"An evaluation of clinical effects of i-PRF as an adjunctive to non-surgical periodontal therapy versus non-surgical periodontal therapy alone in treatment of chronic periodontitis patients – a split mouth randomized controlled clinical trial"

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Aim- *The aim of the present study is to investigate whether there is difference in therapeutic effect between initial treatments of chronic periodontitis i.e. scaling and rootplanning (SRP) alone and SRP in conjunction with injectable platelet-rich fibrin (I- PRF) application, comparing clinical parameters after 6 weeks.*
Materials &method- *10 patients with chronic moderate to severe periodontitis having minimum 2 sites with PPD ≥5mm were selected from the OPD of the department of periodontology. After phase I therapy two sites were randomly divided as test and control group. Test site is treatedwith i prf and other site was considered as control group.*
Results- *compared to baseline, both treatment modalities demonstrated an improvement in investigate clinical parameters .the mean value CAL decreased from 6.2± 0.63 to 5.1±0.65 in test group while in control group it was reduced from 6.3±0.94 to 5.6±0.69. Total reduction of 1.1±0.31 in test group while 0.7±0.34 in control group similarly the corresponding values for BOP, PI and PPD showed statistically significant difference between the groups. The collected data is compared and analyzed by applying suitable statistical software and the results are calculated.*
Conclusion- Regardless the limited number of patients in the study, initial periodontal therapy in conjunction with injectable platelet-rich fibrin proved to display significant improvement in all clinical parameters compared to initial periodontal therapy alone.

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I.   Introduction

Periodontitis may be a chronic multifactorial disease, characterized by the progressive destruction of periodontal supporting tissues. Periodontitis presents an inflammation developed by disorders of the host immune response to the Infections caused by periodonto pathogens [1]. Chronic periodontitis represents a sort of destructive periodontitis that's generally characterized by slow progression [2]. The World Workshop on the Classification of periodontal And peri-implant disease and Condition In 2017 agreed that the diseasepreviously described as "chronic" or "aggressive" will Be grouped under a category "periodontitis"[3]. Periodontitis was regarded as the sixth most prevalent disease globally in 2010 and it affected approximately 50% of the adult population worldwide in 2014. [4]

Considering the increased prevalence rate it is necessary to upgrade theknowledge and techniques for treatment of periodontal diseases.

Nonsurgical periodontal therapy (NSPT) is the cornerstone of periodontaltherapy and therefore the first recommended approach to the control of periodontalinfections. It is also known as "Cause related therapy," [5] NSPT has evolved over the years, it is still considered to be the "gold standard" to which other treatment methods are compared.[6,7] However, conventional mechanical debridement procedures don't remove all periodontopathic bacteria from the subgingival environment, especially those in inaccessible areas like furcations, grooves, concavities, and deep pockets. It appears that the effects of mechanical therapy might be augmented using adjunctive agents which may further suppress theremaining pathogens or enhance the healing

of the tissues.

The periodontal wound healing after SRP usually induces the development of a long junctional epithelium, causing recurrence of periodontal pockets. To enhance the method of regeneration, the adjunctive therapeutic procedures are added to the traditional therapy since the top of the last century. Over the past 3 decades plateletshave been applied in dentistry these autologous regenerative tools are concentrated suspensions of supra-physiological amount of growth factors (GFs) and, when appliedlocally, can induce soft and hard tissue regeneration [8]. Various GFs and cytokines Are reserved in platelets, which are vital in wound repair and homeostasis [8]. The periodontal wound healing process implies a series of cell-to-cell interactions and molecular signals that are primarily mediated by cytokines and GFs. GFs control enhancing collagen production, cell proliferation and differentiation, as well as blood vessel formation [9]. Platelet concentrates have advanced from the first generation. platelet-rich plasma (PRP) to the second generation platelet-rich fibrin (PRF). PRF, developed by Choukroun et al. [10], enables a scaffold enriched with platelets and GFs, as well as leukocytes. The concentrate is generated from a blood harvest without any artificial biochemical modifications and anticoagulants.

