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TO EVALUATE AND COMPARE THE EFFECTIVENESS OF ADVANCED PLATELET-RICH FIBRIN (A-PRF) COMBINED WITH 1% METRONIDAZOLE GEL VERSUS A-PRF ALONE IN THE TREATMENT OF CHRONIC PERIODONTITIS OVER A 12-WEEK PERIOD.

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ABSTRACT

Aim
To evaluate and compare the effectiveness of advanced platelet-rich fibrin (A-PRF) combined with 1% metronidazole gel versus A-PRF alone in the treatment of chronic periodontitis over a 12-week period.

Introduction
Periodontitis is a prevalent inflammatory condition characterized by the destruction of periodontal tissues, largely driven by microbial infection. Regenerative therapies such as advanced platelet-rich fibrin (A-PRF) have shown promising outcomes due to their ability to promote healing and tissue regeneration. Metronidazole, a widely used antimicrobial agent, has demonstrated efficacy in targeting anaerobic pathogens involved in periodontitis. This study investigates the potential synergistic effect of combining A-PRF with 1% metronidazole gel to enhance clinical outcomes in patients with chronic periodontitis.

Objective
To assess and compare the clinical efficacy of A-PRF in combination with 1% metronidazole gel versus A-PRF alone in reducing plaque, gingival inflammation, probing pocket depth, and improving clinical attachment levels in chronic periodontitis patients.

Methodology
This 12-week randomized clinical trial included 60 periodontal sites from patients aged between 30 to 65 years, randomly allocated into two groups.

Group A: Received A-PRF combined with 1% metronidazole gel

Group B: Received A-PRF alone
Clinical parameters including Plaque Index (PI), Gingival Index (GI), Probing Pocket Depth (PPD), and Clinical Attachment Level (CAL) were recorded at baseline, 4 weeks, and 12 weeks. Statistical analysis was conducted to evaluate intra- and intergroup differences.

Results
Both groups exhibited statistically significant improvements in all clinical parameters over the 12-week period. However, Group A showed significantly greater reductions in PI, PPD, and CAL compared to Group B at 12 weeks ($p < 0.001$). Although GI improved significantly within both groups, the intergroup difference was not statistically significant.

Conclusion
The combination of A-PRF and 1% metronidazole gel provides enhanced therapeutic benefits in the management of chronic periodontitis compared to A-PRF alone. This dual-action approach not only reduces the microbial load effectively but also supports tissue regeneration. Further clinical studies with larger sample sizes and extended follow-up periods are recommended to validate and extend these findings.

INTRODUCTION

Periodontitis is a chronic, multifactorial inflammatory disease associated with dysbiotic biofilms and characterized by progressive destruction of the tooth-supporting apparatus, including alveolar bone and periodontal ligament [1]. It is the most prevalent periodontal condition globally, typically exhibiting a slow to moderate rate of progression and is strongly

linked to the accumulation of subgingival plaque biofilms and calculus deposits [2]. In recent years, there has been growing emphasis on the use of locally delivered adjunctive therapies, particularly due to the site-specific nature of periodontitis. Local drug delivery offers the advantage of achieving higher antimicrobial concentrations at the disease site while reducing systemic exposure and minimizing side effects [3]. Periodic local chemotherapeutic interventions have demonstrated clinical benefits, including reduced bleeding on probing (BOP), stabilization of clinical attachment level (CAL), and reduction in probing pocket depth (PPD).

A variety of site-specific antimicrobial agents are currently utilized in periodontal practice, including tetracycline fibers (Actisite), metronidazole gel (Elyzol), minocycline gel and microspheres (Arestin), chlorhexidine gluconate chip (PerioChip), and doxycycline hyclate gel (Atridox) [4]. Metronidazole (MTZ), a nitroimidazole-based antimicrobial, has demonstrated bactericidal activity against key anaerobic periodontal pathogens such as *Porphyromonas gingivalis* and *Prevotella intermedia* [5]. It exerts its antimicrobial effect by disrupting bacterial DNA synthesis, leading to microbial cell death [6,7]. MTZ can be used as both a systemic and a local adjunct to subgingival debridement [6,8], with a plasma half-life of approximately 8 hours [9]. Its minimum inhibitory concentration (MIC) varies depending on the target microbial species.

Periodontal regeneration relies heavily on the presence of bioactive molecules that stimulate wound healing. Autologous platelet concentrates, such as platelet-rich fibrin (PRF), have emerged as biologically active scaffolds capable of enhancing regeneration of both soft and hard periodontal tissues [10]. PRF is classified as a second-generation platelet concentrate, prepared by centrifugation of the patient's own venous blood without the addition of anticoagulants [11]. It contains a three-dimensional fibrin network rich in platelets, leukocytes, cytokines, and growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-ß), and insulin-like growth factor-1 (IGF-1) [12], as well as thrombospondin-1, a protein involved in cellular adhesion and repair.

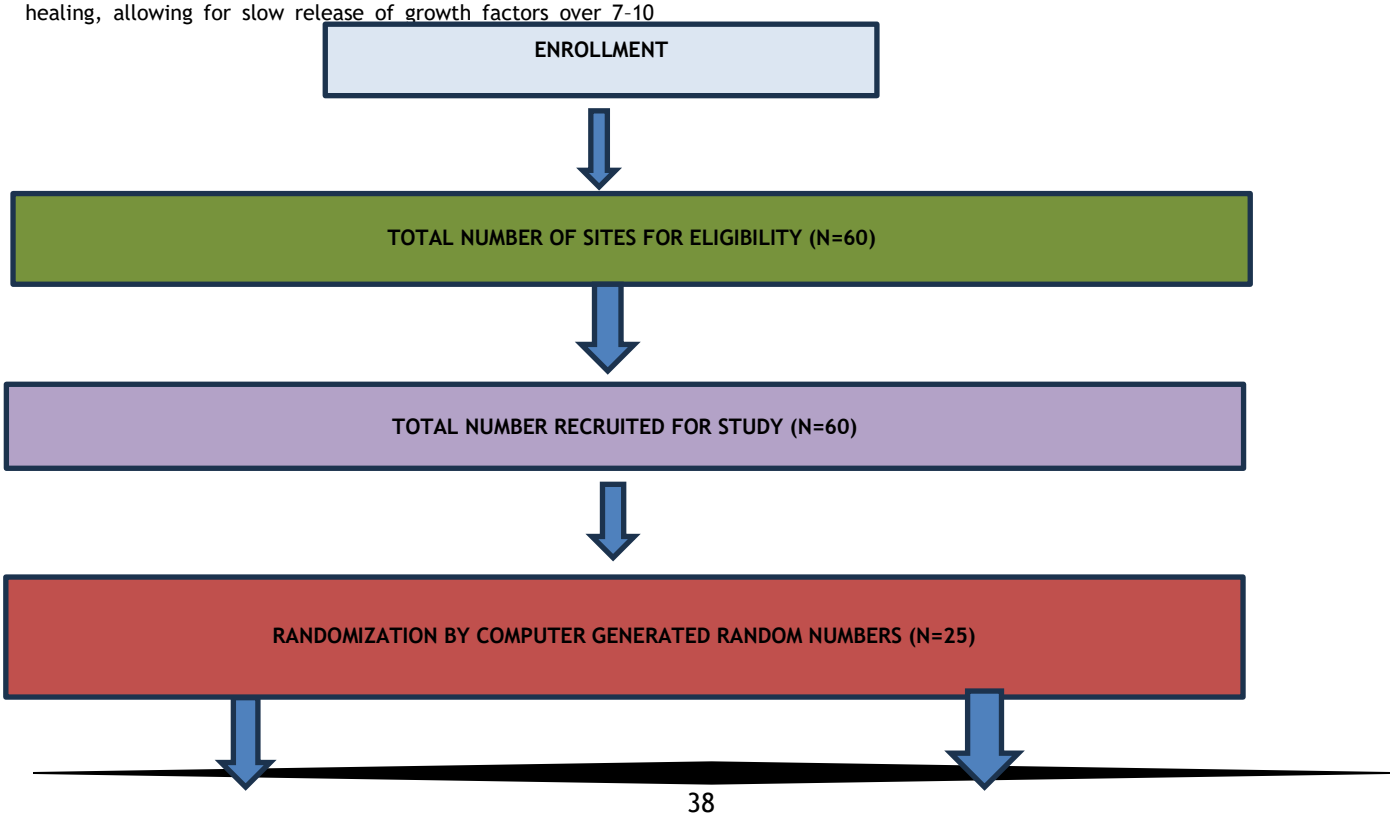
PRF has shown promising outcomes in enhancing periodontal wound healing and promoting bone regeneration [13]. First introduced by Choukroun et al. in 2001 [14], the classical PRF preparation involves centrifuging a 10 mL whole blood sample at 2700 rpm for 12 minutes [15]. PRF is biologically superior to first-generation concentrates such as PRP, as it does not require thrombin or other additives [16,17]. It promotes physiologic wound healing, allowing for slow release of growth factors over 7–10 days, while its natural fibrin matrix serves as a scaffold for cellular migration and proliferation [19]. This matrix also supports space maintenance, which is essential for osteogenesis [20-22].

