COMPARISON BETWEEN ANTIMICROBIAL PHOTODYNAMIC THERAPY AND INJECTABLE PLATELET RICH FIBRIN AS AN ADJUNCT TO NON-SURGICAL PERIODONTAL TREATMENT (A RANDOMIZED CONTROLLED CLINICAL TRIAL WITH MICROBIOLOGICAL ASSESSMENT)

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ABSTRACT

Background: The aim of this study was to compare the efficacy of injectable form of PRF to antimicrobial photo dynamic therapy as an adjunctive treatment to non-surgical periodontal therapy in patients with stage III grade B periodontitis in terms of clinical improvement and antimicrobial ability.

Subjects and Methods: 39 patients of each gender with age vary from 30 to 60 years diagnosed with stage III grade B periodontitis. The patients were divided randomly into three groups. (Group I) 13 patients treated by SRP (scaling and root planning) with application of i-PRF, (Group II) 13 patients treated by SRP with application of 940 nm diode laser and Indocyanine green (ICG), (Group III) treated by SRP alone as a control group. Clinical parameters such as GI (gingival index), PI (plaque index), CAL (clinical attachment level) and PD (probing depth) were recorded preoperatively and 3 months post operatively. Site-specific measure of bactericidal effect against *Pg (Porphyromonas gingivalis)* preoperative, 1 week postoperative and 1 month postoperative for all groups.

Results: group I who receiving i-PRF resulted in a significant decrease in the percentage of *Pg* at the end of 1 month when compared to the other groups. Comparison of clinical parameters revealed significant differences in patients treated with aPDT in relation to GI, and CAL while i-PRF group , was better in PD at the end of the study period.

Conclusion: i-PRF and aPDT may enhance the potential benefits of SRP in periodontitis patients and can be used as an adjunct to nonsurgical periodontal therapy.

KEYWORDS: Stage III Grade B periodontitis, Photodynamic therapy, i-PRF, *Porphyromonas gingivalis*, Egypt.

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INTRODUCTION

Periodontitis is a chronic multifactorial inflammatory disease associated with dysbiotic plaque biofilms, characterized by continuous destruction of the tooth-supporting tissues .It accounts for a substantial proportion of masticatory dysfunction .Periodontitis results in significant increased dental care costs and has a marked negative impact on general health [1].

There are several risk factors for periodontal disease such as smoking, poor oral hygiene, medication, diabetes, age, stress, and heredity [2]. In United States, recent studies suggest that periodontal disease affects fifty percent of population over thirty years of age and is the utmost cause of tooth loss among adults. Periodontal disease affects 10–15% of adult populations worldwide. WHO had reported incidence of 80% of periodontal diseases in Egypt 2014. Despite this high prevalence of periodontal diseases, no definite preventive measures are undertaken to screen, prevent or to address this health issue to establish a stable periodontal health protocol program [3, 4].

A multi-dimensional periodontitis, staging and grading system was proposed, Grade A (slow progression rate), Grade B (moderate progression rate) and Grade C (rapid progression rate). Staging is largely dependent upon the severity of disease as well as on the complexity of disease management, while grading provides supplemental information about biological features of the disease including a history-based analysis of periodontitis progression rate; assessment of the risk for further progression; [1].

Initial non-surgical therapy for periodontal disease consists of professional removal of both supragingival and sub-gingival dental plaque and calculus with scaling and sub-gingival debridement [5].

Non-surgical periodontal therapy, with or without adjunctive therapies, is an effective treatment for periodontitis. To enhance treatment outcomes, several adjuncts to non-surgical periodontal treatment have been proposed, that include antibiotics, either systemic such as amoxicillin and metronidazole, or localized antimicrobials, such as chlorhexidine. [6]. In local delivery drugs (LDDS), antimicrobial agents are directly placed in the periodontal pocket [7].

