BMC Oral Health

RESEARCH

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The clinical efficacy of injectable platelet-rich fibrin (i-PRF) as an adjunct to nonsurgical periodontal therapy in smokers with periodontitis

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Abstract

Background Smokers with periodontitis generally respond less favorably to nonsurgical treatments compared to nonsmokers. Injectable platelet-rich fibrin (i-PRF) is an effective autogenous material that positively influences various biological processes, including inflammation, wound healing, angiogenesis, and regeneration. This split-mouth randomized controlled study aims to investigate the effects of subgingival i-PRF application on clinical periodontal parameters as an adjunct to scaling and root planning (SRP) in smokers with periodontitis.

Methods This study included twenty-five patients with Stage 2 to 3 Grade C periodontitis. For each patient, four contralateral deep pockets (two for each side) were randomly treated with SRP + i-PRF (test group) or SRP + saline (control group). Subgingival i-PRF/saline application was repeated on the 7th day, and clinical periodontal parameters were recorded at baseline and 1 and 3 months following the treatments.

Results Compared with the baseline measurements, both groups presented significant improvements in clinical parameters. The probing depth (PD) was significantly lower in the test group than in the control group at the 1st and 3rd months ($P < 0.05$). The 3-month gingival index (GI) and bleeding on probing (BOP) values were significantly lower in the test group than in the control group ($P < 0.05$). No significant differences were observed in the Turesky modified Quigley-Hein Plaque Index (TQHPI) or clinical attachment loss (CAL) score between the groups during the follow-up visits ($P > 0.05$). However, greater PD reduction and clinical attachment gain were found in the test group than in the control group at the 1st and 3rd months ($P < 0.05$).

Conclusions Greater PD reduction and clinical attachment gain in the test group indicate that i-PRF may play a beneficial role in improving the clinical outcomes of nonsurgical periodontal treatment in smokers with periodontitis.

Trial registration ID NCT06605547 (https://clinicaltrials.gov/); September 23, 2024.

Keywords Injectable platelet-rich fibrin, Periodontal debridement, Periodontitis, Smokers

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Introduction

Periodontitis is a chronic, destructive, and irreversible inflammatory disease, is characterized by the destruction of the periodontal tissues supporting the tooth, which can eventually lead to tooth loss [1]. While nonsurgical periodontal treatment, including scaling and root planning (SRP), oral hygiene instructions, and patient motivation, can achieve clinical success in most cases of periodontitis, complex cases may require additional treatment modalities [2–4].

Smoking is recognized as the most significant environmental risk factor for periodontal disease. Smoking negatively affects immune system functions such as leukocyte formation, neutrophil function, cytokine and chemokine expression, fibroblast activities, vascular factors, and antibody and inflammatory mediator production. Smokers are more prone to an increase in periodontal pocket depth, clinical attachment loss, and pathogenic bacteria count [5, 6]. Since smoking disrupts periodontal healing, various treatment modalities, including the application of subgingival therapeutic agents in addition to nonsurgical periodontal therapy, have been used to increase the effectiveness of SRP and minimize the need for surgical periodontal treatment in smokers [7–11].

Platelet concentrates, autogenous materials with unique properties, are of interest in dentistry, especially in periodontology. These materials are obtained by centrifuging blood collected from the antecubital vein at a specific rotation speed and time. Platelet-rich fibrin concentrates are typically in a dense gel or solid form [12–15]. However, these forms are unsuitable for injection, which led to the recent development of i-PRF in an injectable form [16].

Recent studies have shown that i-PRF becomes a dynamic gel containing platelets, leukocytes, type I collagen, and osteocalcin 10–15 min after preparation/application, providing a three-dimensional fibrin network containing growth factors [14, 17]. Compared to other platelet concentrates, i-PRF induces fibroblast migration and platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), osteocalcin, and collagen 1 expression more [18]. Research indicates that i-PRF influences immunity by inhibiting dendritic cell maturation and suppressing M1 (pro-inflammatory) type macrophage polarization [19]. Since it is obtained by slower and shorter centrifugation than other platelet concentrates do, regenerative cells with higher growth factor concentrations are more common in i-PRF [14]. This results in an increase in the number of leukocytes and the release of stimulated growth factors. Increased leukocyte and platelet counts contribute to the increase in antimicrobial activity of i-PRF [20, 21]. In an in vitro study, i-PRF inhibited the growth of *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* [21]. The aforementioned properties of i-PRF have prompted researchers to explore its impact on the outcomes of nonsurgical periodontal treatment.

Aydınyurt et al. investigated the effects of subgingival i-PRF injection in rats with experimental periodontitis. They noted that subgingival i-PRF application was as effective as SRP in reducing bone loss and modulating the inflammatory response during experimental periodontitis. However, no additional benefits from using i-PRF in conjunction with SRP were observed [22]. While some clinical trials in which i-PRF was applied in addition to SRP to periodontitis patients reported that i-PRF had additional benefits, another study reported that no additional benefit was observed [23–25].

Although previous studies have investigated the effects of subgingival i-PRF application on treatment outcomes in the nonsurgical treatment of periodontitis, these studies were conducted with nonsmokers [23–25]. Considering the antimicrobial, anti-inflammatory, and biological properties of i-PRF, it is hypothesized that the subgingival application of i-PRF in conjunction with SRP in smokers will improve clinical outcomes more than SRP alone. The aim of this study was to investigate the effects of subgingival i-PRF application in addition to SRP on periodontal clinical parameters in smokers with Stage 2 to 3 periodontitis.