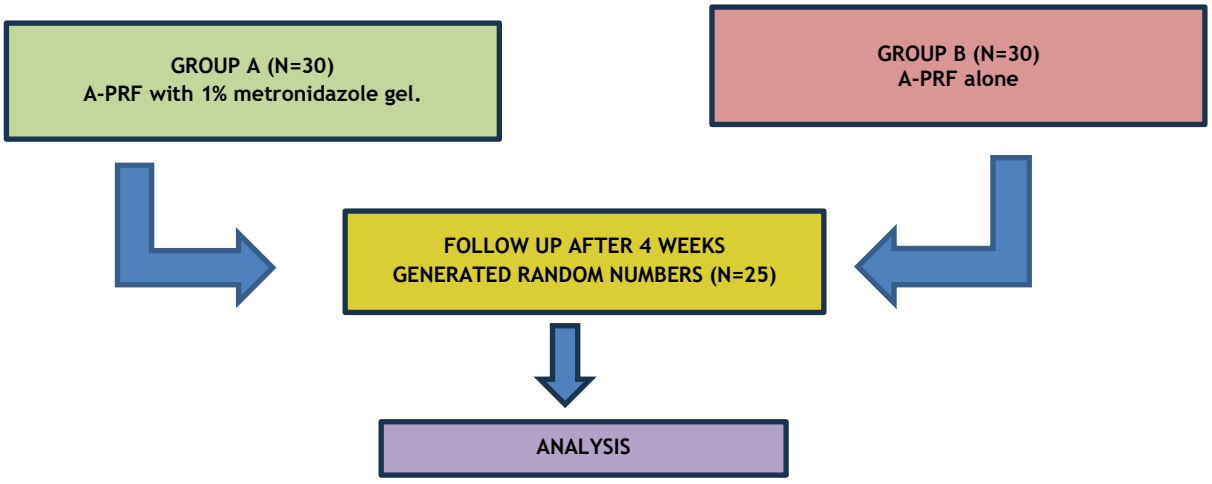
Advanced PRF (A-PRF) is a modified form of PRF obtained by reducing the relative centrifugal force (RCF) and time, resulting in increased leukocyte and growth factor content [11]. According to findings by Caruana et al., adjusting centrifugation parameters significantly alters the release of TGF-ß1 and VEGF concentrations [23]. A-PRF has been shown to contain more neutrophils, which facilitate angiogenesis and tissue remodeling by modulating macrophages toward a reparative phenotype [25,26].

Given the bactericidal efficacy of 1% metronidazole gel and the regenerative capacity of A-PRF, their combined application may offer synergistic benefits in treating Stage II–III periodontitis. This study is thus designed to evaluate and compare the clinical outcomes of A-PRF alone and in combination with 1% metronidazole gel as adjuncts to non-surgical periodontal therapy. The aim is to assess whether the combined approach enhances periodontal tissue healing and improves clinical parameters beyond those achieved by A-PRF alone.

MATERIALS AND METHODS:

This study was a 12-week single-blind, randomized controlled clinical trial conducted in the Department of Periodontology at Inderprastha Dental College and Hospital, Sahibabad. It involved patients diagnosed with periodontitis who reported to the outpatient department for treatment. A total of 60 periodontal sites were selected from systemically and mentally healthy patients aged between 30 and 65 years, exhibiting a probing pocket depth of ≥5 mm and maintaining adequate oral hygiene with a Plaque Index score of <1 following Phase I therapy. Patients were randomly allocated into two groups using computer-generated random numbers. Group A (n=30) received treatment with advanced platelet-rich fibrin (A-PRF) combined with 1% metronidazole gel, whereas Group B (n=30) was treated with A-PRF alone. Individuals with systemic or infectious diseases (e.g., HIV or hepatitis), tobacco users, those on immunosuppressants or corticosteroids, pregnant or lactating women, those with a history of regenerative therapy at the site, or known allergies to study materials were excluded. Clinical parameters recorded at baseline, 4 weeks, and 12 weeks postoperatively included Plaque Index (Silness & Löe, 1964), Gingival Index (Löe & Silness, 1963), Probing Pocket Depth (PPD), and Clinical Attachment Level (CAL), the latter two measured at the mid-buccal site using a UNC-15 periodontal probe.



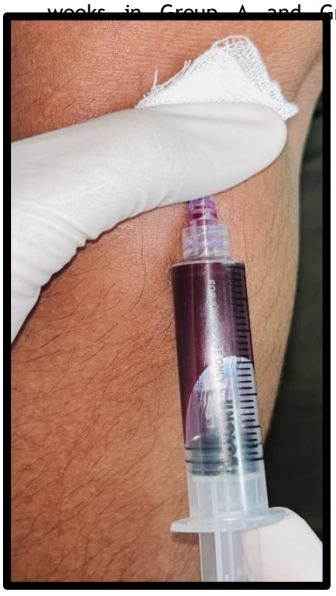


FLOWCHART 1: CONSORT FLOWCHART OF THE STUDY

STATISTICS

This in vivo study assessed clinical parameters—Plaque Index (PI), Gingival Index (GI), Probing Pocket Depth (PPD), and Clinical Attachment Level (CAL)—at baseline, 4 weeks, and 12 weeks in Group A and Group B. Statistical analysis was performed using SPSS version 27.0. Tests included the Friedman test, Post hoc Bonferroni, Student's t-test, One-Way ANOVA, and Mann-Whitney U test, with significance set at $p < 0.05$ and a 95% confidence interval.

