ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)

IJDSIR : Dental Publication Service

Available Online at: www.ijdsir.com

Volume – 6, Issue – 3, June - 2023, Page No. : 169 – 182

Efficacy of advanced platelet-rich fibrin (A-PRF) adjunct with diode laser application in periodontal therapy- 3 months clinical study

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Citation of this Article: Preeti Upadhyay, Pragya Tripathi, Vikram Blaggana, Rashi Adhikari, Anamika Singh, Neeru Verma, "Efficacy of advanced platelet-rich fibrin (A-PRF) adjunct with diode laser application in periodontal therapy- 3 months clinical study", IJDSIR- June - 2023, Volume – 6, Issue - 3, P. No. 169 – 182.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Introduction: The periodontal disease is a chronic inflammatory disease, characterized by bacterial etiology and cyclic evolution, which determines a progressive, site-specific destruction of the supporting tissues of the tooth, and proceeds from the superficial periodontium to the deep periodontium (alveolar bone, periodontal ligament, cementum), resulting in typical pathological lesions (periodontal pockets, gingival recessions, vertical and/or horizontal bone resorption, bifurcation lesions). Diode laser-assisted periodontal treatment is superior to SRP alone and serve as a significant adjunctive treatment tool. A-PRF release significantly more total growth factor than PRF. The procedure of preparing A-PRF by converting the centrifugation process to 1,500 rpm for 14 minutes shows more evenly distributed granulocyte neutrophils and loose fibrin matrix.

Neutrophil granulocytes have soft and hard tissue regeneration capabilities, direct monocytes to phagocytosis, and produce proteases such as MMP9 for wound healing process.

Objectives of Study: Efficacy of advanced platelet-rich fibrin (A-PRF) adjunct with diode laser application in periodontal therapy- 3 months clinical study

Materials and Method: A 3 months randomized controlled clinical trial. 15 sites having 4 – 6 mm of periodontal pocket depth were selected for the study. All 15 sites were treated with A- PRF and diode laser application. The clinical parameters of the study were Probing depth (PD) ,Clinical Attachment Level (CAL), Gingival index – Loe and silness, Plaque index (PI) – silness and Loe H (1964) were recorded at Baseline and at 3 months.

Results: PI, GI, PD and CAL has shown statistically significant results via using A-PRF and laser therapy.

Conclusion: This study concluded that, the therapeutic application of A-PRF adjunct to Laser curettage showed marked reduction and provide beneficial effect in terms of PI, GI, PD and CAL.

Keywords: A - PRF, Diode Laser , Laser Curettage, Periodontal pocket depth

Introduction

Periodontitis is an inflammatory disease of periodontal tissue that results in damage to periodontal ligament and alveolar bone[1]. One of the clinical signs of periodontitis is the presence of a periodontal pocket and CAL. Periodontal pockets are divided into suprabony pocket and infrabony pocket.

The primary goal of periodontal treatment is to regenerate periodontal tissue[9]. Periodontal tissue regeneration is the formation of new bone, cementum, and new periodontal ligaments on tooth root surfaces that are damaged to restore anatomy and function[10]. The clinical parameters for evaluating the success of periodontal regeneration are probing depth (PD), attachment loss, and bone height[8]. Bone height can be seen through radiographic examination at 3 - 6 months[11]. Ideal periodontal tissue regeneration is to improve periodontal and bone attachment, reduce pocket depth, and little gingival recession[12]. Some types of regenerative periodontal treatment are root conditioning, addition of bone graft, guided tissue regeneration (GTR), a combination of GTR-bone graft, and the addition of growth factor[13]. Growth factors that contribute to periodontal regeneration include platelet-derived growth factor (PDGF), transforming growth factor (TGF-β), and insulin-like growth factor (IGF)[14].

The use of PRF in OFD treatment is to enhance tissue regeneration in the treatment of intrabody pocket[15]. Platelet rich fibrin (PRF) is a second-generation platelet concentrate[16]. Which is processed with whole blood taken from a patient fed into a 10 ml tube and centrifuged immediately at 2,700 rpm, 12 mins, with PRF results in clot in the middle between acellular plasma and red blood cells[17,18,19].

Platelet rich fibrin contains leukocytes, platelets, and growth factors contained in a three-dimensional fibrin matrix that acts as a scaffold[20], thereby slowing the release of growth factors during wound healing[16]. Some growth factors that can be found in PRF include PDGF, vascular endothelial growth factor (VEGF), TGF-β, IGF-1, IGF-2, and epidermal growth factor (EGF)[20,21].