Since the quality PRF isn't entirely appropriate for injection,a replacement injectable formulation of PRF (termed I-PRF) enables easier use of the platelet concentrate during a liquid state. It maintains its liquid viscosity for about 15 minutesafter being generated during centrifugation, [11, 12].

So far, patients with CHRONIC PERIODONTITS have not been treated with IPRF during SRP treatment. Therefore, the aim of this study was to work out the consequences of local I-PRF application in conjunction with SRP, compared to application of SRP alone, on periodontal clinical parameters of chronic periodontits.

II. Methodology

The randomized, split-mouth, controlled clinical trial was carried out in the department of periodontology SMBT dental college on patients seeking treatment for chronic periodontitis. The trial evaluated clinical periodontal outcomes after the initialtreatment with or without conjunction of I-PRF. This trial had been approved by the Ethics Committee of the Department of Periodontology, SMBT Dental College After being informed of the research methods.

12 patients with chronic periodontitis was included in the study. Two patients out of the 12 recruited for the study, failed to continue the follow-ups and were excluded from the study. Selection was done on the basis of the inclusion and exclusion criteria

Inclusion criteria
- Patients in the age group of 30-50 years.
- Both male and female Patients with chronic periodontitis.
- Patients having minimum 2 sites with pocket probing depth $\geq$ 5mm after SRP.
- Patients willing to give written informed consent

Exclusion criteria
- Patients having general contraindications to surgery.
- Patients with active systemic diseases and having habit of smoking
- Patients taking medications or having treatment which may affect mucosalhealing.
- Patients who were on antibiotic therapy since past 6 months.

Clinical charting was performed immediately before the treatment and after 6 weeks. The research included the site specific examination of all teeth and tooth, except the third molars. The following variables were recorded from the mesio-buccal, mid-buccal, disto-buccal, disto-lingual, mid-lingual, and mesio-lingual surfaces ofeach tooth: CAL, PPD, BOP, and PI. The examiner, a specialist of periodontology, performed and noted all the examinations. Prior to the start of thestudy and 6 weeks later.

Treatment procedure
Full mouth scaling and root planning was done in all the patient at baseline minimum 2 sites in each patient which was divided randomly as site A and site B
.Site A was treated with SRP and i-PRF as an adjunt to it while site B was treatedwith SRP alone.

Preparation of i-PRF
Blood samples were taken into two 10 ml tubes and prepared for I-PRF preparation. The blood without anticoagulant was then centrifuged at 700 rpm forthree minutes (60 g) at room temperature by a Remi R-8C Laboratory Centrifugeprocesser. The upper liquid layer was taken as I-PRF by using a syringe.

Afterwards, by injecting i-PRF into periodontal pockets the i-PRF was applied in one quadrant (study group) of the chosen jaw (mandible or maxilla), whereas the physiological saline was injected in the opposite side (control group). Treatment allocation was decided by a toss of a coin.

Statistical analysis

Data entries were done in Microsoft Office Excel 2010 and analyses of results were done using Statistical product and service solution (SPSS) version 21 software. Descriptive statistics such as mean and standard deviation were calculated. Unpaired t test was used to compare between both studies groups in relation to periodontal parameters at baseline and 6 weeks post-operative. Paired ttest was used to compare changes in periodontal parameters from baseline to 6 weeks post-operative in each group. The p value was fixed at 0.05.

III. Results

All the patients' tooth sites did not display any clinical signs of deterioration after 6 Week's period. The mean age was 39.2 ±4.10 years and maximum was 48 years.(table no 1,fig 1) At baseline, none of the assessed clinical parameters showed a statistically significant difference between the study and control groups.