Materials and methods

Study population

This randomized, split-mouth clinical trial was approved by the Ethics Committee of the School of Medicine, Bolu Abant Izzet Baysal University (decision number: 2023/201) and registered in Clinical Trials (NCT06605547). The study protocol was conducted in accordance with the revised Helsinki Declaration 2013. Before the study, the research protocol was explained to all participants, and written informed consent was obtained from them.

This clinical trial was carried out from September 2023 to January 2024 in the Periodontology Department at the Faculty of Dentistry, Bolu Abant Izzet Baysal University. Five hundred eighty-two individuals who applied to our clinic were examined. Thirty-five patients who agreed to participate in the study and met the inclusion criteria were enrolled. However, 10 participants did not attend their follow-up appointments. Ultimately, the study was completed with 25 subjects. The CONSORT flow diagram of the study is depicted in Fig. 1.

The inclusion criteria were as follows: aged 20–65 years, systemically healthy, had at least 20 natural teeth (excluding third molars), had contralateral periodontal pockets (PD ≥ 5 mm) and a CAL ≥ 2 mm on a minimum of two premolar and molar teeth on each side, smoked more than 10 cigarettes per day for at least 5 years, and

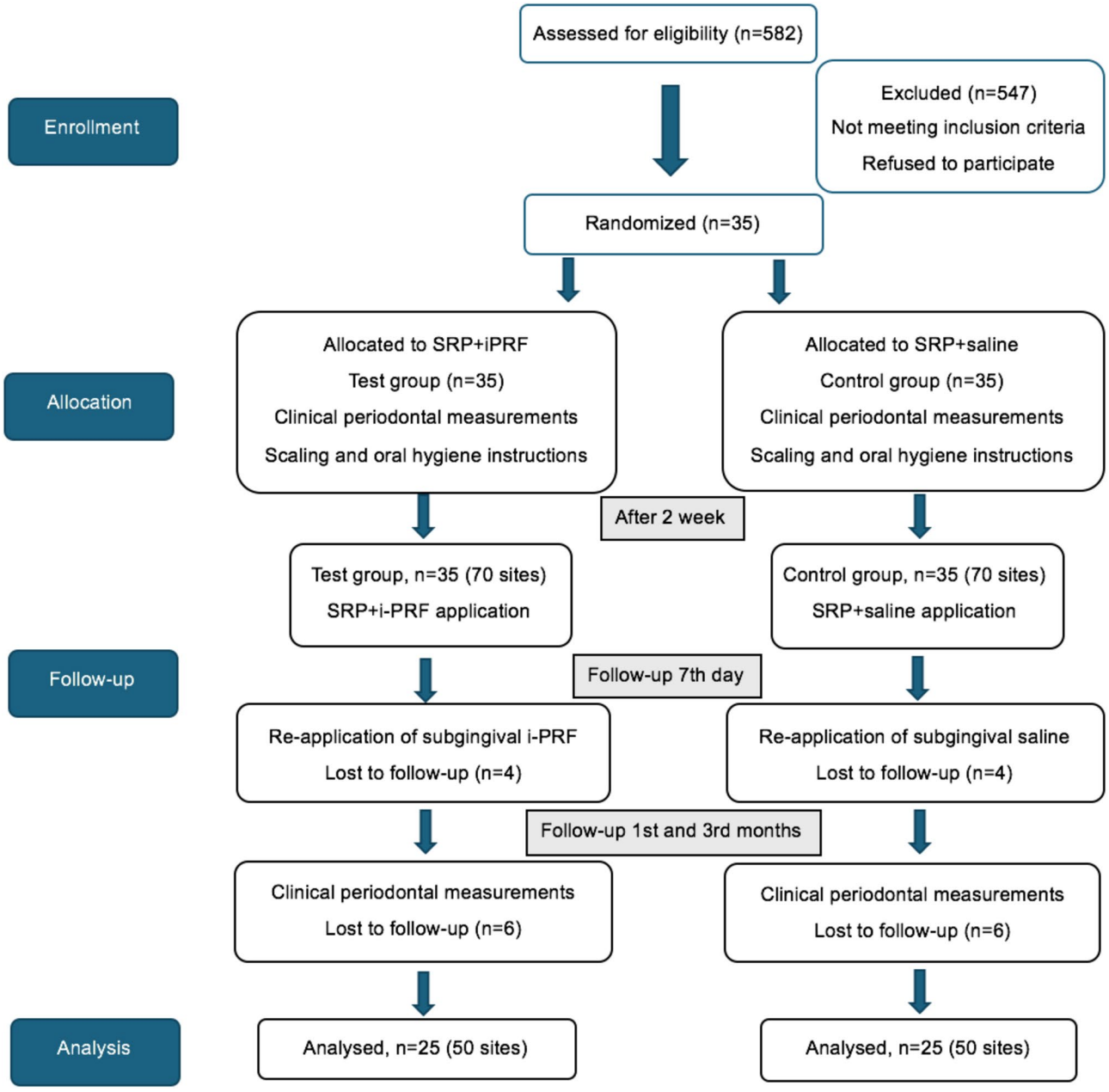

Fig. 1 CONSORT chart showing the study design

were diagnosed with Stage 2 to 3 periodontitis [26, 27]. Smoking history was obtained through self-reports and a standardized questionnaire. Subjects were excluded if they had received periodontal treatment in the past six months, used systemic antibiotics in the last six months, or taken anti-inflammatory medications in the previous three months. Additionally, individuals with hematological disorders, those on immunosuppressive drugs, those using medications that affect natural coagulation processes or the health of gingival and periodontal tissues, and pregnant or breastfeeding females were also excluded. Teeth that exhibited furcation involvement, a periapical lesion, or mobility were excluded from the study.