Some clinical applications of PRF are socket preservation after extraction, gingival recession treatment, intrabody defect regeneration, and sinus elevation[15]. Treatment of intrabody defects by combining OFD and PRF gives better results than OFD alone[22]. A study showed that the administration of demineralized freeze-dried bone allograft (DFDBA) as

graft material in the treatment of intrabody pockets gave no significant difference with PRF[10].

Advanced platelet-rich fibrin (A-PRF) is a further development of PRF by using the concept of lower rotational speed. Research on the effect of centrifugation forces on PRF protocol showed centrifugation pressure has an effect on cell distribution[23]. Leukocytes in the PRF are mostly present at the bottom of the tube, due to centrifugation pressure. The procedure of preparing A-PRF by converting the centrifugation process to 1,500 rpm for 14 minutes shows more evenly distributed granulocyte neutrophils16 and looser fibrin matrix. Neutrophil granulocytes have soft and hard tissue regeneration capabilities, direct monocytes to phagocytosis, and produce proteases such as MMP9 for wound healing process[23].

A study comparing growth factor release in PRP, PRF, and A-PRF concluded that A-PRF released significantly more total factor growth than PRF[15]. Research comparing PRF and A-PRF is limited to laboratory and animal studies, so further research with human subjects is needed.

Although a number of risk factors can influence the start, progression and prognosis of periodontitis (age, sex, cigarette smoking, hormonal changes, immune system disorders, systemic diseases, diabetes, stress) [24,25,26], the main etiological factor is represented by dental plaque and in particular by anaerobic gram-negative bacilli[27]. For that reason, the first phase of periodontal treatment is always represented by the initial preparation, which is a type of etiological, non-surgical therapy, which recognizes as primary aims the elimination or reduction of bacterial infection and the control of periodontal plaque-associated inflammation[28]. We choose to use laser therapy to personally verify the actual efficiency, where the literature talks to us for a long time, of this treatment option in the treatment of periodontally compromised patients and to evaluate their satisfaction. In addition to SRP the use of laser therapy, as shown by several studies, appears to improve and facilitate the healing of treated sites. Recently, Yilmaz et al. (2013) have shown that in the sites treated with the use of laser Er:YAG in addition to SRP, reached statistically significant improvements in terms of attachment gain and reduction in PD compared to sites treated with only srp or only topical gaseous ozone[29]. Other study that compares, like treatment options, Nd:YAG laser alone, SRP alone, and Nd:Yag plus SRP has demonstrated that the last option of treatment is the best in term of reduction of PI, GI, PPD and GCF volume values[30]. Another type of laser (KTP: potassium-titanyl-phosphate) has shown to be a significant help in SRP, like demonstrated in a study of Romeo et al. (2010). In this study, treated sites are divided into four groups and the best results were obtained in the groups in which the laser has been used[31]. A diode laser has a wavelength of 810-980 Nm, and there are many different laser used in periodontology with a different wavelength; Ktp laser has a wavelength of 532 Nm, Nd:YAG laser of 1064 Nm, Er:Yag of 2940 Nm and CO2 laser of 9600-10600 Nm[32]. We used diode laser cause has an easier learning curve and a more affordable price than others.

Materials And Methods

Source of data: The study was conducted on patients visiting the outpatient department of Periodontology, Inderprastha Dental College and Hospital, Ghaziabad, Uttar Pradesh with clinical findings Periodontal pocket depth (4-6mm) were screened for possible participation in this study. 15 sites were identified with 4-6mm ppd and selected for the non-surgical treatment. After an explanation of the proposed study criteria, including treatments and potential risk and benefits, all participants

signed a consent form prior to surgery. The study was approved by ethical committee of institute (Institutional Review Broad), Annexure I (Ethical Clearance Certificate).

Selection Criteria

Inclusion criteria

• Patients aged between 20 to 55 years.

• Both male and female patients.

• Patients maintaining good oral hygiene with plaque index (PI) (score<1.0).

• Patients willing to participate in the study by giving written consent and ready to comply with maintenance program.

• Systemically healthy patients with one or more sites having 4-6 mm PPD and those who can understand and follow oral hygiene instructions properly.