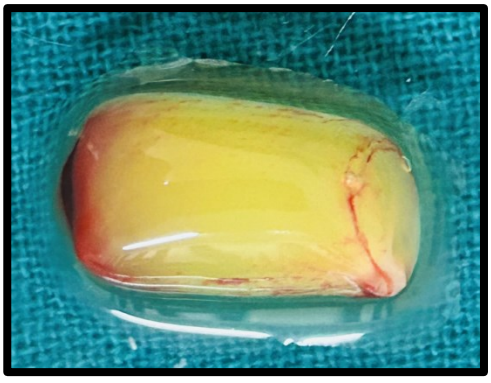
A-PRF MEMBRANE PREPARATION



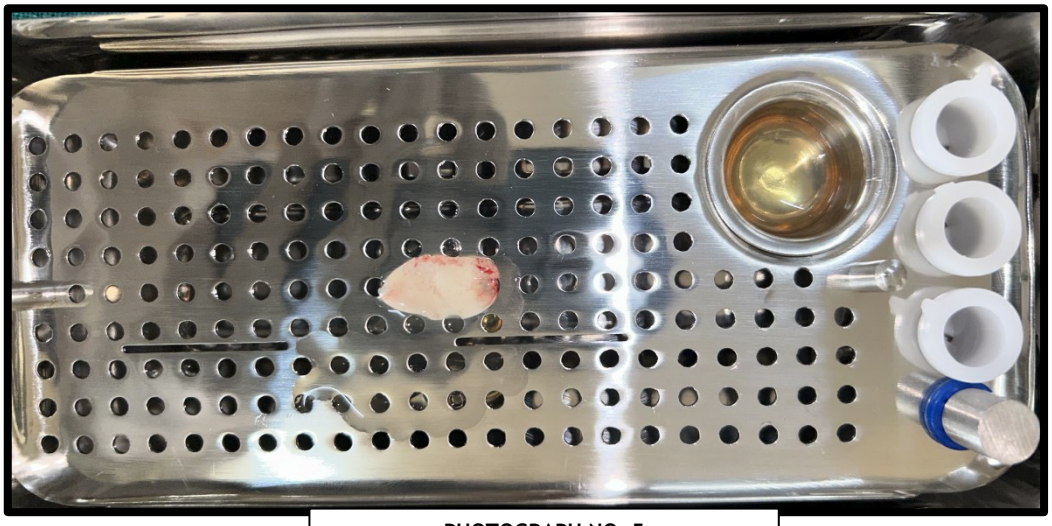
PHOTOGRAPH NO. 1
Blood withdrawn from medial cubital vein

PHOTOGRAPH NO. 2
Blood transferred in glass test tube

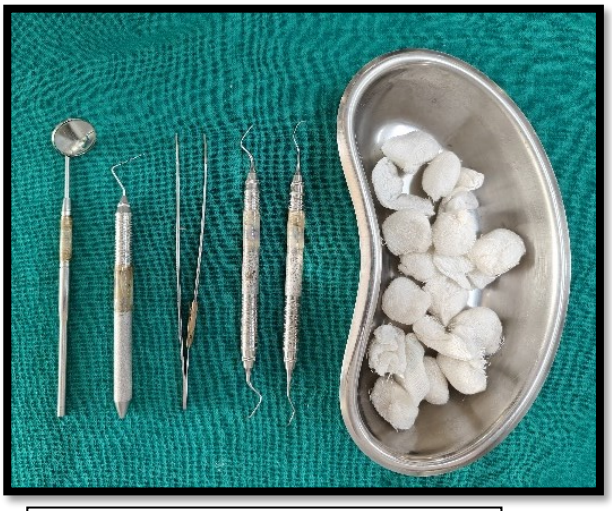
PHOTOGRAPH NO. 3
CENTRIFUGATION



PHOTOGRAPH NO. 4
A-PRF



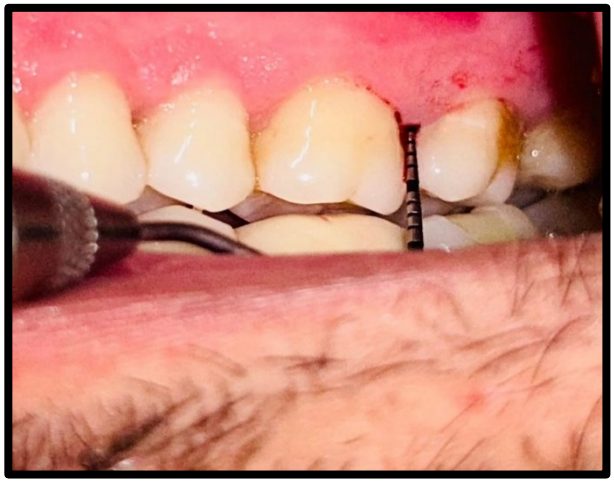
PHOTOGRAPH NO. 5
A -PRF MEMBRANE IN PRF BOX



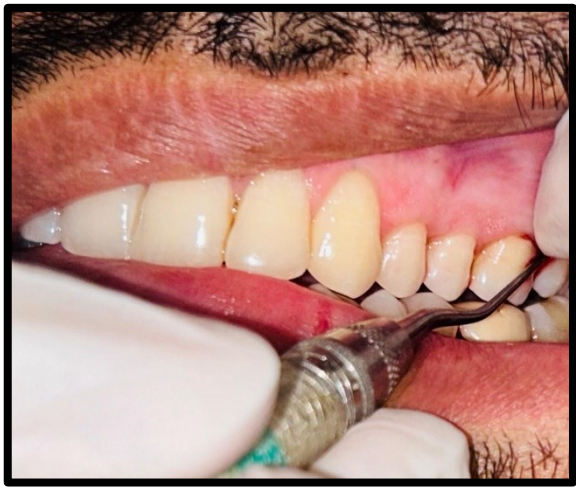
PHOTOGRAPH NO. 6
Surgical Armamentarium

PHOTOGRAPH NO. 7
Periodontal Dressing (Coe-pak)

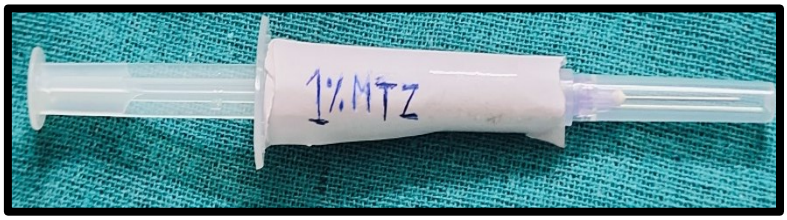
GROUP A: A-PRF MEMBRANE & 1% METRONIDAZOLE GEL



PHOTOGRAPH NO. 8
Baseline Measurement of Pocket Probing Depth (5mm) by using UNC- 15 (Hu-Friedy)



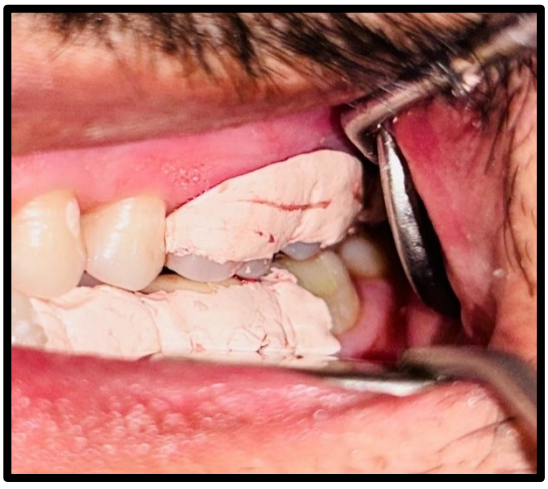
PHOTOGRAPH NO. 9
Curettage done by using Hu-Friedy 1/2Gracey Curette