Sample size calculation

The sample size was calculated at the 95% confidence level in this trial using the G. Power-3.1.9.2 program. Based on the analysis, at the $\alpha = 0.05$ significance level, the standardized effect size was determined to be 0.8232 from a previous study [23]. Consequently, the minimum sample size required per group was calculated to be 25, with a theoretical power of 0.80. Taking potential dropouts into account, the sample size was increased by more

than 30% of the minimum requirement (7.58 observations). Therefore, the final sample size per group was set at 35.

Clinical periodontal parameters

All participants were examined at baseline and 1 and 3 months after nonsurgical periodontal treatment. The evaluations included measurements of full-mouth probing depth (PD), clinical attachment loss (CAL), the presence of bleeding on probing (BOP), the gingival index (GI), and the Turesky modified Quigley-Hein Plaque Index (TQHPI), excluding third molars [28, 29]. TQHPI was evaluated at each facial and lingual non-restored surface of all the teeth. The GI was assessed at four sites (mesio-buccal, disto-buccal, mesio-lingual, and disto-lingual), PD and CAL were measured at six sites (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual) per tooth using a Williams periodontal probe (Hu-Friedy, Chicago, IL, USA). The primary outcome measures of the study were baseline-1st month and baseline-3rd month PD reduction and clinical attachment gain, whereas the TQHPI, GI, and BOP were the secondary outcome measures.

Following the clinical measurement, four contralateral deep pockets (two for each side) in the premolar and molar areas were selected for subgingival application in each patient. The same blinded and calibrated examiner (TÇG) performed all the measurements and nonsurgical periodontal treatment. For intraexaminer calibration, PD, CAL, and GI measurements were performed at 24-hour intervals in 5 periodontitis patients who were not included in the study. The intraclass correlation coefficients for PD and CAL (0.888–0.950 and 0.980–0.991, respectively) and Cohen's kappa value for the GI ($\kappa = 0.806$) were acceptable.

i-PRF preparation

For each patient, peripheral blood was collected in a sterile, noncoated 9-mL plastic tube without any anticoagulant. The blood was then immediately centrifuged at 700 rpm for 3 min via a centrifuge device (INSTRASPIN, USA) according to the manufacturer's instructions. After centrifugation, the upper liquid layer was retrieved, and placed into an insulin syringe connected to a 29G needle (Fig. 2a, b).

Periodontal treatment

The nonsurgical periodontal therapy included SRP, saline irrigation of deep pockets, and oral hygiene instructions. SRP was performed under local anesthesia with an ultrasonic instrument (Woodpecker, UDS-P LED, CHINA) and Gracey curettes (Hu-Friedy, Chicago, IL, USA) within 24 h.

Following the nonsurgical periodontal treatment, i-PRF was applied to the test sites, while saline was applied to the control sites. The test and control sites were randomly selected from the tooth sites chosen during clinical measurements. Randomization was performed via the sealed envelope method. A person not involved in the study randomly selected one of the sealed envelopes, containing a piece of paper labeled "right" or "left" to determine which sites would be treated with i-PRF.

Before applying i-PRF, the teeth were isolated with cotton rolls and dried using a cotton pellet. The 29-gauge needle tip was gently inserted at the bottom of the periodontal pocket, and i-PRF was injected in an apicocoronal direction until it reached the gingival margin, allowing it to overflow from the sulcus (Fig. 2c, d). For saline application, an insulin syringe was filled with saline, and a 29-gauge needle tip was carefully placed into the pocket. Saline was then injected into the pocket until it overflowed from the gingival margin (Fig. 2e, f). After applying i-PRF subgingivally, a waiting period of 10 min was observed to prevent i-PRF from being removed from the sulcus with oral fluids until it turned into a gel. The subgingival application of i-PRF and saline was carried out by a periodontist (BMY). Patients were instructed not to drink or eat anything for at least 30 min after the procedure. They were also informed about proper oral hygiene practices, including tooth brushing and interdental cleaning, and were motivated to maintain daily oral care. Patients were scheduled for a follow-up appointment for a second application of i-PRF or saline 7 days later. During this session, the application was performed carefully at both the test and control sites to avoid negatively impacting wound healing. The blunt needle tip was gently positioned 1–2 mm into the pocket, and i-PRF or saline was slowly released until the excess fluid was excreted from the sulcus. At the 1st and 3rd month follow-ups, full-mouth periodontal clinical measurements were repeated, and oral hygiene instructions were reinforced when necessary. During the 3-month follow-up period, participants were asked to avoid using anti-inflammatory, antibiotic, or immunosuppressant medications whenever possible and to inform the researchers if they had to use them.