Exclusion criteria

- Debilitating systemic or infectious diseases (HIV or hepatitis) or any diseases that affect the periodontium.
- A known allergy to any of the materials used in the study.
- Poor compliance or failure to maintain good oral hygiene.
- Pregnancy or lactation.
- Use of tobacco products through smoking or a smokeless tobacco habit.
- Patients taking immunosuppressive drugs or corticosteroids which may compromise the treatment outcome.
- Failure to sign the informed consent.

Materials used

A-PRF: Platelet rich fibrin is a second-generation therapeutic platelet concentrate, the first being the platelet rich plasma. Prf was first described by choukroun et al. In the

Year 2001.

Advanced Platelet Rich Fibrin (A-PRF) is a new advanced technology that helps heal wounds anywhere in the body, using the patient's own blood. A-PRF shows more neutrophilic granules in distal part mostly at red blood cells-buffer coat interface. Because in the process of A-PRF lower centrifugation, the number of leukocytes obtained was higher because it did not sediment to the bottom of tube. Leukocytes play an important role in bone healing, especially macrophages. Macrophages improve the differentiation of osteoblasts that increase bone formation and promote tissue integration. Leukocytes also prevent pathogen infiltration thereby reducing the risk of infection. Another modification of A-PRF has been suggested by Kobayashi & co-workers in 2016 where they have reduced the centrifugation time to 1300 rpm for 8 minutes. They called this modification as A-PRF+ and suggested that less time would result in a decrease in the amount of forces that the cells of the blood would be exposed to & hence, would increase the number of cells contained in the PRF matrix.[31] The number of growth factors produced by A-PRF, such as PDGF, TGF, and VEGF, was significantly higher than that by PRF.

VEGF plays an important role in the process of angiogenesis that stimulates the proliferation and migration of endothelial cells and maintains blood vessels formation. PDGF helps tissue regeneration and increases osteoblast precursor cells to stimulate bone regeneration.

TGF increases the proliferation of mesenchymal cells, collects osteoblast precursor cells, and osteoblast differentiation. Advanced platelet-rich fibrin (A-PRF) is a further development of PRF by using the concept of lower rotational speed. A research on the effect of centrifugation forces on PRF protocol showed centrifugation pressure has an effect on cell distribution.Leukocytes in the PRF are mostly present at the bottom of the tube, due to centrifugation pressure. The procedure of preparing A-PRF by converting the centrifugation process to 1,500 rpm for 14 minutes shows more evenly distributed granulocyte neutrophils and looser fibrin matrix. Neutrophil granulocytes have soft and hard tissue regeneration capabilities, direct monocytes to phagocytosis, and produce proteases such as MMP9 for wound healing process.

Diode laser

Diode is a solid active medium laser, manufactured from semiconductor crystals using some combination of aluminium or indium, gallium, and arsenic and depending on wavelength either aluminium or indium is used.

Benefits from the use of diode laser in addition to the traditional procedures of srp in the treatment of periodontal pockets like bactericidal effect; curettage effect; bio-stimulating effect. Combining laser therapy with conventional procedures is more effective decontamination of the pocket, with also a recolonization slower than sites treated only mechanically debrided.

According to kreisler (2005) the greatest reduction in the degree of tooth mobility and probing depth in the group of patients who underwent srp + laser therapy can be mainly attributed not to the killing of bacteria in periodontal pockets, but it helps in complete removal of infected sulcular epi thel ium lining, which leads to proper healing of tissue.

Figure 1: Pre-Operative Probing Depth

Figure 2: Diode Laser Curettage Being Performed

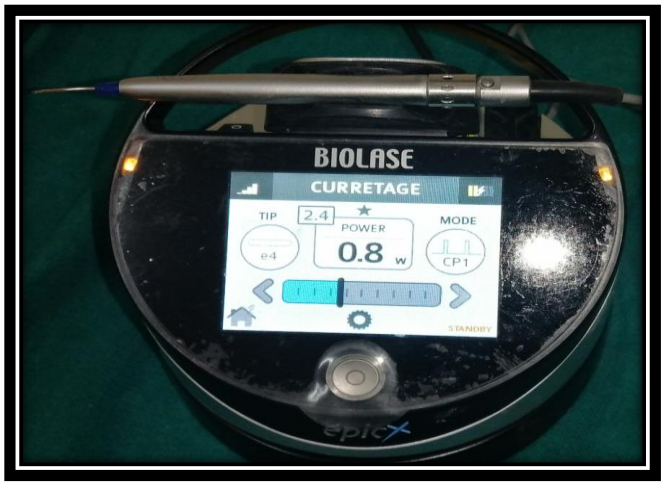


Figure 3: Diode Laser

Figure 4: A- PRF Made

Figure 5: PRF Membrane Placed

Figure 6 : COE – PAK Placed

Results and Observations

Clinical Parameters

Plaque Index (Pi)

The mean score of plaque index (pi) ascertained clinically at baseline and 3 months are statistically non-significant ($p>0.05$). The mean score at baseline (0.8 ± 0.140791) and at 3 months (0.666 ± 0.106249) (table i and graph 1).