Plaque index and bleeding on probing

The results of the mean plaque index and bleeding on probing of the two groups at the baseline, 6th week are presented in Table 2 and Fig. 2. The reduction in bleeding on probing of Group A were significantly higher than the mean bleeding on probing of Group B at the 6th week examination (P < 0.024). The mean reduction in the plaque index was non-significant between group A and group B. (P=1)(table no 3 fig.3)

Probing measurements

Table 4 presents the summary results for probing depth (PD) and clinical attachment loss (CAL). At baseline mean PPD was 5.6 ±0.69 in group A and 5.5 ±0.7 in group B. A statistically significant decrease was observed after treatment at 6 weeks in both groups. The mean reduction of 1.85±0.41 in test and 1.4±0.31 in control group. Showing more reduction in test group. At the baseline, the mean CAL was 6.2±0.63 in group A and 6.3±0.94 in group B. A statistically significant gain of attachment (Table 5 and Fig 5) was observed at 6 weeks after therapy. The mean value of CAL decreased from 6.2 ± 0.63 to 5.1±0.65 in test group while in control group it was reduced from 6.3±0.94 to 5.6±0.69, total reduction of 1.1±0.31 in test group while 0.7±0.34 (table no 5) in control group. Showing more reduction in test group. There was significant reduction in the plaque index from baseline to 6 weeks in both the groups.(table no 2,fig2) Reduction in bleeding on probing was from 0.9±0.31 to 0.2±0.42 in the test group while from 0.9±0.31 to 0.7±0.48 in control group showing more reduction in test group.(table no 3 fig 3)

IV. Discussion

Long-term improvement in clinically measured parameters is the prime aim of the periodontal therapy. This randomized clinical trial with a split-mouth design displayed the difference between the effects of SRP in conjunction with I-PRF *vs.* SRP alone in terms of changing clinical periodontal outcomes during the initial treatment of chronic periodontitis.

The purpose of SRP is to remove local irritants such as calculus from the surfaces of the teeth and to minimize tooth surface roughness which may facilitate the accumulation of local irritants around the teeth.[13] However, the non-surgical mechanical treatment of root surfaces does not necessarily eliminate all of the pathogens harboured in the sub gingival environment [14,15]. This is particularly true for deep periodontal pockets that significantly hamper the effectiveness of non- surgical procedures. It was reported that in pockets with probing depths (PDs) >4 mm, up to 66% of the instrumented root surfaces retained plaque and calculus.[16,17,18]

Hence antibiotics and antiseptics were administered systemically and locally[19] have been used successfully to treat moderate to severe periodontal disease. Over the years, the conventional therapy of periodontitis (SRP) has been enhanced by using various adjunctive therapies, mostly by systemically or locally administered antibiotics and antiseptics [20] since their use involves some risk, they should be prescribed only for specific situations under optimal conditions. Although the influence of nonsurgical use of lasers on the initial treatment of chronic periodontitis has been considered recently, some studies have shown that its impact on PPD and CAL reduction is less effective than that of antibiotics [20].

This research is currently focused on novel adjunctive regenerative methods of chronic periodontitis treatment. A liquid injectable form of platelet concentrate known as i-PRF was discovered in 2006 by Choukroun, but till now only the PRFin the form of fibrin membrane was applied during the surgical therapy of chronic periodontitis. For the first time, i- PRF was used as an adjunt to SRP in treatment of chronic periodontitis in the study done by Mila at el in the year 2020.

The obtained results of current study showed that both therapeutic modalities could result in

statistically significant improvement of all explored clinical parameters 6 weeks after initiating the therapy. Clinical findings of the study is in accordance with the study done by Mila et al. At baseline, no significant differences in terms of PPD and CAL were recorded between the two groups.

After 6 weeks the positive clinical outcomes seen in control group which correspond with the previous findings concerning clinical efficacy of SRP in treatment of chronic periodontitis. This indicates that in subjects with chronic periodontitis, SRP was successful in reducing PPD and improving CAL [21]All the patients were trained to maintain oral hygiene regularly. This might have improved the clinical parameters in both groups throughout the study period.