Statistical analysis

Statistical analyses were performed using the statistical analysis software (SPSS v.25.0; IBM). The Shapiro–Wilk test was used to assess the normality of the data, whereas the Levene test was used to check for homogeneity of variance. For intergroup comparisons, the Mann–Whitney *U* test was used for nonnormally distributed data, while independent samples t-test were conducted for normally distributed data. The intragroup comparisons were performed using the Friedman test. Post hoc

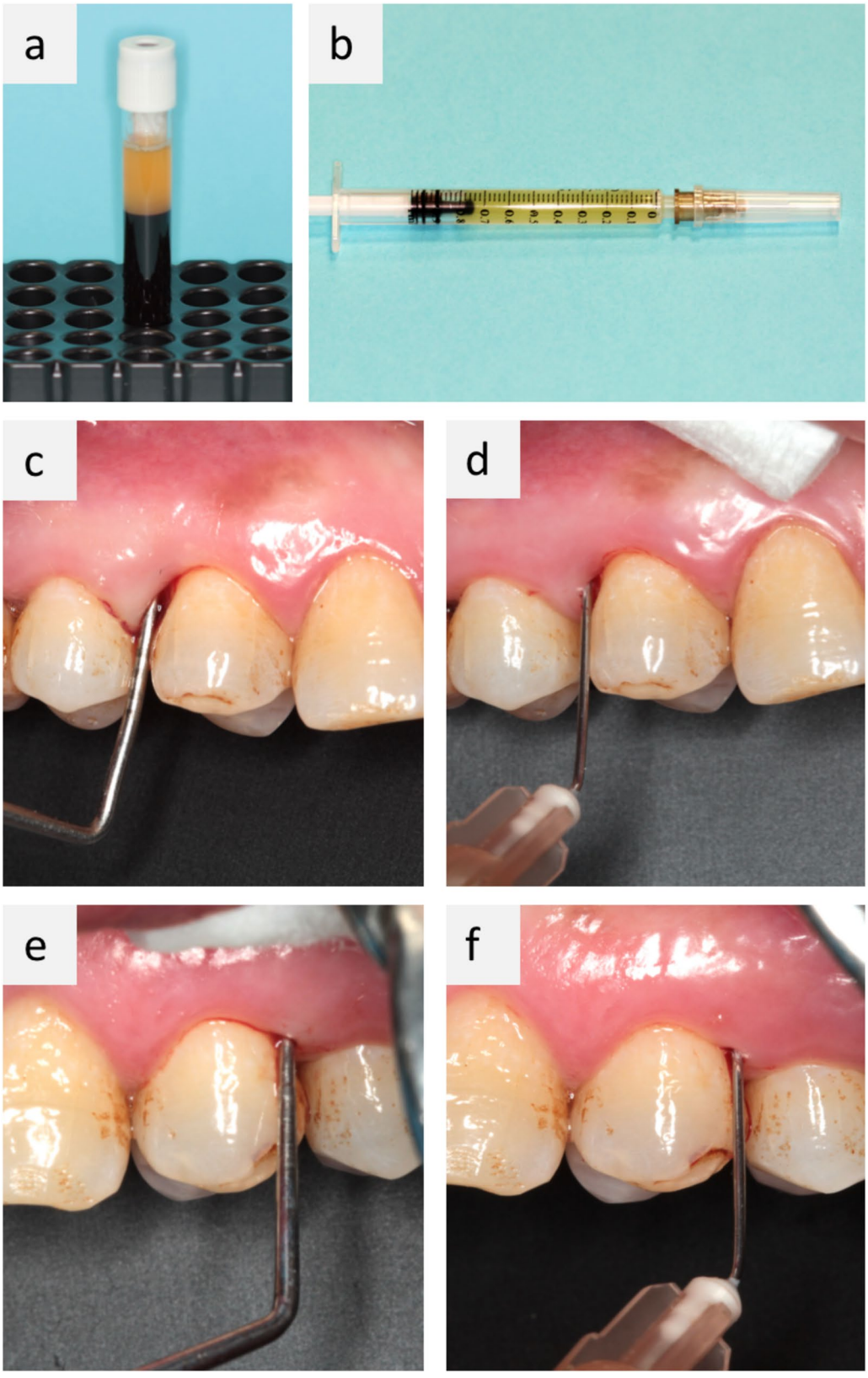

Fig. 2 Subgingival i-PRF and saline application following SRP. **a**) i-PRF was prepared from peripheral blood collected from patients. **b**) i-PRF was transferred into an insulin syringe for subgingival application. **c**) Probing depth measurement in the test site. **d**) Subgingival i-PRF application in the test site. **e**) Probing depth measurement in the control site. **f**) Subgingival saline application in the control site

Bonferroni correction was applied to identify which specific group or groups contributed to the observed differences. A statistically significant level of $P<0.05$ was considered acceptable.

Results

The study was completed with 25 patients (8 females and 17 males). The mean age of the subjects was 44.16 ± 7.73 years. The average number of cigarettes smoked by the participants was 18.28 ± 3.32 per day.