Antimicrobial photodynamic therapy (a-PDT) using diode laser and relevant photosensitizer has been demonstrated to exert potent antimicrobial effects against biofilms. Studies have shown that biofilms of oral bacteria are much more difficult to eradicate by conventional means because of the strong tissue adherence and physical exclusion of antimicrobial substances in biofilms. The fact that a-PDT was found to be so effective against biofilms and this suggests an advantage over other antimicrobial periodontal therapies [8].

The topical uses of Platelets Rich Fibrin (PRF) have achieved great popularity in various fields of medicine, especially in dentistry, oral maxillofacial surgery, cosmetics and plastic surgery. PRF is a second-generation platelet concentrate comprising of complex network of micro fibrins with entrapped platelets and leucocytes. Injectable Platelet rich fibrin (i-PRF) is a platelet concentrate that has been extensively used for multiple medical purposes and is a valuable adjunct for the regeneration of damaged tissues in surgical procedures. The enriched bioactive substances in i-PRF are responsible for speeding the wound healing process. [9].

i-PRF has also antimicrobial effect against periodontopathic bacteria. i-PRF showed maximum zone of inhibition around oral micro-flora, antimicrobial efficacy of i-PRF was performed against *Porphyromonas gingivalis (Pg)* and *Aggregatibacter actinomycetemcomitans (Aa)* [10].

Therefore, the hypothesis of this study considers that aPDT and i-PRF can provide additional clinical benefits to the conventional non-surgical periodontal therapy. The main objectives of this study is to compare between aPDT and i-PRF as an adjunct to

non-surgical periodontal therapy in the treatment of generalized stage III grade B periodontitis in relation to clinical parameters as a primary objective and to assess their bactericidal effect on *Pg* as a secondary objective.

SUBJECTS AND METHODS

Study design

This is a randomized controlled clinical trial in which the patients were divided into 3 groups. Each patient was provided with detailed verbal and written information on the study protocol. Understanding and agreement to enrol in the study was confirmed with written consent and the study received the ethical approval no. (FDASU-Rec IM012013) from the ethical committee of Faculty of Dentistry, Ain Shams University.

A 39 patients diagnosed with generalized stage III grade B periodontitis were selected from the outpatient clinic of Oral Medicine, Periodontology and Oral diagnosis department, Faculty of Dentistry, Ain Shams University. Sample Size Calculation: A power analysis was calculated based on the results of Christodoulides et al., (2008). The predicted sample size (n) was a total of 39 cases i.e.13 for each group. Sample size calculation was performed using G*Power version 3.1.9.4. The participants were included or excluded according to the following criteria: Inclusion criteria: Both genders aged between 30-55 years. Generalized stage III grade B periodontitis: CAL more than 4 mm, PD more than 5 mm, Bone loss extends to the middle or apical third of affected roots, Percentage of Radiographic bone level(RBL) per age is less than 2mm over 5 years [12]. Patients ready to comply with oral hygiene measures and Patients free from any systemic disease or taking drugs that affect healing. Exclusion criteria: Smokers, Pregnant females, Drug abusers, vulnerable groups of people (prisoners and handicapped) In addition Patients with previous antibiotic therapy in the past six months.

Patient grouping and Treatment protocol

Group (I): Included 13 patients diagnosed with generalized stage III grade B periodontitis and treated with non-surgical periodontal treatment SRP + intra pocket injection of i-PRF. Group (II): Included 13 patients diagnosed with generalized stage III grade B periodontitis and treated with SRP + aPDT. Group (III) (Control group): Included 13 patients diagnosed with generalized stage III grade B periodontitis and treated with just SRP.

