rich Fibrin group along with Open Flap Debridement (Group II). Clinical pocket depth (PD), clinical attachment level (CAL) and radiographic (bone fill) measurements were made at baseline and at a 9 -month evaluation. *Results*: At 9 months postoperatively, upon comparing the PD reduction, defect depth reduction, and clinical attachment level gains, it was noted that group II showed statistically-significant improvements compared with group I in PD (3.62 ± 0.52 vs 5.30 ± 0.86 mm) CAL Gain (4.30 ± 0.87 vs 3.12 ± 0.29 mm), bone fill (5.12 ± 0.54 vs 8.96 ± 0.99mm). *Conclusion*: The results of this study indicate that PRF in comparison to OFD improve clinical and Radiographic Parameters associated with treatment of 3 walled intrabony Periodontal Defects.

Keywords: Regeneration, Intrabony defects, Platelet Rich Fibrin, Open Flap Debridement.

1. INTRODUCTION

Periodontitis, a long-lasting multifactorial inflammatory disease (Bueno et al., 2015) associated with dysbiotic dental biofilm is characterized by destruction of the tooth supporting tissues (Pihlstrom, 2001). Intrabony defects, a specific osseous defect with definite morphology portray the apical spread of plaque in the course of periodontitis (Waerhaug, 1979), and if left untreated, are at an elevated risk for disease progression (Papapanou & Wennstrom, 1991).

The purpose of conventional clinical therapy for Periodontitis is to eradicate infectious sources, and reduce inflammation to arrest disease progression, but the regeneration of lost periodontal tissues is curtailed. Regeneration, a complex biological process entails the replacement of tissues lost to disease or injury with physiologically identical engineered tissues (Giannobile, 1996). In recent decades, a plethora of clinical protocols have been suggested to regenerate the periodontal tissues and restore interproximal intrabony defects. These include the use of various surgical techniques in conjunction with different types of bone grafts, barrier techniques, growth factors, enamel matrix derivative (Cortellini & Tonetti, 2000; Hiatt, 1973). Current regenerative therapies own little potential in attaining complete periodontal restoration (Greenwell, 2001; Sander & Karring, 1995). Consequently the quest on devising an autologous bioactive material that is most effective in its regenerative potential had been escalating.

The Choukroun's Platelet-rich fibrin (PRF) is one such product that has proved its worth interms of accelerated wound healing and regeneration (Gupta et al., 2011). PRF, a second generation platelet concentrate, encompassing a tetra molecular framework (Choukroun et al., 2006) is an immune and platelet concentrate collected on a single fibrin membrane having a synergistic effect on healing and immunity (Mosesson et al., 2001) there upon, culminating this biomaterial to be a favourable matrix for the development of coherent healing, without any inflammatory excess. Concerning specific procedures with regards to dentistry, PRF possess broad applicability and has manifested reassuring results when used in combination with bone grafts to hasten the healing process, ridge augmentation procedures, socket preservation, root coverage procedures, regeneration of intrabony defects, furcation defects, and palatal wound healing after free gingival grafts (Choukroun et al., 2006), to treat gingival fenestrations along with coronally positioned flap (Pradeep et al., 2012) in the management of complicated oral wounds (Deepa & Jain, 2015) and as suitable scaffold for bone tissue engineering applications (Jain et al., 2012).

PRF induces a significant and continuous stimulation and proliferation of various cells in vitro with the strongest induction effect on osteoblasts (Gassling et al., 2010). Appraising the soft tissue and hard tissue healing potential of PRF in various procedures, the present study selected PRF for the therapy of IBDs. So far research conducted to evaluate the periodontal intrabony defect regenerative capacity of autologous PRF has been few. Therefore, this study focuses to explore the additional efficacy of autologous PRF with OFD in the treatment of 3-wall IBDs compared to OFD alone

2. MATERIALS AND METHODS

This was a double-blind non randomized clinical trial, was carried out at the Department of Periodontics, Rural Dental College, Loni from 16/01/2019 to 30/12/2020. This was a 9 months follow up study and the recordings were done at start and at 9 months. After ethical approval (Pravara Institute of Medical Sciences, PIMS/IEC-DR/2019/14) all participants were verbally informed and written assent was collected for participation in the study.