I-PRF is suitable for periodontal pocket application due to its advantage of being in a liquid form. The injectable form of PRF preparation is based on a slower and shorter centrifugation spin. Moreover, this protocol of centrifugation leads to a higher presence of regenerative cells with higher concentration of GFs, and cytokines, which together may enhance the healing potential of both bone and softtissues [22]

CAL is used in clinical trials to examine various therapeutic modalities that could either reduce the progression of periodontal disease or enable the regeneration of supporting structures. In this study, the progress was made in reducing CAL in the test group more than in the control group 6 weeks after the initial treatment. The previous systematic reviews on SRP with different adjuncts, showing that a three month therapy leads to the CAL value ranging 0.08–1 mm [23, 24]. The results demonstrated CAL gain by much as 1.1 mm in test group and 0.7 in control group representing better outcome in test group with i-PRF compared to the control group after SRP.

The greater clinical value of CAL gain may be due to more rapid wound healing, less short-term gingival inflammation, and sustained reduction of periopathogenicbacteria [25].

IPRF contains more GFs than PRF, which is six to seven times more loaded with GFs than PRP shown in the study done by Miron et al. [26]. The use of i-PRF enabled due to the fact that after a short period of time, approximately 15 minutes,I-PRF is formed into a matrix scaffold [26]. The scaffold was proved to have a direct impact on the ability of human gingival fibroblasts to migrate, proliferate, release additional GFs and periodontal ligament cell growth, as well as to increase the differentiation of osteoblasts [27]. By preventing the down-growth of junctional epithelium to the root surfaces and suppressing its interference between the root and soft tissue, a new attachment on root surfaces can be formed.

Furthermore, antimicrobial and anti-inflammatory effects of PRF have also been described [28]. Dohan et al. [29] stated that PRF has immunological and antibacterial properties due to its leukocyte degranulation, and possess some cytokines that may induce angiogenesis and pro/anti-inflammatory reactions. The decrease of microorganism concentration in this area results in reducing inflammation. Reducing the inflammation level brings about the decrease of PPD,BOP values.

PPD in the study group was reduced by 1.85 mm after a 6weeks period, while thecontrol group showed a significantly less reduction in PPD ($p < 0.05$). BOP was also reduced in both groups after 6 weeks along with reduction in PI after three months and the improvement in oral hygiene.

V.   Conclusion

Regardless of the limited number of patients, the results of the present study indicated that local application of IPRF in conjunction with SRP,compared to SRP alone, had significant effect on periodontal clinical parameters in the treatment of CP.

Acknowledgement

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Age distribution in group A and B table 1 ,fig 1

| Mean	SD	S.E.	Minimum	Maximum
39.2	4.10	1.29	35.0	48.0
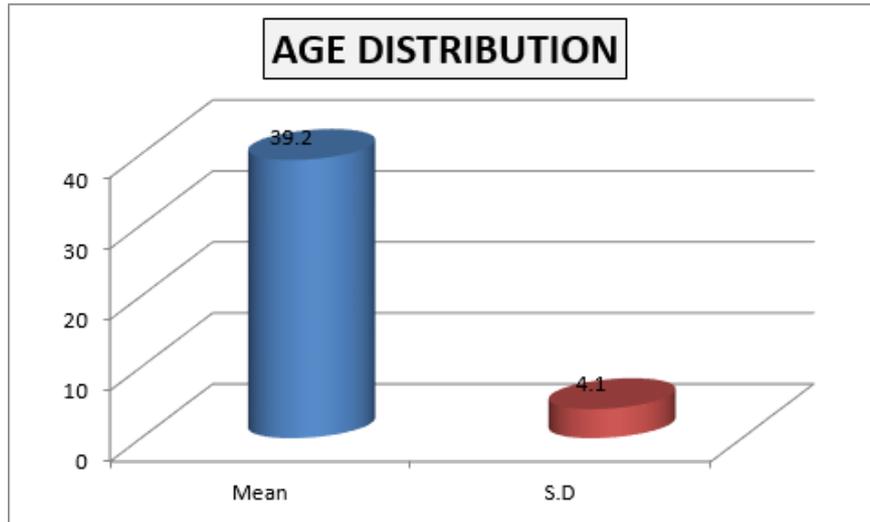
Comparison of mean plaque index between group A and group B table no 2,fig 2