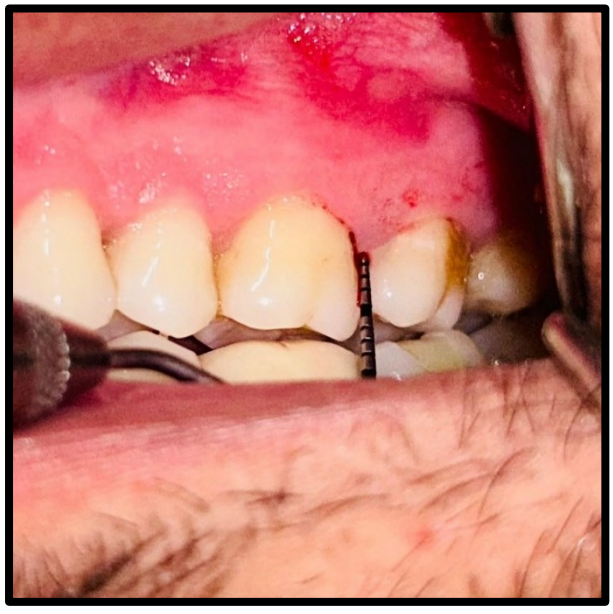
PHOTOGRAPH NO. 10
1% METRONIDAZOLE GEL

PHOTOGRAPH NO. 11
A-PRF MEMBRANE & 1% METRONIDAZOLE GEL

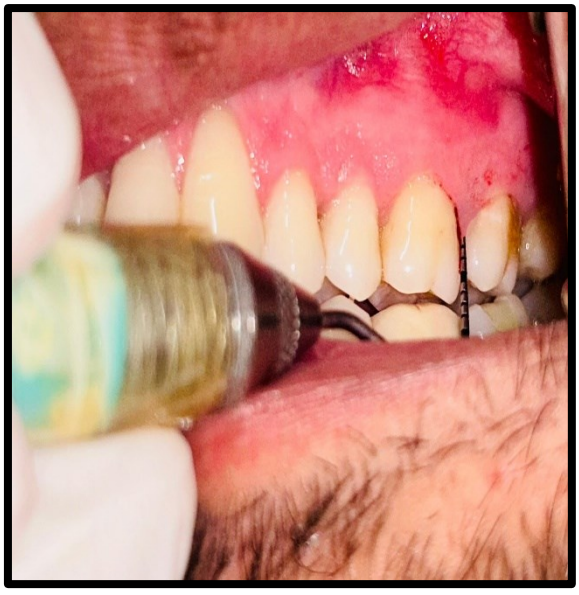
PHOTOGRAPH NO. 12
A-PRF & 1% METRONIDAZOLE GEL MIXED



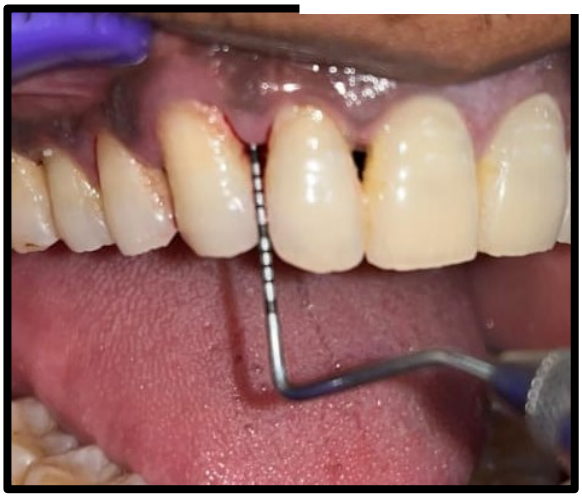
PHOTOGRAPH NO. 13
Periodontal dressing (Coe-Pak)



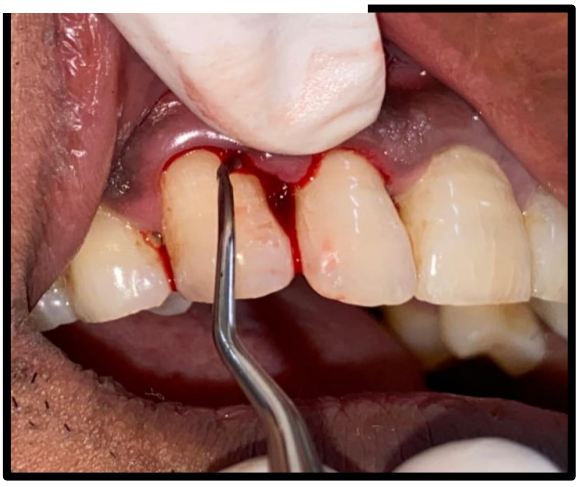
PHOTOGRAPH NO. 14
Measurement of Pocket Probing Depth at 4th week by using UNC- 15 (Hu-Friedy)



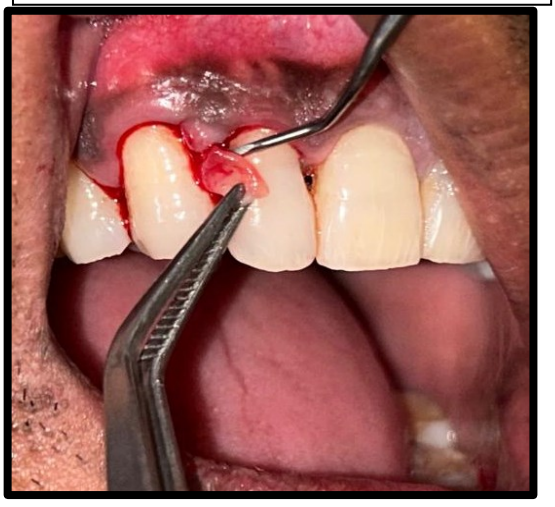
PHOTOGRAPH NO. 15
Measurement of Pocket Probing Depth at 12th week by using UNC- 15 (Hu-Friedy)



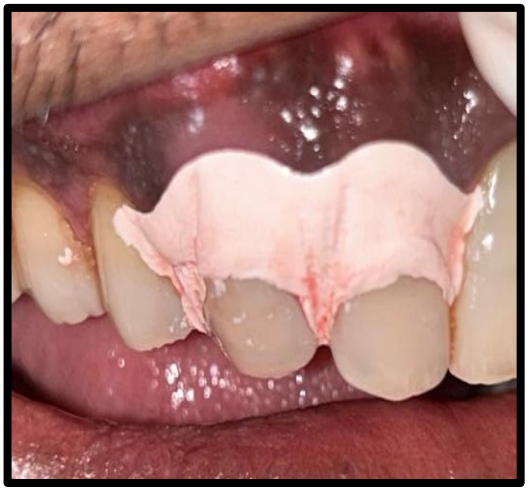
PHOTOGRAPH NO. 16
Baseline Measurement of Pocket Probing Depth (5mm) by using UNC- 15 (Hu-Friedy)



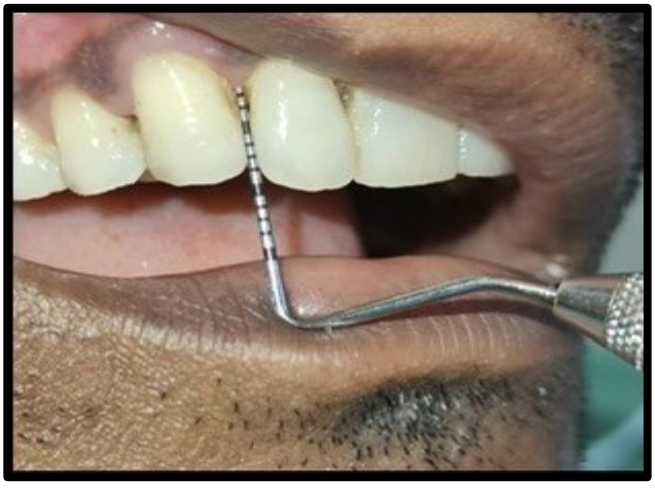
PHOTOGRAPH NO. 17
Curettage done by using Hu-Friedy 1/2Gracey Curette