Clinical periodontal measurements were evaluated at 50 test sites and 50 control sites across a total of 25 patients, with 2 test and 2 control sites per patient. Table 1 presents the initial clinical periodontal parameters and the measurements taken at the 1st month and 3rd month for both the test and control groups. The initial periodontal measurements were similar between the two groups ($P>0.05$). Following both treatment methods, all the clinical parameters significantly improved ($P<0.05$). However, no significant differences in the TQHPI or CAL were observed between the groups at the 1st and 3rd months ($P>0.05$). At 3 months, the values for GI and PD were significantly lower in the test group than in the control group ($P<0.05$). Additionally, BOP values were significantly lower in the test group than in the control group, and PD reduction and clinical attachment gain were significantly greater in the test group than in the control group during the follow-up visits ($P<0.05$) (Figs. 3 and 4, and 5).

Table 1 Clinical periodontal parameters of the study groups at different time intervals

Periodontal index	Test group (mean ± SD)	Control group (mean ± SD)	*P* value
TQHPI			
T0	2.60 ± 0.83	2.54 ± 0.73	0.788
T1	0.52 ± 0.95	0.88 ± 0.98	0.090
T2	0.56 ± 0.73	0.80 ± 0.80	0.254
P value	**< 0.001[a, b]**	**< 0.001[a, b]**	
GI			
T0	1.90 ± 0.25	1.88 ± 0.30	0.951
T1	0.28 ± 0.60	0.6 ± 0.72	0.061
T2	0.08 ± 0.28	0.4 ± 0.58	**0.017**
P value	**< 0.001[a, b]**	**< 0.001[a, b]**	
BOP (%)			
T0	90.00 ± 25.00	90.00 ± 25.00	1.000
T1	10.00 ± 25.00	28.00 ± 32.53	**0.020**
T2	4.00 ± 13.84	20.00 ± 28.87	**0.017**
P value	**< 0.001[a, b]**	**< 0.001[a, b]**	
PD (mm)			
T0	5.92 ± 1.12	5.56 ± 1.10	0.067
T1	2.66 ± 0.83	3.02 ± 1.04	0.118
T2	2.50 ± 0.69	2.86 ± 0.77	**0.038**
P value	**< 0.001[a, b]**	**< 0.001[a, b]**	
Δ PD (T0-T1)	3.26 ± 0.91	2.54 ± 0.79	**0.001**
Δ PD (T0-T2)	3.42 ± 0.80	2.70 ± 0.89	**< 0.001**
CAL (mm)			
T0	6.02 ± 1.12	5.64 ± 1.11	0.064
T1	2.87 ± 0.90	3.22 ± 1.24	0.197
T2	2.70 ± 0.72	3.10 ± 1.00	0.125
P value	**< 0.001[a, b]**	**< 0.001[a, b]**	
Δ CAL (T0-T1)	3.17 ± 0.90	2.42 ± 0.69	**0.001**
Δ CAL (T0-T2)	3.32 ± 0.78	2.54 ± 0.80	**0.001**

Statistically significant differences are indicated in bold ($P<0.05$ and $P<0.001$)

[a] Significant difference between baseline and the first month, [b] significant difference between baseline and the third month

T0: Baseline, T1: First month, T2: Third month, Δ: Changes in clinical parameters during the study period

Discussion

To the best of our knowledge, this study is the first to investigate the effects of subgingival i-PRF application in addition to SRP on clinical periodontal parameters in smokers with periodontitis. The results revealed lower GI and BOP values at the test sites than at the control sites. Furthermore, the test sites demonstrated a greater gain in clinical attachment and a higher reduction in probing depth.

Nonsurgical periodontal treatment encompasses traditional procedures aimed at infection control, reducing probing pocket depth, and improving clinical attachment levels. SRP is widely regarded as the gold standard for treating periodontitis [30, 31]. However, smokers typically show a poorer response to SRP [5]. Smoking is known to increase neutrophil activity and suppress the immune response [32]. Various studies highlight that smoking adversely affects alveolar bone height by influencing bone metabolism, and nicotine inhibits osteoblast activity while promoting osteoclast activity [33–35]. Additionally, smoking negatively impacts fibroblasts, leading to a reduction in collagen and fibronectin production [36]. It also alters the oral microbiota, increasing the prevalence of bacteria such as *Prevotella intermedia*, *Campylobacter rectus*, *Tannerella forsythia*, *Treponema denticola*, and *Porphyromonas gingivalis* [37, 38].

i-PRF is an autogenous material that aids the periodontal healing process by secreting various growth factors essential for regulating wound healing and tissue regeneration [39]. i-PRF has shown the ability to enhance osteoblast proliferation and promote bone mineralization [22, 40]. Furthermore, it has been demonstrated to inhibit M1 macrophage polarization and important inflammatory pathways [19]. Clinical studies indicate that i-PRF increases the gingival crevicular fluid (GCF) levels of vascular endothelial growth factor (VEGF) and interleukin-10 (IL-10) while decreasing tumor necrosis factor-α (TNF-α), thereby helping to reduce inflammation [24]. Additionally, i-PRF has been reported to possess antibacterial properties against *Porphyromonas gingivalis*, a significant periodontal pathogen [21]. In