Treatment protocol

At baseline all candidates underwent phase 1 therapy, single session of full mouth supra gingival scaling using ultrasonic device combined with sub gingival debridement using universal curettes. All patients were instructed to maintain thorough oral hygiene measures, including brushing with a medium toothbrush and regular tooth paste three times daily, as well as the use of dental floss or interdental brush. Patients were checked for their oral hygiene measures after one week and those who did not follow the instructions were excluded from the study. Preoperative evaluation: After one week, all candidates underwent full mouth periodontal examination and full charts using UNC 15 probe. The following parameters were assessed preoperatively and after three months. PI, GI, PD and CAL

For Group I patients (i-PRF): after performing phase 1 therapy, a venous blood sample was collected in 9 ml dry glass tube and was immediately centrifuged using duo machine for three minutes at 700 rpm, without anticoagulant or another gelling agent. After centrifugation, i-PRF was immediately collected using a 3 mm plastic syringe to avoid coagulation. The plastic syringe tip was changed into narrow plastic blunt tip to avoid injury to tissues during application. i-PRF was injected immediately to the deepest pocket intra sulcularly. The tip was inserted intra sulcular without doing any pressure until the slightest resistance was felt. The i-PRF was injected until it appeared from the gingival margin as shown in figure (1), it was done only 1 time immediately after finishing phase 1 therapy.

Fig. (1)

For Group II patients (a-PDT): after finishing phase 1 therapy, 1 ml of the Indocyanine green (ICG) dye was withdrawn from the vial by a sterile plastic syringe. The regular tip of the plastic syringe was discarded and replaced with a plastic narrow blunt tip to avoid injury to the sulcus. The tip was inserted intra sulcular related to the selected deepest pocket without doing any pressure until the slightest resistance was felt. The ICG (0.2ml photosensitizer solution) was injected until it appeared from the gingival margin figure (2).

Fig. (2)

The irrigated pocket was then immediately illuminated via the LASER hand piece using Diode LASER Epic X with wavelength 940nm and light-diffusing tip E3 for a period of 60 seconds at a power of 0.5 watt. Residual photosensitizer was suctioned from the buccal margin after the activation cycle was completed [13]. It was done only 1 time immediately after finishing phase 1 therapy. Group III patients: - (control group) recall visits were given to them every two weeks. During these visits, supra gingival deposits was removed and were checked for their oral hygiene measures. No medications were prescribed to them.

Postoperative instructions (For group I and II): All subjects were instructed with the following: After SRP and application of the locally delivered agent, avoid eating, drinking, or rinsing for one hour. Rinse mouth 2-3 times a day with warm saline. Brushing twice a day with a medium bristled toothbrush. Using fluoride rinses in case of sensitivity. No flossing for three days after treatment. All groups were followed up every 2 weeks to maintain oral hygiene and removal of supra-gingival deposits. Regarding clinical parameters: All groups were assessed preoperatively and three months postoperatively.

Microbiological analysis: PCR of gingival crevicular fluid sample (GCF) of the selected deepest pocket to estimate the count of *Pg* before the start of the treatment, was done at one week and one month postoperatively.

GCF Sampling: Before sampling, the adjacent teeth were isolated with cotton rolls. To standardize site selection and adequate sample volume, crevicular fluid was collected on paper points size (30) placed parallel to the long axis of the tooth in the most affected site for 1mm depth in the gingival sulcus until mild resistance is felt and kept for 30 seconds and pooled in reduced transport fluid (RTF) medium for microbiological analysis. GCF collected samples contaminated with saliva were discarded. The samples were immediately transferred for microbiological culturing of *Pg* which was then separately vortexed and inoculated in anaerobic jar according to the requirement for culturing and quantification of anaerobic bacteria [14].

Statistical analysis

Categorical were presented as frequency and percentage values and were analyzed using Fisher's exact test. Numerical data were presented as mean and standard deviation values. Parametric data were analyzed using one-way ANOVA followed by Tukey's post hoc test for intergroup comparisons and repeated measures ANOVA followed by Bonferroni post hoc test for intragroup comparisons. Non-parametric data were analyzed using Kruskal Wallis test followed by Dunn's post hoc test with Bonferroni correction for intergroup comparisons and Friedman's test Subjects and Methods followed by Nemenyi post hoc test for intragroup comparisons.