Patient selection

Patients were classified as having stage II and stage III Periodontitis, on the basis of the 2017 consensus classification of periodontal diseases (Papapanou et al., 2018). Patients of both sexes with an age range of 30-65 years having 3-walled intrabony defects bilaterally, presence of probing pocket depth more than or equal to 5 mm and clinical attachment level greater than or equal to 3 mm after phase I therapy were included in the study.

Medically compromised patients and those consuming medications (corticosteroids/bisphosphonate therapy) that affect the end results of periodontal therapy, smokers, pregnant or lactating, who had undergone periodontal procedure within a time span of 1 year, and with Hematological disorders and insufficient platelet count (< 200000/mm3), were excluded. In addition patients with grade III and grade II tooth mobility, teeth with furcation defects, teeth requiring endodontic treatment, carious teeth necessitating restorations, below par oral hygiene (plaque index >1.5) after reassessment of non-surgical Therapy were precluded.

Initial phase I therapy involved performing full mouth supra and sub gingival scaling and root planning along with oral hygiene measures. Following phase I therapy the subjects were re-evaluated after 6 to 8 weeks, to confirm the suitability of the sites for this study.

Study design

The study used a split-mouth design, in which two interproximal sites were assigned. 50 selected sites from 25 patients were designated into two categories. The test group comprised of PRF -OFD and control group consisted of OFD (conventional flap surgery). All the surgeries were performed by a Periodontist while an examiner other than surgeon performed all the measurements without knowledge of the groups. Patients were blinded for allocation to particular group and treatment.

Presurgical clinical measurements and radiographic measurements

Clinical parameters were recorded before the surgical procedure and at 9 months post-operatively. Customised acrylic occlusal stent with grooves were fabricated for each site to standardize and reproduce the position and angulation of University of North Carolina-15 (UNC-15, Hu Friedy, Chicago, IL, USA) periodontal probe. With the acrylic stent in position, the periodontal probe was inserted into the pocket, and pocket depth (from gingival margin to base of pocket) and clinical attachment level (from the apical extent of occlusal stent to base of pocket) were recorded. Plaque index (PI) (Silness & Loe, 1964) were also measured.

Radiological assessments

Pre-operatively and 9 months post-operatively, intra-oral standardized radiographs were taken for the evaluation of radiographic bone level (RBL) applying paralleling technique. Radiographic bone loss/gain was calculated as the subduction between RBL measurements pre and postoperatively. Radiographic measurements were done as (1) depth from the CEJ to the deepest point of the vertical bone defect (BD), (2) space between CEJ to the alveolar crest (AC) and (3) interval from the AC to BD. Measurements were obtained utilizing a millimetre grid.

The most coronal area where the periodontal ligament (PDL) maintained an even width was identified to measure the most apical extension of the defect. The crossing of the silhouette of the alveolar crest with the root surface was defined as the alveolar crest. The differences between 9 months and baseline values of CEJ-BD indicated the amount of bone fill.

Materials

The PRF was processed in congruence with the protocol developed by Choukroun et al., (2000). Preceding surgery, venous blood was drawn in 10-ml sterile tube without anticoagulant and immediately centrifuged in REMI 4 (R-4C, REMI Laboratory Instruments, Mumbai, India) centrifugation machine at 3,000 revolutions (approximately: 400 g)/min for 10 min. The centrifuged blood presented three basic fractions: the red corpuscles at the bottom and acellular plasma at the top and a structured fibrin clot in the intermediate portion. PRF was isolated from base of red corpuscules utilising scissors in such a manner as to preserve a small RBC layer since the most potential regenerative area, i.e., platelets and WBCs is concentrated in an intermediate layer located between RBCs and the PRF clot. The resultant PRF clots were compressed in a sterile syringe to obtain a plug.