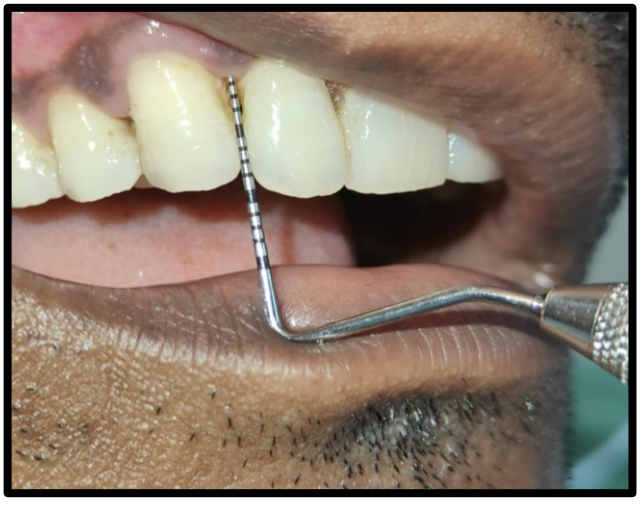
PHOTOGRAPH NO. 18
A-PRF MEMBRANE placed at baseline



PHOTOGRAPH NO. 19
Periodontal dressing (Coe-Pak)



PHOTOGRAPH NO. 20
Measurement of Pocket Probing Depth at 4th week by using UNC- 15 (Hu-Friedy)



PHOTOGRAPH NO. 21
Measurement of Pocket Probing Depth at 12th week by using UNC- 15 (Hu-Friedy)

RESULTS:

Intragroup comparison of Plaque index

Group	Interval	Mean	SD	p-value	Pairwise comparisons
Group A	**Baseline**	0.42	0.18	<0.001*	Baseline vs 4 weeks: 0.005* Baseline vs 12 weeks: <0.001* 4 weeks vs 12 weeks: <0.001*
	4 weeks	0.30	0.12		
	12 weeks	0.17	0.07		
Group B	**Baseline**	0.42	0.18	<0.001*	Baseline vs 4 weeks: 0.117 Baseline vs 12 weeks: <0.001* 4 weeks vs 12 weeks: <0.001*
	4 weeks	0.36	0.14		
	12 weeks	0.25	0.08		

Friedman test; Post hoc Bonferroni test; * indicates a significant difference at p≤0.05

TABLE 1: This table compares plaque index scores at baseline, 4 weeks, and 12 weeks. Group A showed significant reductions at each interval, with the lowest score at 12 weeks. In Group B, no significant change was seen between baseline and 4 weeks, but a significant reduction was observed at 12 weeks.

Intergroup comparison of plaque index

Interval	Group A		Group B		Difference	p-value
	Mean	SD	Mean	SD		
Baseline	0.42	0.18	0.42	0.18	0.00	0.946
4 weeks	0.30	0.12	0.36	0.14	-0.06	0.082
12 weeks	0.17	0.07	0.25	0.08	-0.08	<0.001*

Mann Whitney test

TABLE 2: Intergroup comparison of plaque index

Intragroup comparison of gingival index

Group	Interval	Mean	SD	p-value	Pairwise comparisons
Group A	**Baseline**	0.24	0.06	<0.001*	Baseline vs 4 weeks: 0.660 Baseline vs 12 weeks: <0.001* 4 weeks vs 12 weeks: 0.001*
	4 weeks		0.21	0.03	
	12 weeks		0.14	0.05	
Group B	**Baseline**		0.25	0.06	<0.001*	Baseline vs 4 weeks: 0.413 Baseline vs 12 weeks: <0.001* 4 weeks vs 12 weeks: <0.001*
	4 weeks		0.21	0.06	
	12 weeks		0.14	0.06	

Friedman test; Post hoc Bonferroni test; * indicates a significant difference at p≤0.05

TABLE 3: This table compares each group's baseline, 4-week, and 12-week plaque index. In both Group A and Group B, the 12-week gingival index was significantly lower than the baseline and 4-week gingival index and there was a non-significant difference between the baseline and 4-week gingival index.

Intergroup comparison of gingival index

Interval	Group A		Group B		Difference	p-value
	Mean	SD	Mean	SD		
Baseline	0.24	0.06	0.25	0.06	-0.01	0.522
4 weeks	0.21	0.03	0.21	0.06	0.00	0.843
12 weeks	0.14	0.05	0.14	0.06	0.00	0.672

Mann Whitney test; * indicates a significant difference at p≤0.05

TABLE 4: This table compares the CAL between the two groups. At each interval, the GI score did not differ significantly between the two groups.

Intragroup comparison of PPD

Group	Interval	Mean	SD	p-value	Pairwise comparisons
Group A	**Baseline**	4.77	0.43	<0.001*	Baseline vs 4 weeks: <0.001* Baseline vs 12 weeks: <0.001* 4 weeks vs 12 weeks: 0.001*
	4 weeks	3.47	0.51		

	12 weeks	2.20	0.41		
Group B	**Baseline**	4.63	0.49	<0.001*	Baseline vs 4 weeks: <0.001* Baseline vs 12 weeks: <0.001* 4 weeks vs 12 weeks: <0.001*
	4 weeks	3.53	0.51		
	12 weeks	2.63	0.49		

Friedman test; Post hoc Bonferroni test; * indicates a significant difference at p≤0.05

TABLE 5: This table compares each group's baseline, 4-week, and 12-week PPD values. In Group A and Group B, the baseline PPD value was significantly greater than the PPD after 4 weeks and 12 weeks and the 12-week PPD value was significantly lower than the PPD at baseline & after 4 weeks.

Intergroup comparison of PPD

Interval	**Group A**		**Group B**		**Difference**	**p-value**
	Mean	**SD**	**Mean**	**SD**		
Baseline	4.77	0.43	4.63	0.49	0.14	0.264
4 weeks	3.47	0.51	3.53	0.51	-0.06	0.609
12 weeks	2.20	0.41	2.63	0.49	-0.43	0.001*

Mann Whitney test; * indicates a significant difference at p≤0.05

TABLE 6: This table compares the PPD between the two groups. There was a non-significant difference in the PPD value of the two groups at baseline as well as after 4 weeks. However, after 12 weeks, the PPD value of Group A was significantly lower than that of Group B.