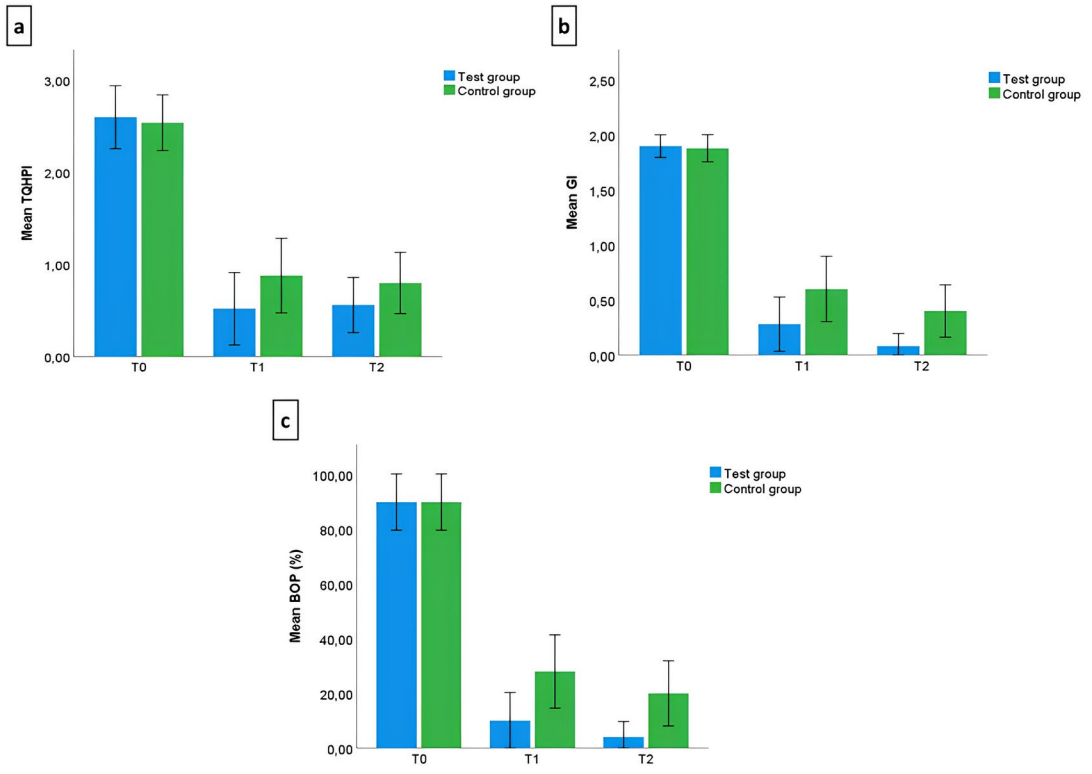

Fig. 3 Graphs comparing **a**) the Turesky modified Quigley-Hein Plaque Index (TQHPI), **b**) the gingival index (GI), and **c**) the presence of bleeding on probing (BOP) between test and control groups over different study periods (T0: Baseline, T1: First month, T2: Third month)

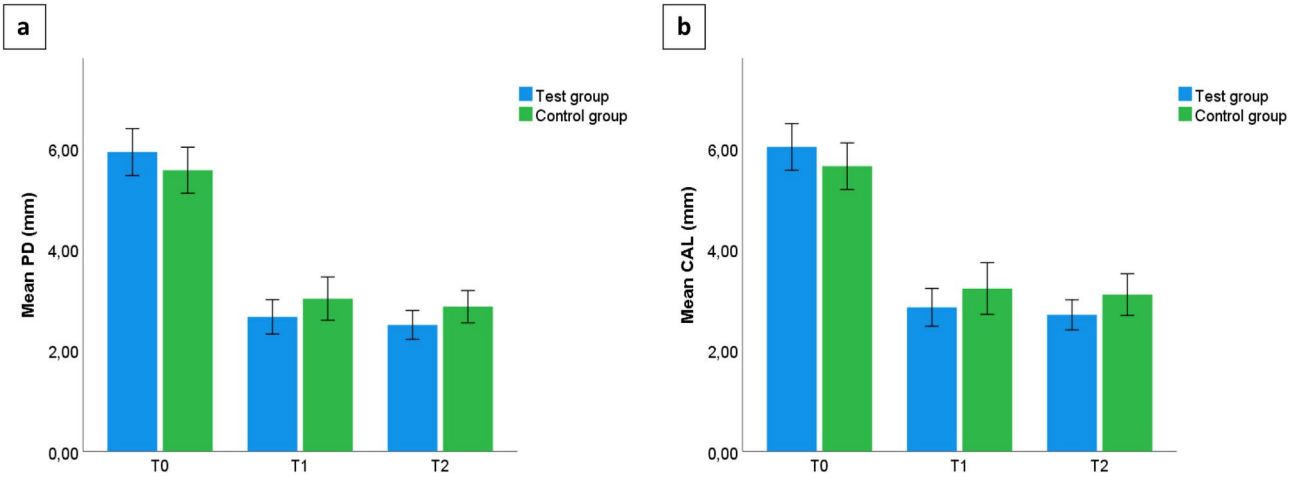

Fig. 4 Graphs comparing **a**) probing depth (PD) and **b**) clinical attachment loss (CAL) between test and control groups over different study periods (T0: Baseline, T1: First month, T2: Third month)

light of this information, the current study was based on the idea that the properties of i-PRF could improve the effectiveness of nonsurgical periodontal treatment in smokers by mitigating the adverse effects of smoking on periodontal healing.