RESULTS

I- Demographic data

There was no complications and all patients completed the study. There was 4(30.8%) males in i-PRF group and 9(69.2%) females. In aPDT, there was 6(46.2%) males and 7(53.8%) females. In the control group, there was 3(23.1%) males and 10(76.9%) females. The mean age in i-PRF group was 40.40±4.38 years, in aPDT, it was 43.29±2.50 and in the control group, it was 39.15±5.98. There was no significant difference between the three groups regarding sex (p=0.582) and age (p=0.212).

II- Clinical assessment

The mean and standard deviation of all clinical parameters and bacterial load of the three groups patients are summarized in Table (1)

In the intragroup comparisons there was a significant decrease in the mean gingival index after 3 months (p<0.05). in addition the results showed that group II demonstrated greater reduction in the mean percentage change of gingival index than the other two groups, but with no significant difference between the three groups.

Regarding the Probing depth (mm): At baseline, intergroup comparison showed no significant difference between the three studied groups (p=0.956). After 3 months, there was a significant difference between values of different groups (p=0.013). The highest value was found in the control group, followed by aPDT group while the lowest value was found in i-PRF. Post hoc pairwise comparisons showed value of the control group to be significantly higher than i-PRF group (p<0.001). Although intragroup comparisons there was a significant decrease in the mean probing depth value after 3 months (p<0.05).

There was a statistically significant difference in percentage change between the different groups (p=0.006). The highest reduction in probing depth

TABLE (1) The mean and standard deviation of all clinical parameters and bacterial load of the three groups patients

Parameter / Grouping	Gingival index (%) (Mean±SD)	Probing depth (%) (Mean±SD)	Clinical attachment loss (%) (Mean±SD)	Pg load (%) (Mean±SD)		
				Baseline1 week	1 week – 1 month	Baseline1 month
i-PRF	73.33±19.56[A]	41.90±7.87[A]	44.17±14.95[AB]	49.00±19.00[A]	50.97±18.08[A]	75.18±13.30[A]
aPDT	85.71±17.82[A]	41.50±8.00[A]	52.86±7.56[A]	30.48±17.64[B]	27.92±14.30[B]	49.38±15.89[B]
Control	66.67±16.67[A]	30.95±8.81[B]	36.79±10.94[B]	26.43±14.36[B]	23.06±18.71[B]	43.99±16.83[B]
p-value	0.095ns	0.006*	0.025*	0.004*	<0.001*	<0.001*

Different superscript letters indicate a statistically significant difference within the same horizontal row; significant (p ≤ 0.05) ns; non-significant (p>0.05)*

was found in i-PRF followed by aPDT while the lowest value was found in the control group. Post hoc pairwise comparisons showed that the control group has significantly lower value than the other groups (p<0.001).

Clinical attachment level Baseline intergroup comparison showed no significant difference between the studied groups (p=0.981). After 3 months, there was a significant difference between values of different groups (p=0.022). The greatest attachment gain was found in aPDT followed by i-PRF while the least attachment gain was found in the control group. Post hoc pairwise comparisons showed the value of the control group to be significantly higher than aPDT group (p<0.001) while in intragroup comparisons for all groups, there was a significant decrease in the mean clinical attachment level value i.e attachment gain after 3 months (p<0.05).

Intergroup comparisons of percentage change: There was a significant difference between the different groups (p=0.025). The highest change was found in aPDT (52.86%) attachment gain followed by i-PRF (44.17%) attachment gain while the lowest value was found in the control group (36.79%) attachment gain. Post hoc pairwise comparisons showed aPDT group has a significantly higher value than the control group (p<0.001) as shown in figure (3)
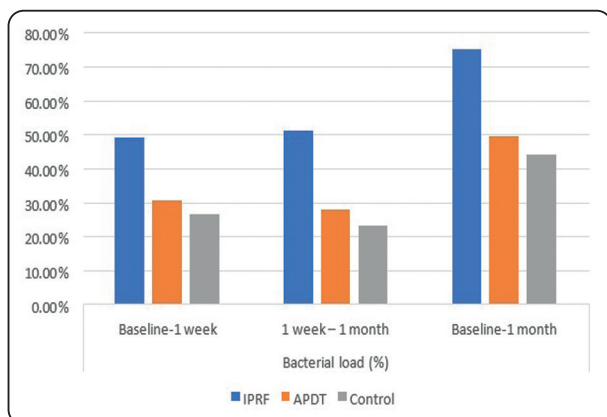