Intragroup comparison of CAL

Group	**Interval**	**Mean**	**SD**	**p-value**	**Pairwise comparisons**
Group A	**Baseline**	3.93	0.37	<0.001*	Baseline vs 4 weeks: 0.158 Baseline vs 12 weeks: <0.001* 4 weeks vs 12 weeks: <0.001*
	4 weeks	3.43	0.50		
	12 weeks	2.17	0.38		
Group B	**Baseline**	3.77	0.63	<0.001*	Baseline vs 4 weeks: 0.035* Baseline vs 12 weeks: <0.001* 4 weeks vs 12 weeks: 0.001*
	4 weeks	3.17	0.59		
	12 weeks	2.37	0.49		

Friedman test; Post hoc Bonferroni test; * indicates a significant difference at p≤0.05

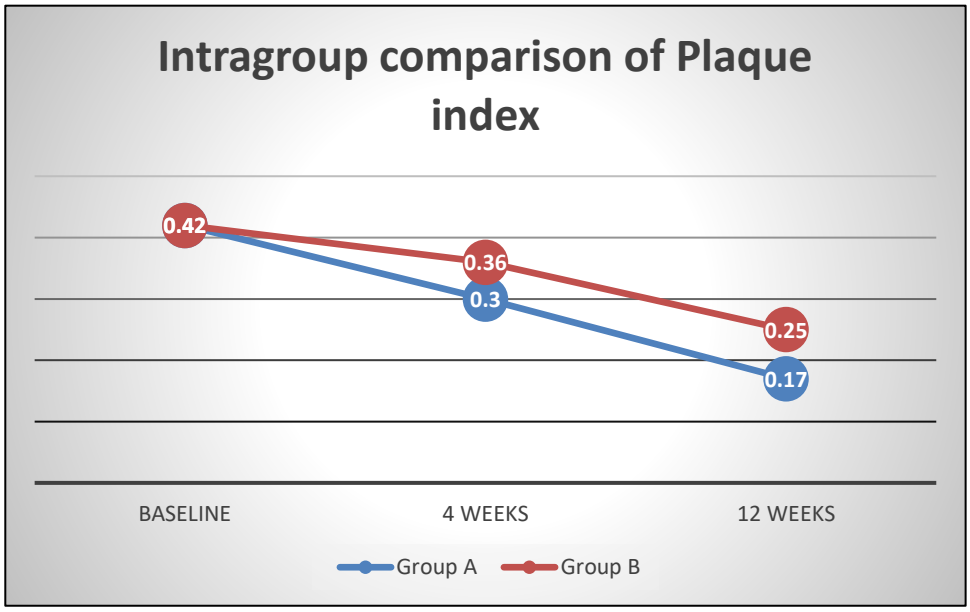
TABLE 7: This table compares each group's baseline, 4-week, and 12-week CAL values. In Group A, the 12-week CAL value was significantly lower than the baseline and 4-week CAL value and there was a non-significant difference between the baseline and 4-week CAL values. In Group B, the baseline CAL value was significantly greater than the CAL after 4 weeks and 12 weeks and there was a non-significant difference between the 4-week and 12-week CAL.

Intergroup comparison of CAL

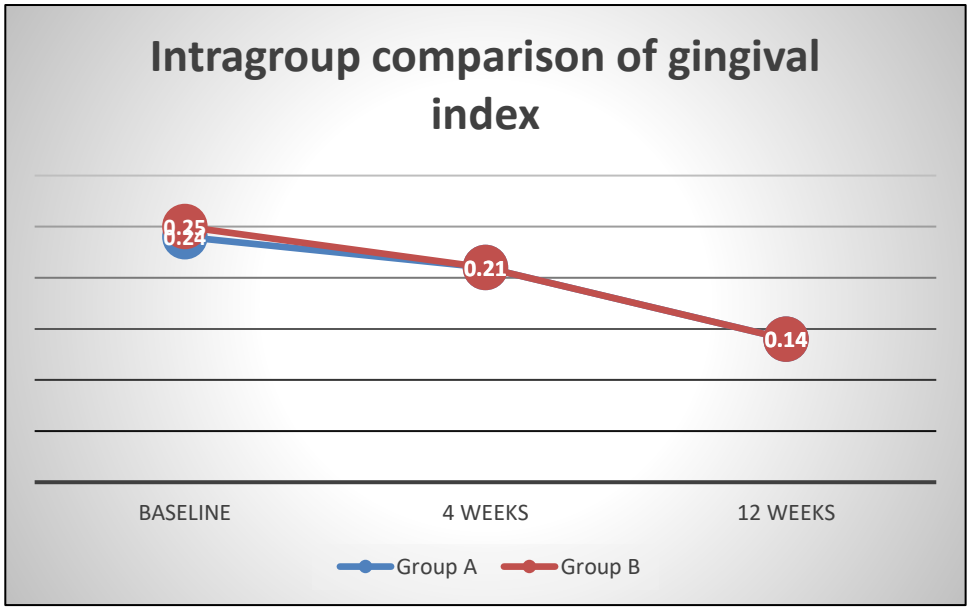
Interval	**Group A**		**Group B**		**Difference**	**p-value**
	Mean	**SD**	**Mean**	**SD**		
Baseline	3.93	0.37	3.77	0.63	0.16	0.162
4 weeks	3.43	0.50	3.17	0.59	0.26	0.084
12 weeks	2.17	0.38	2.37	0.49	-0.20	0.082

Mann Whitney test; * indicates a significant difference at p≤0.05

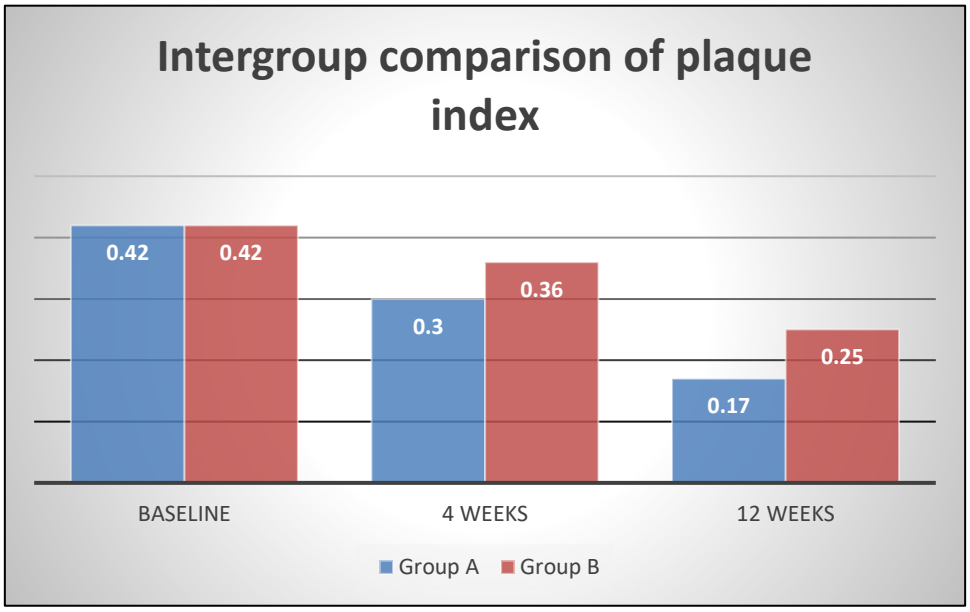
TABLE 8: This table compares the CAL between the two groups. At each interval, there was a non-significant difference in the CAL of the two groups.