Gingival Index (Gi)

The Mean Score of Gingival Index (Gi) Ascertained Clinically at Baseline And 3 Months Are Statistically Non-Significant ($P>0.05$). The Mean Score at Baseline (0.8 ± 0.108321) And At 3 Months (0.56 ± 0.59333) (Table Ii and Graph 2).

Probing Depth (Pd)

The mean score of probing depth (pd) ascertained clinically at baseline and 3 months are statistically non-significant ($p>0.05$)). The mean score at baseline (5.13333 ± 0.5933) (table iii and graph 3).

Clinical Attachment Level (Cal)

The mean score of clinical attachment level (cal) ascertained clinically at baseline and 3 months are statistically non-significant ($p>0.05$) the mean score at baseline **(2 +** 2.828427) (table iv and graph 4).

Table 1: Distribution of Mean And S.D Of Pi at Different Time Intervals

	N	Mean	SD	P - Value
Baseline PI	15	0.8	0.140791	0.03
3 Months PI	15	0.66666	0.106249	

NS Not significant p>0.05, *Significant p<0.05, ** Highly significant <0.01

Table 2: Distribution of mean and S.D of GI at different time intervals.

	N	Mean	SD	P- Value
Baseline GI	15	0.8	0.108321	0.0001
3 Months GI	15	0.56	0.59333	

NS Not significant p>0.05, *Significant p<0.05, ** Highly significant <0.01

Table 3: Distribution of mean and S.D of PD at different time intervals.

	N	Mean	SD	P - Value
Baseline PD	15	5.13333	0.5933	0.0001
3 Months PD	15	3.5	0.718	

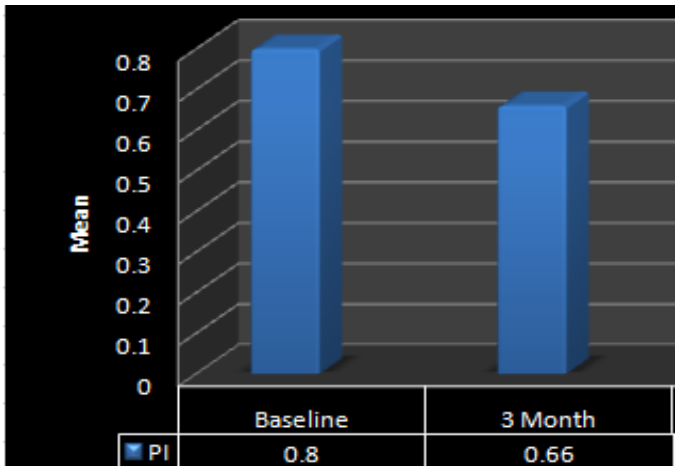
NS Not significant p>0.05, *Significant p<0.05, ** Highly significant <0.01

Table 4: Distribution of mean and S.D of CAL at different time intervals.

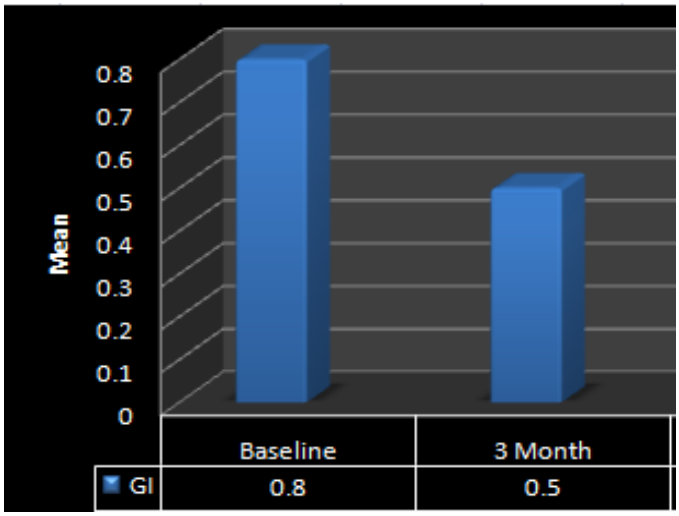
	N	Mean	SD	P - Value
Baseline CAL	15	2	2.828427	0.02
3 Months CAL	15	1.6	2.274496	

NS Not significant p>0.05, *Significant p<0.05, ** Highly significant <0.01.