Surgical procedure

Iodine solution was used to conduct extraoral asepsis and intraoral asepsis was carried out with 0.12% chlorhexidine digluconate rinse. The operating procedure was performed by administration of local anaesthesia comprising of 2% lidocaine and epinephrine at a concentration of 1:100,000. Surgery was performed by placing intrasulcular incisions and reflection of a full-thickness mucoperiosteal flap. Complete debridement of the defects, as well as scaling and root planning to ensure root smoothness, were achieved with the use of an ultrasonic device and hand instruments. After thorough debridement, the flaps in the test sites (OFD and PRF), were sutured loosely and left untied following which the PRF clot was positioned at the base of the defect and compacted to the level of the bordering bony walls. Flaps in both groups were repositioned and sutured with 3–0 non-absorbable black silk surgical suture (Ethicon, Johnson & Johnson, Somerville, NJ) using an interrupted technique. Periodontal dressing was used to protect the surgical area. The defects of different groups were neither under the same flap nor in the similar quadrant.

Postoperative Care included prescription of antibiotics and analgesics (amoxicillin 500 mg, four times per day for 7 days and ibuprofen 800 mg three times per day), along with chlorhexidine digluconate (0.12%) two times a day for 2 weeks. Each patient was examined at 1, 3 and 9 months postoperatively.

Statistic analysis

Analysis of statistics was done by descriptive statistics as mean, SD, percentage, proportions etc. To attain a 90% power and determine mean differences of clinical parameters among groups, 25 sites for every group was required. Comparison of Plaque Index (from Baseline to 1 month, Baseline to 3 months, Baseline to 6 months, Baseline to 9 months), Pocket Depth, Clinical Attachment Level and Radiological Bone level from Baseline to 9 months in two groups was done by applying Student's Paired 't'

test at 5% ($p<0.05$) level of significance. Statistical analysis software namely SYSTAT version 12 (made by Crane's software, Bangalore) a licensed copy was used to analyse the data.

3. RESULTS

A total of 50 sites from 25 patients completed the study. Demographic data showed that 56% of the sample group were males and 44% were females aged 25-40 (M=35.84 years, SD= 4.03 years). Descriptive findings of research subscales are demonstrated in Table 1. Group I consisted of 25 sites, treated by OFD alone (Control Group); group II comprised of 25 sites, treated with OFD and PRF (Test Group). All treated sites healed uneventfully. Baseline analysis did not demonstrate any substantial variation amid groups for the assessed variables, suggesting that any final disparities among treated groups were not influenced by initial defect characteristics, thus allowing post-treatment results to be compared. A statistically valid reduction in the Plaque index scores were observed during the various intervals ($P<0.001$) (Table 2 & Figure 1).

Table 1 Age and sex wise distribution in Group I (Open Flap Debridement), Group II (Leukocyte Rich Platelet-rich Fibrin along with Open Flap Debridement)

Age in years	Males	Females	Total
25-30	1	1	2(8%)
30-35	5	3	8(32%)
35-40	8	7	15(60%)
Total	14(56%)	11(44%)	25(100%)
Mean ± SD	35.84 years ± 4.03 years		

Table 2 Comparison of Plaque Index from Baseline and follow up visits

	Baseline	Baseline -1 Month	Baseline -3 Months	Baseline - 6 Months	Baseline -9 Months
Mean ± SD	1.93±0.42	1.17±0.27	0.83±0.42	0.74±0.39	0.53±0.23
t*		11.0144	13.0952	14.6913	21.5385
'p' value		p = 0.0001	p = 0.0001	p = 0.0001	p = 0.0001

* Paired t test.

Comparative evaluation of Pocket Depth, Clinical Attachment gain and defect fill Test and Control Groups at Baseline and 9 Months are reported in Table 3. Both OFD and PRF–OFD groups showed significant pocket depth reduction at 9 months compared with baseline. However mean pocket reduction was greater significantly in the test group (PRF +OFD) 3.62±0.52 mm when compared to control group (OFD Alone) 5.30±0.86. The differences noted amidst the groups were significant in favour of the PRF–OFD group ($P<0.001$) Figure 2.