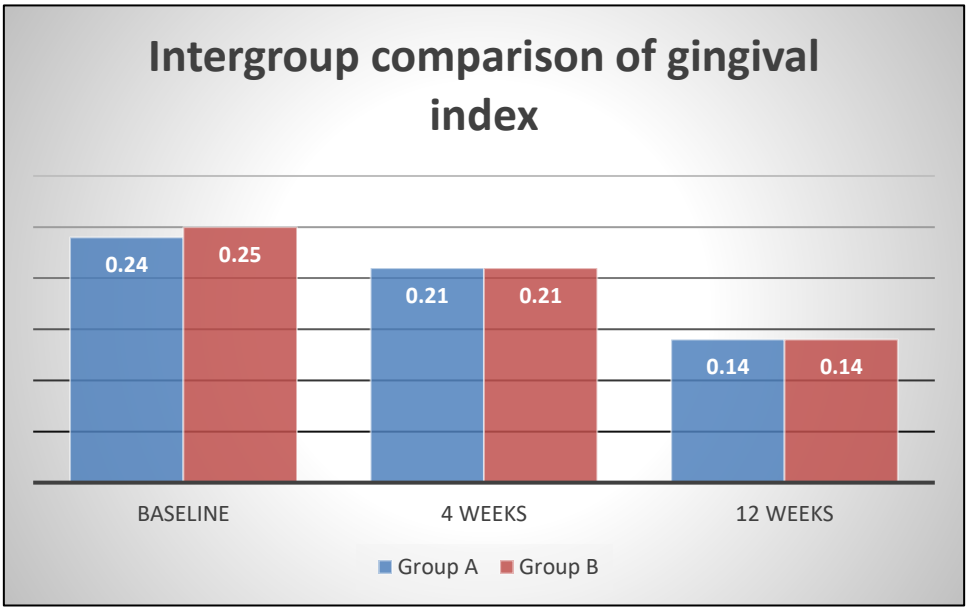
GRAPH 1: Intragroup comparision of plaque index in Group A and Group B



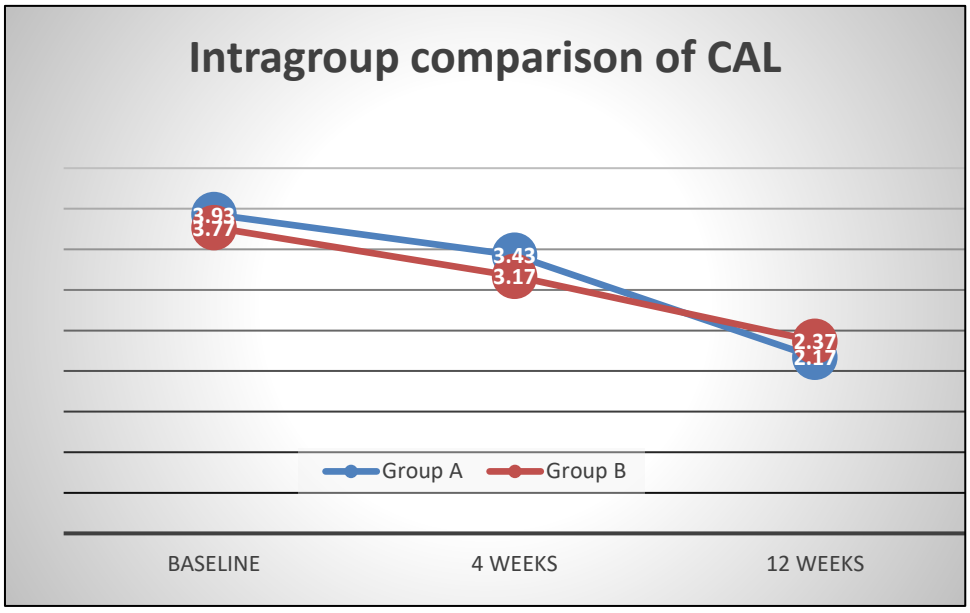
GRAPH 2: Intragroup comparision of gingival index in Group A and Group B



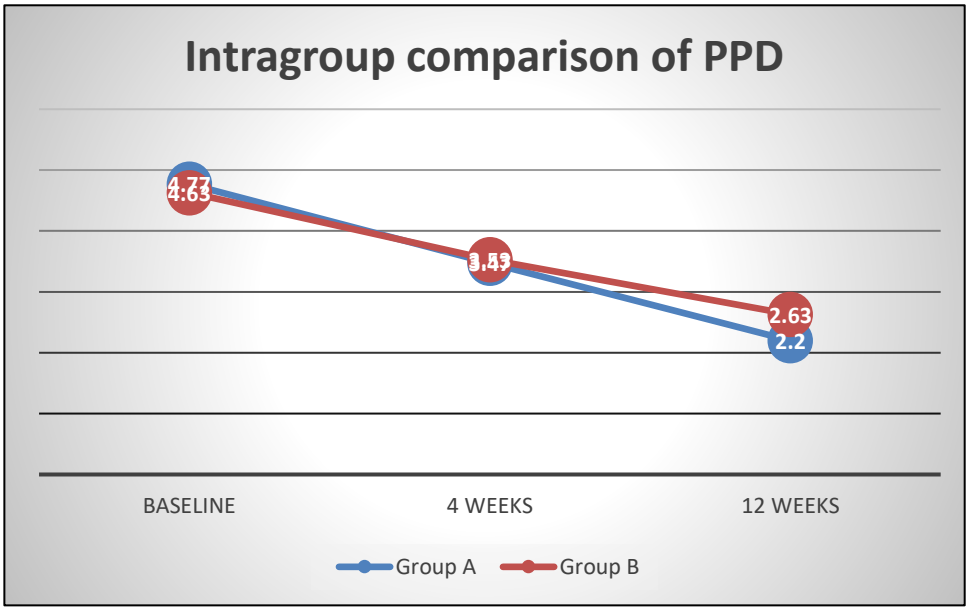
GRAPH 3: Intergroup comparision of plaque index in Group A and Group B



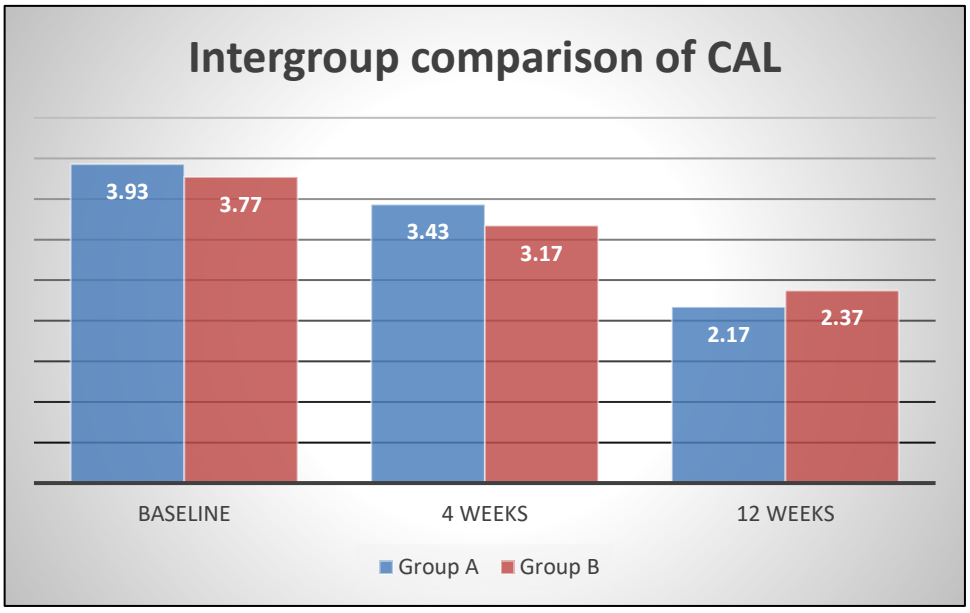
GRAPH 4: Intergroup comparision of plaque index in Group A and Group B