Fig. (3): Bar chart showing mean clinical attachment level percentage change for different groups

III- Microbiological assessment

Bacterial load: (*Pg*)

Intergroup comparisons: At baseline, there was no significant difference between the studied groups (p=0.086). After 1 week and 1 month, there was a significant difference between the different groups (p<0.05). The lowest amount of *Pg* load was found in i-PRF, followed by aPDT while the highest amount of *Pg* load was found in the control group. Post hoc pairwise comparisons showed i-PRF group to have a significantly lower value than the other groups (p<0.001).

Intragroup comparisons: For all groups, there was a significant decrease in the mean *Pg* load values measured at different intervals (p<0.05). The highest value was measured at baseline, followed by 1 week, while the lowest value was measured after 1 month. Post hoc pairwise comparisons were all statistically significant (p<0.001).

Figure (4) show that at all intervals, there was a significant difference between the different groups (p<0.001). The highest change which was found to be 75.18% in i-PRF decrease in bacterial load at the end of the study followed by aPDT 49.38% while the lowest value was found in the control group 43.99%. Post hoc pairwise comparisons showed i-PRF group to have a significantly higher percentage reduction value than the other groups (p<0.001).
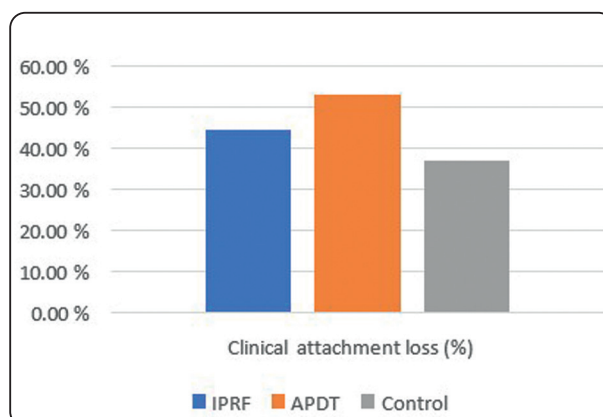

Fig. (4): Bar chart showing mean bacterial load percentage change for different groups

DISCUSSION

Sub-gingival debridement is considered the gold standard of periodontal treatment and its clinical efficacy is well documented in systematic reviews. Meanwhile, previous studies reported that a period of 4–6 weeks may be sufficient to evaluate the effectiveness of non-surgical periodontal therapy in periodontal tissues and that post-treatment recovery occurs in 3–6 months in patients with good mechanical plaque control. In the current study, GCF samples were obtained at baseline, one week and one month postoperatively to distinguish the short term antimicrobial effects of both adjunctive treatments [15].

i-PRF was introduced based on the concept of PRF with added advantage being in an injectable form. It can be utilized alone or combined easily with various biomaterials such as enamel matrix derivative and natural bone mineral. Its protocol is based on the concept that slower and shorter centrifugation results in a higher presence of regenerative cells with higher concentrations of growth factors which can remain beyond 10 days [16].

According to Karde et al., (2017), since i-PRF is autogenous, it decreases the chances of adverse reactions to the implanted material, especially immune-mediated ones. Similar to other types of grafting, it is qualified as a viable option in regenerative procedures. In addition, a study by Miron et al., (2017) revealed that i-PRF showed maximum zone of inhibition around oral microflora.