OFD group presented with an attachment gain of 3.12±0.29, while the gain for the PRF-OFD group was 4.30±0.87. The differences in attachment gain observed among the two groups were significantly better in the PRF–OFD group ($P<0.001$) Figure 3. Test sites presented with significantly greater defect fill (5.12±0.54mm) than the control sites (8.96±0.99mm) ($P<0.001$) at 9 months. The PRF-OFD category exhibited with substantially higher defect fill (5.12±0.54mm) than the OFD group (8.96±0.99mm) ($P<0.001$) Figure 4.

Table 3 Comparative Evaluation of mean change in pocket depth, and attachment Level and intrabony defect depth from baseline to 9 Months in test and control groups

		Test Group			Control Group		
	VISIT	Mean ± SD	t*	P	Mean ± SD	t*	p
Pocket Depth	Baseline	7.84±1.03	27.2258	<0.001	7.84±1.03	13.4391	<0.001
	9 Months	3.62±0.52			5.30±0.86		
Clinical Attachment Level	Baseline	6.80±1.04	27.6691	<0.001	6.80±1.04	13.0890	<0.001
	9 Months	3.12±0.29			4.30±0.87		
IBD Depth	Baseline	9.08±0.99	3.0303	<0.001	6.80±0.86		<0.001
	9 Months	8.96±0.99			5.12±0.54	60.001	

* Paired t test.

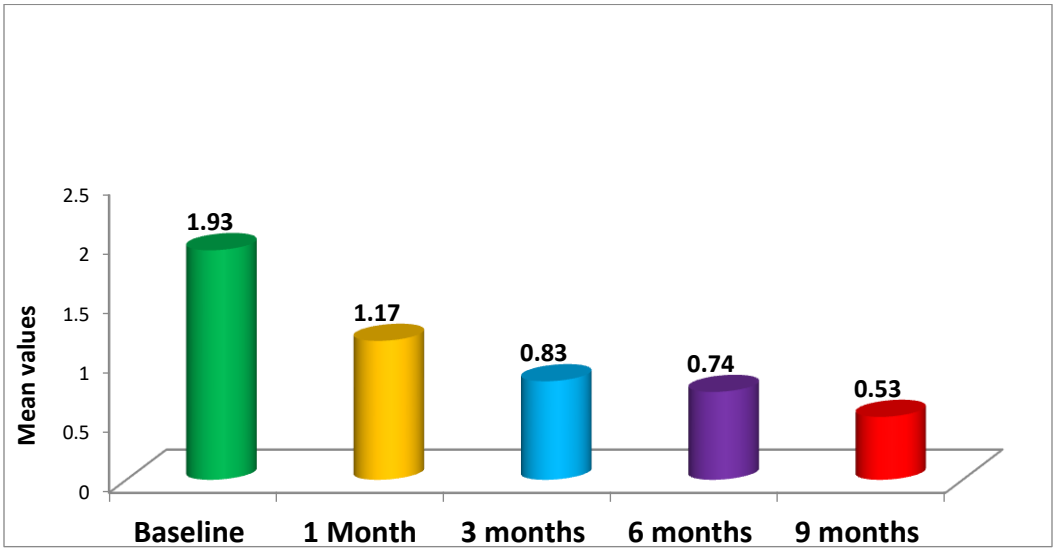

Figure 1 Comparison of Plaque Index from Baseline to 1 month, 3 months, 6 months and 9 months follow up