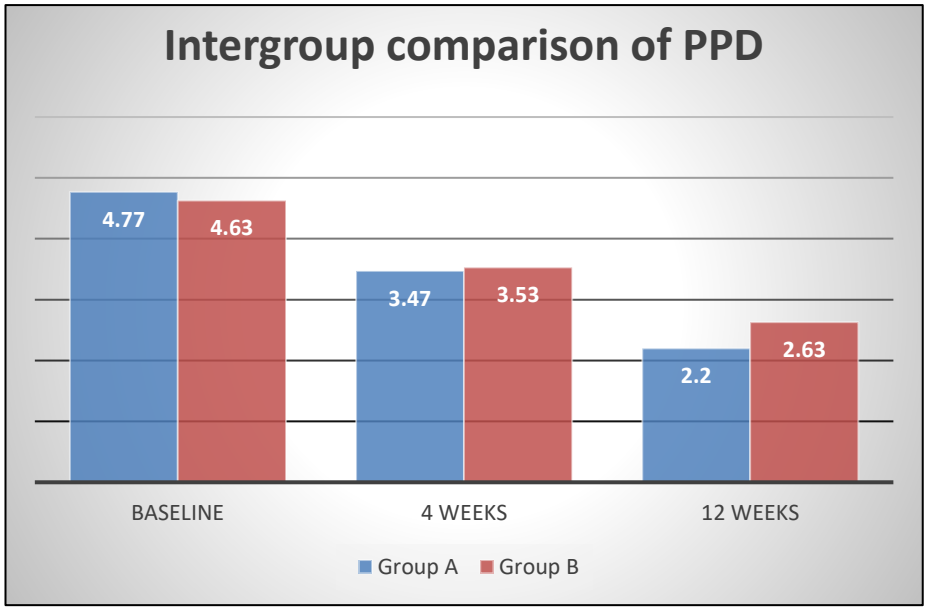
GRAPH 5: Intragroup comparision of CAL in Group A and Group B



GRAPH 6: Intragroup comparision of PPD in Group A and Group B



GRAPH 7: Intergroup comparision of CAL in Group A and Group B



GRAPH 8: Intergroup comparision of PPD in Group A and Group B

The present study was carried out to evaluate the clinical periodontal parameters in patients diagnosed with periodontitis when treated with Advanced Platelet Rich Fibrin and 1% metronidazole gel. In this study, to evaluate and compare the efficacy of local drug delivery at baseline, 4 weeks and 12 weeks.

A total of 60 sites were initially selected and screened for periodontitis. Data of 60 sites were finally collected and analyzed. The post-operative follow up was done at 4 weeks and 12 weeks after Phase 1 therapy comprising of full mouth scaling and root planing using hand and ultrasonic instruments. Thus, the observations made were statistically analyzed.

The results of the study were subjected to statistical analysis using the following test: the statistical analysis was done using the SPSS (Statistical Package for Social Science) version 27.0 version. The mean values observed were represented by mean SD. The normality of data was tested by Friedman test; Post hoc Bonferroni test. The significance difference of parameters between groups (Intergroup comparison) at different time intervals was tested by Student's t- test, One-Way ANOVA and Mann Whitney U test. The 95% C.I. and 5% level of significance was used for analysis of data. Level of significance was set at $p < 0.05$. The present in vivo study constituted assessment of clinical parameters viz. plaque index (PI), gingival index (GI), pocket probing depth (PPD), clinical attachment level (CAL) at baseline, 4 Weeks and 12 weeks in Group A and Group B.

DISCUSSION

This study evaluated the comparative efficacy of advanced platelet-rich fibrin (A-PRF) combined with 1% metronidazole gel versus A-PRF alone in the treatment of chronic periodontitis. Periodontitis, a multifactorial inflammatory disease initiated by microbial plaque, results in the progressive destruction of the

periodontal ligament and alveolar bone, leading to clinical attachment loss and pocket formation. Contemporary periodontal therapy aims to eliminate infection, control inflammation, and regenerate lost periodontal structures.

In this randomized clinical trial, clinical parameters including Plaque Index (PI), Gingival Index (GI), Probing Pocket Depth (PPD), and Clinical Attachment Level (CAL) were assessed at baseline and after 12 weeks of treatment. The primary objective was to assess whether the addition of 1% metronidazole gel to A-PRF enhances clinical outcomes compared to A-PRF alone.

Plaque accumulation plays a pivotal role in the initiation and progression of periodontal disease. Both groups in this study demonstrated statistically significant reductions in PI from baseline to 12 weeks. However, Group A (A-PRF + metronidazole gel) exhibited a more marked reduction in PI compared to Group B (A-PRF alone), with intergroup differences reaching statistical significance at 12 weeks ($p < 0.001$). The enhanced plaque control in Group A can be attributed to the sustained antimicrobial action of metronidazole, which is particularly effective against obligate anaerobes such as Porphyromonas gingivalis and Prevotella intermedia [27,28]. This aligns with the findings of Taneja et al., who reported superior plaque reduction when metronidazole was used adjunctively with platelet-rich fibrin [29].

Gingival inflammation, as measured by the Gingival Index (GI), showed significant reductions within both groups over the 12-week period, reflecting effective management of the inflammatory response. However, intergroup differences were not statistically significant, suggesting that A-PRF alone may be sufficient to manage gingival inflammation. A-PRF has been shown to release key anti-inflammatory cytokines and growth factors such as transforming growth factor-beta (TGF-ß) and platelet-derived growth factor (PDGF), which contribute to reducing inflammation and promoting healing [30,31].

Probing Pocket Depth (PPD) is a critical indicator of disease severity and treatment success. Both groups experienced significant reductions in PPD from baseline to 12 weeks, with Group A showing significantly greater improvement ($p = 0.001$). The combined antimicrobial and regenerative approach likely produced a synergistic effect, with metronidazole reducing the bacterial load and A-PRF enhancing tissue regeneration. This finding is consistent with a study by Mallappa et al., who observed superior pocket depth reduction when adjunctive agents were used alongside A-PRF [32].

Clinical Attachment Level (CAL) reflects the restoration of periodontal support. Both groups exhibited significant intragroup CAL gains, with Group A demonstrating a trend toward greater improvement, although intergroup differences were not statistically significant. This suggests an additive benefit of combining A-PRF with metronidazole gel. Csifó-Nagy et al. reported similar outcomes in their clinical trial on A-PRF in periodontal regeneration, emphasizing its role in promoting soft and hard tissue repair [33].

The biological efficacy of A-PRF stems from its three-dimensional fibrin matrix, which serves as a scaffold for cellular migration and proliferation. It facilitates the release of growth factors such as vascular endothelial growth factor (VEGF), PDGF, and TGF-ß for up to 10–14 days, supporting neovascularization and osteogenic activity [34]. These properties make A-PRF a potent regenerative agent in periodontal therapy.

Metronidazole gel, on the other hand, offers localized antimicrobial activity without systemic side effects. Its use as a local drug delivery system ensures high concentrations at the site of infection, enhancing its bactericidal effects against anaerobic organisms while minimizing the risk of antibiotic resistance [35].

Furthermore, the integration of regenerative and antimicrobial therapies addresses both microbial etiologies and the need for tissue regeneration—key factors in achieving long-term periodontal stability. This dual-targeted approach has been increasingly advocated in recent literature as a comprehensive treatment modality [36].

CONCLUSION

The findings of this study suggest that combining A-PRF with 1% metronidazole gel significantly enhances clinical outcomes in periodontal therapy compared to A-PRF alone. Notable improvements were observed in plaque reduction, pocket depth, and clinical attachment levels, especially at the 12-week interval. The synergistic effect of antimicrobial action and regenerative potential appears to offer a more effective therapeutic strategy for managing periodontitis. Future studies with larger sample sizes, histologic evaluation, and longer follow-up durations are warranted to validate these results and determine the longevity of treatment benefits.

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