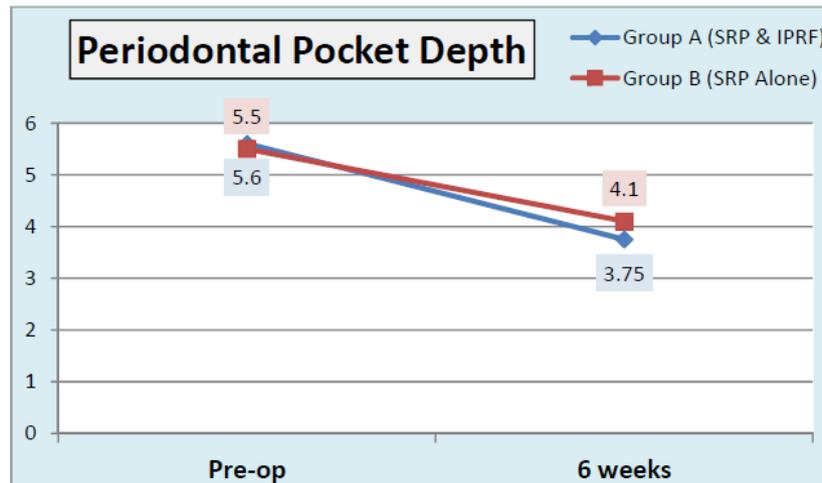| Plaque Index	Group A (SRP &IPRF)	Group B (SRP Alone)	Unpaired 't' test	P value, Significance
Pre-op	1.77 (0.55)	1.77 (0.55)	t =0.00	p =1.000
6 weeks	0.82 (0.37)	0.82 (0.37)	t =0.000	p =1.000
Reduction/ Change in PI	0.95 (0.79)	0.95 (0.79)	t =0.000	p=1.000
Paired 't' test value (Pre vs 6 weeks)	t =4.471	t =4.471		
p value, Significance	p<0.001**	p<0.001**		
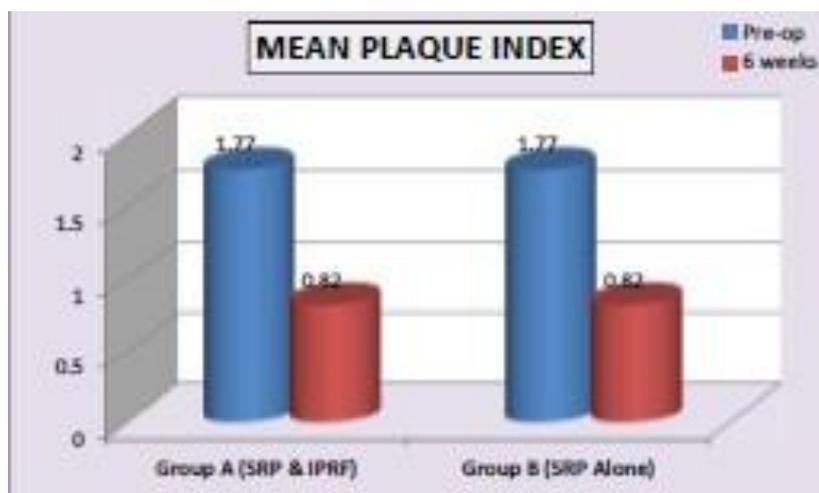
Comparison of mean bleeding index between group A and group B table 3 and fig3