In order to increase the success in the periodontal treatment of smokers, the effects of different treatment methods in addition to nonsurgical periodontal therapy in smokers have been investigated in various studies [7–11]. This study evaluated the impact of i-PRF application on nonsurgical periodontal therapy among smokers, focusing on several clinical parameters: TQHPI, GI, BOP, PD, and CAL. The dental plaque was scored using TQHPI because its scoring structure provides a more accurate assessment of small plaque accumulations compared to

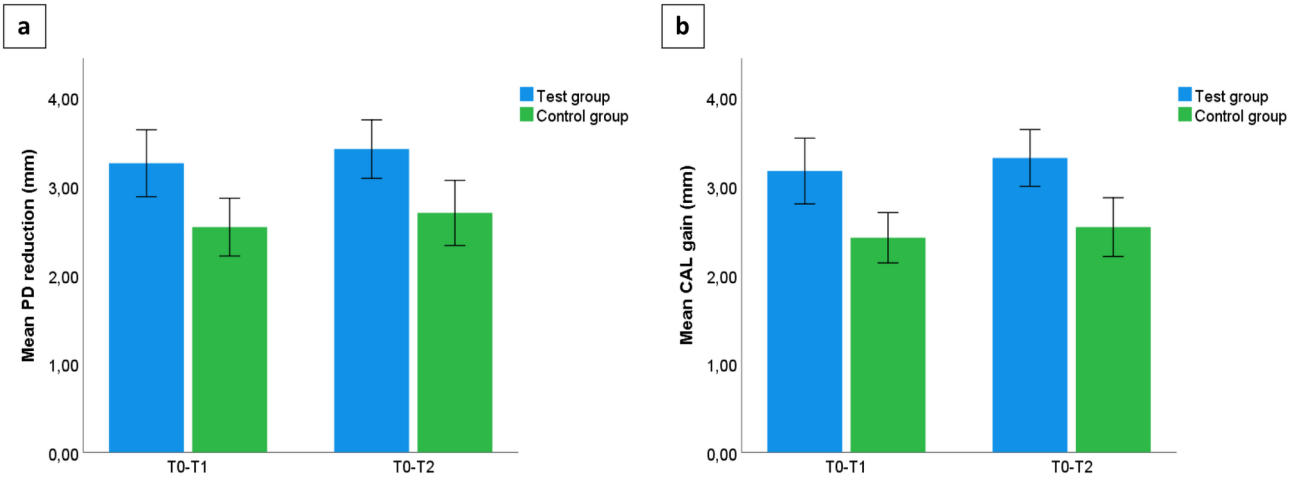

Fig. 5 Graphs showing the changes in **a**) probing depth (PD) and **b**) clinical attachment loss (CAL) in the study periods (T0-T1: Baseline-1 month, T0-T2: Baseline-3 months)

larger ones and allows for easy application in full-mouth clinical measurements [41].

The intragroup analysis revealed a notable reduction in all the periodontal measurements in both groups during the follow-up visits compared with the baseline values. These findings demonstrate the efficacy of SRP combined with oral hygiene education, indicating its role in ensuring effective oral hygiene maintenance, reducing probing depth, achieving clinical attachment gain, and alleviating gingival inflammation in smokers with periodontitis. In the comparison between the study groups, the 1st- and 3rd-month TQHPI and CAL values, and the 1st-month GI and PD measurements were higher in the control group than in the test group; however, these differences were not statistically significant. On the other hand, the 3rd-month GI and 1st- and 3rd-month BOP values were statistically lower in the test group than in the control group. In addition, the baseline-1st month and baseline-3rd month PD and CAL changes were greater at the test sites than at the control sites. These results suggest that subgingival i-PRF application in addition to SRP in smokers with periodontitis may be beneficial in reducing gingival inflammation, decreasing probing depth, and gaining clinical attachment. In our study, the significant reduction in GI and BOP in the test sites may be linked to the beneficial effects of i-PRF on the immune response impaired by smoking. The more significant clinical attachment gain and PD reduction observed in the i-PRF sites may be attributed to the positive effects of i-PRF on fibroblast function, tissue repair, and bone metabolism, which are impaired in smokers. To better understand the mechanisms behind the healing effects of i-PRF application in treating periodontitis in smokers, further studies evaluating the levels of pro-inflammatory and anti-inflammatory cytokine and bone metabolism mediators in GCF and periodontal tissues, as well as the pathogenic bacteria in subgingival plaques are needed.