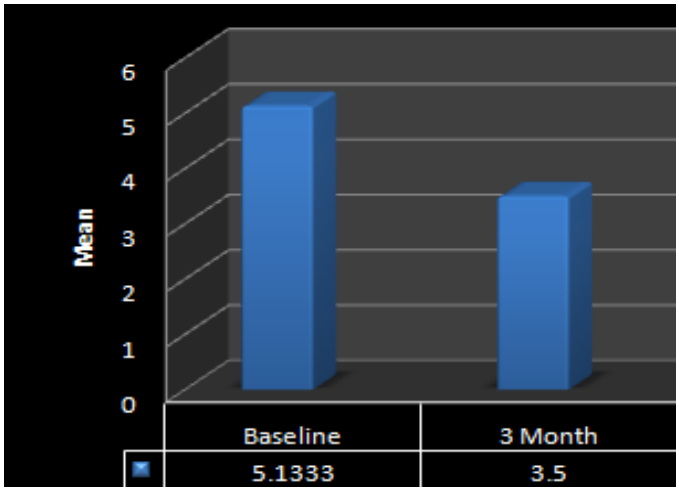
Graph 1 : Comparison of mean PI at different time points



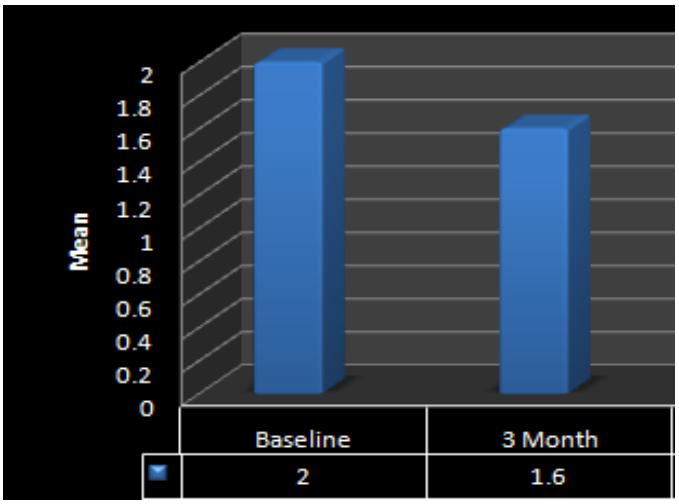
Graph 2 : Comparison of mean GI at different time points



Graph 3: Comparison of mean PD at different time points



Graph 4: Comparison of mean CAL at different time points



Discussion

Despite NSPT being the worldwide acceptable treatment regimen of CP, it has been assessed critically on many circumstances over the past decade for its limitations. As a result of this, various assisted treatment modalities have emerged. Hence, the utilisation of A-PRF & diode laser-assisted treatment as an adjunct therapy, which can be beneficial in NSPT cases unable to offer adequate optimal outcome or in compromised medical health conditions.

The present in vivo study constituted assessment of clinical parameters viz. PI, GI, PD and CAL at Baseline and 3 months. PI and GI is reduced at 3 months it indicates that all participants were maintaining optimum oral hygiene

The results showed PD and CAL reduction in the study at observation time, on day 30 and day 90. This means there was an improvement in clinical conditions. Acc ording to Mani R et al[56] 2015 & Raja S et al[57] 2009 PD and CAL reduction is influenced by growth factor produced by A-PRF, such as PDGF, EGF, and IGF-1 which act as homeostasis factor, increase proliferation and migration of periodontal fibroblasts, and prevent periodontal fibroblast apoptosis. This allows better tissue regeneration with A-PRF As we known, PDGF, VEGF, and IGF-1 increase the proliferation of fibroblasts and angioblasts, the synthesis of extracellular matrix, and angiogenesis process.

In Fujioka-Kobayashi M et al [58] 2017 study abundant amount of neutrophil granulocytes in A-PRF also affects macrophage differentiation, resulting in the regeneration of hard and soft tissues. According to Prabhu P et al[59] study 2014 by 4th day, proliferation of fibroblasts and angioblasts occurs, followed by the formation of new junctional epithelium at the end of the 2nd week. In the end of week 4 to month 3, the process of tissue maturation and bone remodeling occurs.