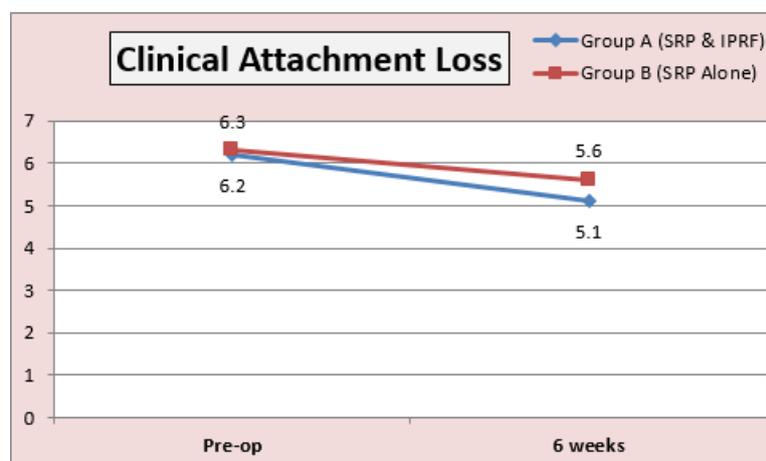| BOP	Group A (SRP &IPRF)	Group B (SRP Alone)	Unpaired 't' test	P value, Significance
Pre-op	0.9 (0.31)	0.9 (0.31)	t = 0.00	p =1.00
6 weeks	0.2 (0.42)	0.7 (0.48)	t =-2.466	p =0.024*
Paired 't' test value	t = 4.2	t = 1.095		
p value, Significance	p =0.001*	p =0.288		
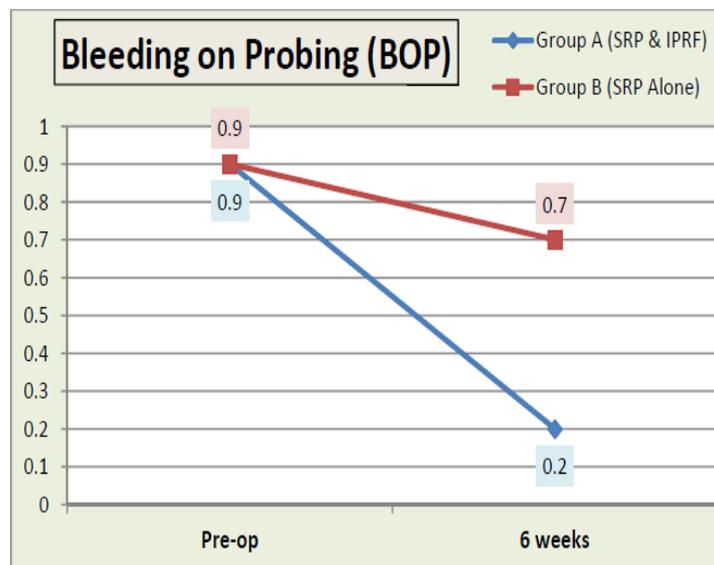
Comparison of mean pocket probing depth between group A and group B table 4fig 4

PPD	Group A (SRP &IPRF)	Group B (SRP Alone)	Unpaired 't' test	P value, Significance
Pre-op	5.6 (0.69)	5.5 (0.7)	t =0.318	p=0.754
6 weeks	3.75 (0.67)	4.1 (0.69)	t = -1.137	p =0.270
Reduction/ Change in PPD	1.85 (0.41)	1.4 (0.31)	t =2.741	p =0.013*
Paired 't' test value (Pre vs 6 weeks)	t =6.011	t =4.452		
p value, Significance	p <0.001**	p<0.001**		

Comparison of mean CAL between group A and group B table 5 ,fig 5

CAL	Group A (SRP &IPRF)	Group B (SRP Alone)	Unpaired 't' test	P value, Significance
Pre-op	6.2 (0.63)	6.3 (0.94)	t = -0.277	p=0.785
6 weeks	5.1 (0.65)	5.6 (0.69)	t = -1.646	p =0.177
Reduction/ Change in CAL	1.1 (0.31)	0.7 (0.34)	t =2.683	p =0.015*
Paired 't' test value (Pre vs 6 weeks)	t =3.811	t =1.878		
p value, Significance	p =0.001*	p =0.077		