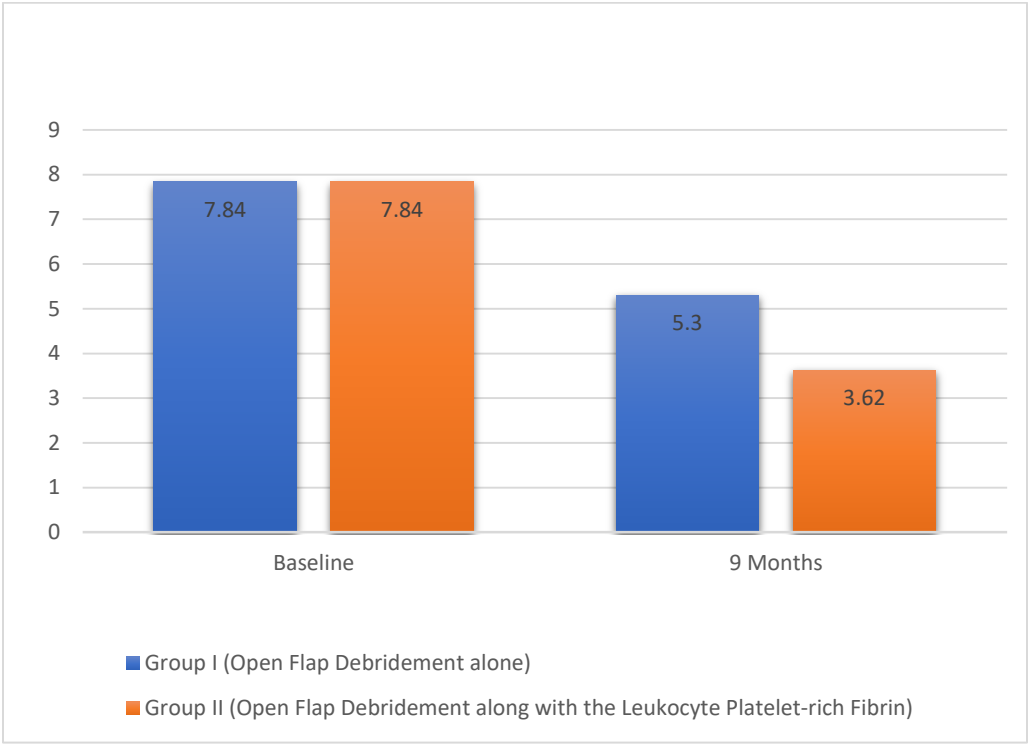

Figure 2 Comparison of Probing Pocket Depth from Baseline to 9 months follow up in Group I (Open Flap Debridement alone) and Group II (Open Flap Debridement along with the Leukocyte Platelet-rich Fibrin)