According to study by Newman MG, Takei HH, Klokkevold PR. Carranza's[60] 2012 Hard tissue regeneration is affected by the association between RANK and RANKL or OPG. RANK binding to OPG may inhibit osteoclast activation and differentiation processes and increase osteoblast proliferation. The results suggest that A-PRF may increase OPG secretion.

In study by Ghanaati S[61] 2014 in the process of A-PRF formation with lower centrifugation, the number of leukocytes obtained was higher because it did not sediment to the bottom of tube. Leukocytes

Play an important role in bone healing, especially macrophages. Macrophages improve the differentiation of osteoblasts that increase bone formation and promote tissue integration.

Fujioka-Kobayashi M[62] 2017 in their study concluded that Leukocytes also prevent pathogen infiltration thereby reducing the risk of infection.

Kobayashi E[63] 2016 in his study stated that the number of growth factors produced by A-PRF, such as PDGF, TGF, and VEGF, was significantly higher than that by PRF. VEGF plays an important role in the process of angiogenesis that stimulates the proliferation and

migration of endothelial cells and maintains blood vessels formation. VEGF also plays a role in bone formation by increasing the migration, proliferation, and differentiation of osteoblasts.

Yun YR[64] 2012 in his study mentioned that PDGF helps tissue regeneration and increases osteoblast precursor cells to stimulate bone regeneration.

Devescovi V in 2008 concluded that TGF increases the proliferation of mesenchymal cells, collects osteoblast precursor cells, and osteoblast differentiation.

Also Borrajo JL,Diode et al [65] 2004 , lebeau J.et al [66] 2012 concluded that laser in adjunct to A-PRF in the treatment of periodontal pockets provide bactericidal ,curettage , bio-stimulating effect.

According to Kreisler[69](2005) the greatest reduction in the degree of tooth mobility and probing depth in the group of patients who underwent SRP + laser therapy can be mainly attributed not to the killing of bacteria in periodontal pockets, but rather to the complete removal of infected sulcular epi thel ium, which leads to greater attack of the connective tissue. According to the studies of Benedicenti [70] (2008), the laser would stimulate mitochondrial activity, with a production of intracellular ATP >22% in irradiated cells compared to those not exposed to radiant energy, resulting in a halving of the times of cell duplication ,the process is Biostimulant Effect.

In an in vitro study of Soares et al. (2013) it has been demonstrated that low-level laser irradiation (LLLI) has a positive

Stimulatory effect on the proliferation of human periodontal ligament stem cells.

Conlan [71] (1996) found an increase of about 50% of the proliferation and differentiation of fibroblasts and collagen synthesis within the periodontal ligament , which process, according to Choi [72] (2010) begins to manifest between the next 24-48 hours to laser treatment, and intensifies especially after the 72 hours ; all these reactions accelerate the healing process and encourages a speedy recovery in clinical attachment.

Laser acts only as an adjunct to etiological non-surgical periodontal therapy, not being able to replace traditional mechanical procedures of SRP; In this regard, the study of Kamma et al. [73] (2009) showed that combining mechanical treatment (SRP) with diode laser therapy produces better results than the laser therapy alone, both in clinical (probing depth and clinical attachment level) and bacteriological terms (total bacterial count of periodontal pathogens) .

Conclusion

This randomized controlled clinical study evaluated "Efficacy of advanced platelet-rich fibrin (A-PRF) adjunct with diode laser application in periodontal therapy- 3 months clinical study''.

The clinical parameters were evaluated at baseline and 3 months for GI, PI, PD, CAL.

The present study resulted in no post-operative discomfort to the patient and healing was uneventful. The PI score was <1 at 3 months post operatively, thereby indicating favourable environment for healing of the periodontium throughout the period of study.

We conclude that Laser acts only as an adjunct to etiological non-surgical periodontal therapy, not being able to replace traditional mechanical procedures of SRP; combining mechanical treatment (SRP) with diode laser therapy produces better results than the laser therapy alone, both in clinical (probing depth and clinical attachment level) and bacteriological terms (total bacterial count of periodontal pathogens) .

Laser in adjunct to A-PRF in the treatment of periodontal pockets provide bactericidal , bio-stimulating effect.

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