On the other hand, antimicrobial efficacy of PRP and PRF was performed against *Pg* and *Aa*. It was seen that *Pg* and *Aa* were inhibited by PRP but not by PRF and that's why the current study is testing the ability of i-PRF to inhibit *Pg* **(18)**. aPDT was first utilized in medicine as a method for the treatment of cancer over a century ago. aPDT using a diode laser with a potential new photosensitizer; indocyanine green-loaded nanospheres, may be effective for the clearance of *Pg* from the diseased periodontal pockets as it was suggested by previous studies [19].

Regarding the selection of stage III grade B of periodontitis in the present study, it is considered the common stage that most of the periodontitis patients suffer from as it is related to the middle and old age people group, also moderate rate of progression due to multiple factors such as dental biofilm accumulation, stress and genetic factors **(1)**. In periodontitis patients, it has been recorded that Stage IV periodontitis occurs less frequently than Stage III periodontitis and the number of regions where GCF can be obtained decreases due to tooth loss in these patients [21]. Periodontitis patients with generalized Stage III and Grade B were preferred in the current study due to the disproportionately high damage of periodontal tissues and rapid progress with plaque accumulation in Grade C patients and the inadequate response to non-surgical periodontal therapy [21].

In the current study, the PI was evaluated to monitor patients' compliance, since this parameter is mostly relied on patients. Moreover, another clinical parameters were recorded such as the gingival index, CAL and probing depth with the main aim to assess the effect of the treatment and the healing potential of the patients.

Pathogenic microflora of the dental plaque causes periodontal diseases. Therefore, inflammation control is achieved by removing the dental plaque with initial periodontal treatment and oral hygiene measures. In addition, *Aa* and *Pg* associated with periodontal infections that invade pocket epithelial cells, dentinal tubules and the biofilm in the mouth forms a reservoir. i-PRF and aPDT can be sustained for a period in the periodontal pocket which allow them to reach the dentinal tubules and pocket epithelial cells [22].

The mean percentage change of GI after 3 months was high in aPDT (85.71±17.82), followed by i-PRF (73.33±19.56) and the least was the control group (66.67±16.67), there was no statistical significant difference between the three groups.

On the other hand, there was a statistical significant decrease in the mean GI in all the studied groups after 3 months. This decrease in the GI is due to resolution of the inflammation and reduction in the proinflammatory mediators. This result is in accordance with a study conducted by Monzavi et al., (2016) who demonstrated that a significant reduction in clinical signs of inflammation can be achieved by SRP in combination with aPDT in patients with chronic periodontitis.

Regarding probing depth, results of the current study revealed that there was a statistical significant decrease in the probing depth in all groups after three months. This reduction in PD is due to shrinkage of gingiva and reduction of inflammation.

Results demonstrated that there was no statistical significant difference in the mean probing depth at baseline in the three studied groups. By comparing the mean percentage change in probing depth between the three groups after three months, results showed statistical significant difference in i-PRF and aPDT (41.90±7.87, 41.50±8.00 respectively) when compared to control group (30.95±8.81). This result is due to the effect of the released growth factors, anti-inflammatory mediators from the i-PRF and the oxidative effect from the aPDT. This was in accordance with Srikanth et al., (2015) who revealed that the adjunctive use of ICG resulted in significantly higher change in PD after 3 months of healing than the sites receiving SRP alone.

Contrary to the current study Alwaeli et al., (2015) applied a diode laser with a wavelength of 670 nm and phenothiazine chloride as a photosensitizer and they failed to show encouraging effects in terms of PD reduction. This difference may be due to difference in the type of photosensitizer and diode laser wavelength 670nm used in that study compared to ICG and 940nm wavelength which was used in the present study.

Regarding clinical attachment level, there was a statistical significant decrease in all groups after three months. i.e., attachment gain. This gain is due to healing with long junctional epithelium. By comparing mean percentage change of CAL after three months between groups, there was a greater decrease in attachment level in aPDT group 52.86% attachment gain when compared to i-PRF group 44.17%. Moreover, i-PRF group showed a higher gain in attachment level when compared to control group 36.79%. This result is due to the effect of laser as it acts as a bio stimulation for alkaline phosphatase enzyme that plays a role in encouraging tissue regeneration and also the ability of i-PRF induce rapid angiogenesis of tissues through release of vascular endothelial growth factor (VEGF) and fibroblast growth factor.