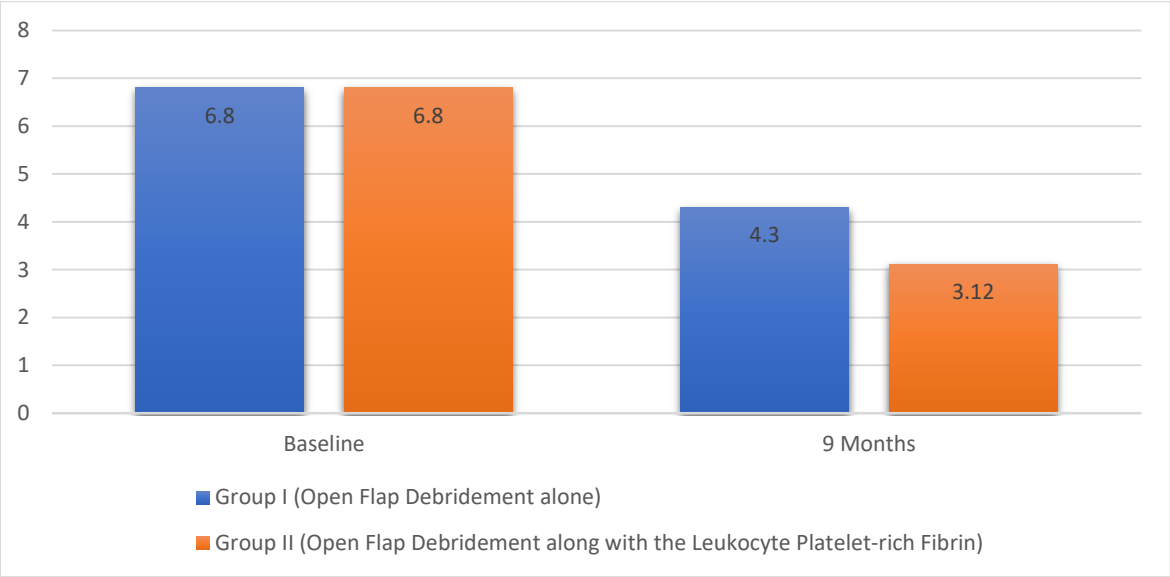

Figure 3 Comparison of Attachment Level from Baseline to 9 months follow up in Group I (Open Flap Debridement alone) and Group II (Open Flap Debridement along with the Leukocyte Platelet-rich Fibrin)

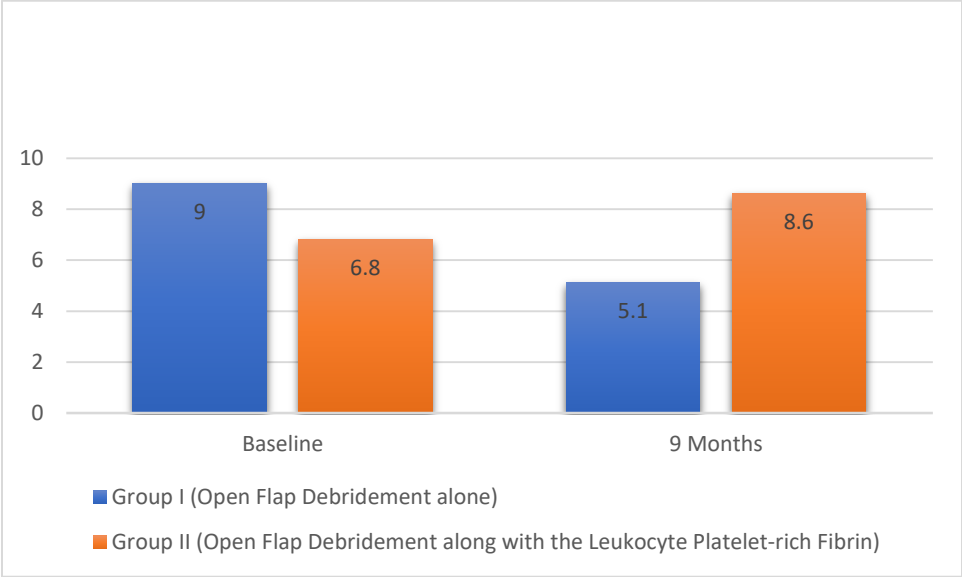

Figure 4 Comparison of Intrabony Defect Depth at Baseline and 9 months follow up in Group I (Open Flap Debridement alone) and Group II (Open Flap Debridement along with theLeukocyte Platelet-rich Fibrin)

4. DISCUSSION

Periodontal Wound healing commencing by clot formation entails interplay amidst epithelial cells, gingival fibroblasts, periodontal ligament cells, and osteoblasts (Bueno et al., 2015). Platelets are used as robust tools for periodontal regeneration for couple of decades due to their vital role in wound healing process. PRF, constituting platelets and growth factors is and devoid of any anti-coagulant or any other biochemical modifications. With asemblance of a cicatricial matrix, PRF behaves as a powerful healing biomaterial with inherent regenerative capacity which can be embodied in various dental procedures (Dohan et al., 2006).

The pursuit for an ideal natural source of autologous product, to support bone repair or regeneration, have led the search for Platelet Rich Fibrin. Considering only limited studies involving the analysis of PRF in the therapy intrabony defect depth reduction, the current investigation was designed to compare PRF to the open debridement controls in the treatment of 3 walled vertical osseous defects (three walled). In the present study, three walled intrabony defects were selected as the end result of the regenerative methods in intrabony defects depends to a greater degree on choice of cases to be treated than any other technique

inferring the presence of three bony walls is a necessary topographic feature for a favourable result (Prichard, 1957) as the defect containment by 3 osseous walls was correlated with superior clinical defect fill (Blumenthal et al., 2003).

In this particular study, both treatment modalities achieved a substantial deduction in the plaque index at the treated sites during follow-up evaluations compared with baseline scores, the findings of which were in accordance with those of Chacko et al., (2014). The reduction in PI may be attributed to periodic (monthly) supragingival plaque maintenance along with reinforcement of oral hygiene directives, the absence of which, will eventually lead to failure of treatment. Combined evaluation of Periodontal parameters like probing pocket depth, CAL and the bleeding on probing, are essential to evaluate and supervise periodontal status. Pocket depth reduction being a prudent result of periodontal treatment, is a key factor for clinician as it influences ones ability to instrument a treated area during maintenance visits. Clinical attachment gain an important outcome of periodontal therapy could possible be the result of true periodontal regeneration (new attachment) or, alternatively, healing by repair long junctional epithelium (Chang & Zhao, 2011).

In the present study decline of PPD and CAL gain displayed a notable variation from at 9 months in comparison to baseline irrespective of the sites. Nonetheless on comparison experimental sites revealed a better pocket reduction and gain in attachment than control site. These findings were in congruity with those of Thorat et al., (2011) which could be ascribed to the presence of various growth factors and a better organised fibrin matrix of PRF that efficiently directs stem cell migration and accelerates the periodontal tissue healing (Choukroun et al., 2000). Dohan et al., (2006) observed better healing properties with PRF owing to slower release of growth factors from PRF than PRP.

The present study also reflects the percentage of depth reduction in IBD at test sites (46.92%) is greater than the conventionally treated subjects (28.66%). Similar to the present results Pradeep et al., (2012) also showed increased level of radiographic bone gain after treatment with PRF when compared to PRP. In short term trials, Thorat et al., (2011) reported increased bone fill after 9months post treatment in the defects treated with. The supremacy of PRF in promoting the healing of osseous defects can be attributed to promotion of protein kinase (p-ERK) and stimulation of the production of osteoprotegerin (OPG) which inturn causes proliferation of osteoblasts (Chang & Zhao, 2011). Tsai et al., (2009) in a culture study noted that PRF incites proliferation of osteoblasts, periodontal ligament cells and growth factors and subdues oral epithelial cell growth suggesting that these distinct actions may be favourable for periodontal regeneration. The inherent osteoconductive and/or osteoinductive property of PRF is beneficial for bone regeneration. Distinguishing the effect of PRP and PRF on growth and differentiation of osteoblasts Sanchez et al., (2003) reported the superior affection of osteoblasts to the PRF membrane compared to PRP.

5. CONCLUSION

In conclusion, our study demonstrates that application of PRF in intrabony defects results in substantial improvements of pocket depth reduction, attachment gain and intrabony defect fill compared with OFD alone. PRF is a natural, physiologic and economic source of autologous product annihilating concerns regarding immunogenic reactions and disease transmission. With an innate potential to harbour growth factors PRF promotes periodontal regeneration. In the future prespective long term clinical results analysing the potency of PRF in regenerative procedures, randomized trials implying their clinical implementation, in conjunction with histological nature of newly formed tissues remains to be elucidated.

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Author Contributions

Conceptualization:	G.Pendyala;S.Rao; P. Byakod; S. Magar; A. Lawande; S. Joshi; A. Mani
Data collection:	G. Pendyala
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Investigation:	G. Pendyala; A. Mani
Methodology:	G. Pendyala; A. Mani; A. Lawande
Writing – original draft:	G. Pendyala; S. Joshi
Writing – review & editing:	G. Pendyala, P. Byakod; S. Magar

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval

The study was approved by the Ethics Committee of Pravara Institute of Medical Sciences (ethical code: PIMS/IEC-DR/2019/14).

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Conflicts of interest

The authors declare that they have no conflict of interest.

Data and materials availability

All data associated with this study are present in the paper.

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