This result is in agreement with De Oliveira et al., (2007) who compared SRP with aPDT alone in patients with aggressive periodontitis. Ten patients were treated in a split mouth design. A significant reduction in CAL could be observed in both groups after 3 months with more superiority for aPDT group. Moreover, Srikanth et al., (2015) revealed that the adjunctive use of ICG resulted in a significantly higher reduction in CAL after 3 months of healing than the sites receiving SRP alone.

In another study by Vučković et al., (2020) results demonstrated more CAL gain in i-PRF group than the control group in their study. The greater clinical value of CAL gain may be due to more rapid wound healing, less short-term gingival inflammation, and sustained reduction of periopathogenic bacteria.

On the contrary, another study yielded no significant improvements in CAL gain for SRP in combination with adjunctive aPDT than for SRP alone in treatment of periodontitis using Toluidine blue TBO and diode laser wavelength of 660nm [27]. This result may be due to recording of CAL after 6 months and not 3 months follow up data.

Regarding the microbiological analysis of the *Pg* present within the GCF in the treated sites in the current study, there was a statistical significant decrease in the microbiological load in all groups after one week and one month postoperatively. This

is due to removal of biofilm and hard deposits which is the main habitat for the bacteria. This result is in agreement with that of Nagahara et al., (2013) & Srikanth et al., (2015). The former demonstrated promising bactericidal effect of ICG loaded nanospheres with a 805 nm diode laser irradiation on *Pg*. The latter showed statistically significant reduction of selected bacterial species such as *Pg* and *Aa* when using ICG mediated photodynamic therapy.

At baseline, there was no significant difference in the *Pg* load in the three studied groups. After one week and one month postoperatively, group I (i-PRF) showed greater statistical significant difference favouring reduction in *Pg* when compared to aPDT or the control group. The mean *Pg* load was 2.33 in i-PRF, while it was 5.8 and 7.1 in aPDT and control group respectively. This can be explained on the basis that i-PRF has increased platelet activation and increased numbers of leukocytes formation which can be considered responsible for the higher antimicrobial activity that is related to the presence of antibacterial proteins. These proteins possess a wide spectrum of activity against gram positive and gram negative bacteria, as they initiate the lysis of bacterial cell. This result is similar to Karde et al., (2017) who revealed that i-PRF has maximum antimicrobial efficacy and higher platelet count in comparison to other platelet concentrates.

This result is also in agreement with that of Kour et al., (2018) who had compared three platelet concentrates PRP, PRF, and i-PRF for their antibacterial activity against *Pg* and *Aa*. i-PRF and PRP had showed favorable antimicrobial activity.

There was a marked statistical significant decrease between the mean percentage change of microbiological load in all groups as the i-PRF (75.18±13.30) showed the most reduced microbiological load followed by the aPDT (49.38±15.89) and the least was the control group (43.99±16.83) .This result is due to the good antimicrobial effect released by i-PRF and the oxidative bactericidal effect of aPDT. On the contrary Aydinyurt et al., (2021) had reported that there was no difference between i-PRF and SRP regarding their effect on the bacterial load. This result could be due to missing NSPT in the i-PRF group.

CONCLUSION

Within the limitations of this study, it can be concluded that injectable platelet rich fibrin or antimicrobial photodynamic therapy can be considered an effective adjunct to SRP in routine non-invasive treatment of periodontal disease. Both i-PRF and aPDT showed significant reduction in probing depth when compared to NSPT. aPDT exhibited more gain in CAL and more reduction in GI compared to i-PRF or SRP. I-PRF demonstrated significant reduction in bacterial load of *Pg* compared to aPDT or SRP.

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