To our knowledge, no studies have reported the use of i-PRF in the treatment of periodontitis in smokers. Therefore, it is not possible to compare our results directly with those of other studies. Changes in clinical parameters were compared with studies using i-PRF in the treatment of periodontitis in nonsmokers. Among these studies, only the study by Albonni et al. evaluated TQHPI. However, the study presented only whole mouth TQHPI values and did not provide values specific to the test and control groups. In other studies, consistent with our findings, the plaque index for the test and control groups was found to be similar during the follow-up sessions [23, 24]. Torumtay Cin et al. conducted a split-mouth study that treated 34 deep periodontal pockets in 17 periodontitis patients with SRP + i-PRF and SRP + saline [24]. As a result, they reported that PD reduction and clinical attachment gain values were significantly greater in the SRP + i-PRF group, which is consistent with our results. On the other hand, unlike our results, the GI and BOP values were reported to be similar to those of the control group at follow-up appointments. In another split-mouth study, Vuckociv et al. applied i-PRF in addition to SRP to 24 periodontitis patients [23]. At the 3rd month, BOP, CAL, and PD were observed to be significantly lower in the i-PRF group than in the control group. Nevertheless, some studies indicate that using i-PRF in addition to SRP does not lead to any additional improvement in clinical parameters. Albonni et al. reported no statistically significant difference in BOP, PD, and CAL values between sites with and without i-PRF [25]. Shunmuga et al. applied i-PRF in addition to SRP to the test group and only SRP to the control group in type 2 diabetes mellitus patients with Stage III Grade C periodontitis. In the evaluation between the groups, they concluded that the mean

PD and CAL were similar at the 3rd and 6th months and that i-PRF did not contribute to SRP [42]. The differences between our findings and those of previous research may be attributed to variations in study design, population characteristics, and i-PRF application protocols.

Studies have shown that i-PRF provides long-term growth factor release for up to 10 days [14]. Therefore, we applied subgingival i-PRF, which was repeated 7 days after the first application. Although most previous studies have applied i-PRF once in addition to nonsurgical periodontal treatment, there are also repeated applications, as in our study [22, 43]. In their study on experimental periodontitis in rats, Aydınyurt et al. applied i-PRF with or without mechanical periodontal treatment on the 1st, 3rd, and 7th days. Contrary to our findings, they reported that the addition of i-PRF to SRP in experimental periodontitis did not result in superior outcomes compared to SRP alone [22]. In another study, Khallaf et al. applied piroxicam gel in conjunction with SRP on 20 regions with periodontal pockets deeper than 6 mm, while applying i-PRF to another 20 regions. i-PRF application was repeated every 2 weeks for 3 months. Supporting the results of our study, they also showed significant improvements in the PD, CAL, and BOP measurements in the i-PRF group compared to the piroxicam gel group during follow-up visits [43].

In our study, i-PRF obtained from the venous blood of smokers was used. The effects of smoking on platelet concentrates, which are crucial in many treatment procedures, have been investigated in various studies. Rios et al. investigated the effects of smoking on biomolecule release from leucocyte- and platelet-rich fibrin (L-PRF) and found that both smokers and nonsmokers had similar biomolecule releases associated with wound healing [44]. Srirangarajan et al. examined the influence of smoking on the platelet morphology and fiber structure of both L-PRF and advanced platelet-rich fibrin (A-PRF) membranes. Their electron microscopy results indicated that long-term smoking affects the thickness and arrangement of the membrane fiber architecture, potentially impacting platelet activation [45]. Das et al. assessed the quality of A-PRF in periodontitis patients in three groups, including systemically healthy individuals (group 1), heavy tobacco smokers (group 2), and uncontrolled type 2 diabetic patients (group 3). They concluded that a greater percentage of loose fibrin networks in the A-PRF membranes of smokers. Despite these changes, it has been stated that A-PRF could still provide improved periodontal healing in smokers [46]. Nevertheless, the authors did not find any studies specifically addressing the effects of cigarette smoking on i-PRF. The enhanced clinical healing observed in sites treated with i-PRF in this study suggests that smoking does not significantly impair the healing properties of i-PRF.

Limitations

The current study has several limitations. One of the limitations is that smoking history was assessed through self-reports, and salivary or serum cotinine levels were not analysed. Since the effects of smoking on periodontal health and response to treatment are dose-dependent, further studies are needed to determine whether periodontal healing following i-PRF application is also dependent on tobacco exposure levels. Another limitation is that the gingival biotype and the adequacy of attached gingival width, which could affect periodontal healing and clinical outcomes, were not evaluated in the test and control sites. Additionally, since the study did not determine whether the dominant hand (right or left-handedness) was associated with the control or test site, the clinical parameters may have been affected by variations in brushing efficiency due to hand dominance. This split-mouth study assessed the short-term effects of i-PRF on periodontal clinical improvement following SRP. Further multicenter, randomized, controlled clinical studies with a larger population are necessary to investigate the long-term effects of subgingival i-PRF application in the periodontal treatment of smokers.

Conclusion

Within the limits of this study, it can be concluded that subgingival i-PRF application may contribute to periodontal healing following SRP in smokers with periodontitis. The results of this study highlight the potential role of i-PRF in achieving periodontal health and preventing tooth loss in smokers at risk for edentulism. Furthermore, these results also promise that applying i-PRF may improve treatment outcomes in challenging procedures, including the treatment of recurrent periodontitis, the management of peri-implant diseases, and surgical periodontal therapy in smokers.

Abbreviations

i-PRF	Injectable platelet-rich fibrin
SRP	Scaling and root planning
PD	Probing depth
GI	Gingival index
BOP	Bleeding on probing
TQHPI	Turesky modified quigley-hein plaque index
CAL	Clinical attachment loss
PDGF	Platelet-derived growth factor
TGF-β	Transforming growth factor-β
GCF	Gingival crevicular fluid
VEGF	Vascular endothelial growth factor
IL-10	Interleukin-10
TNF-α	Tumor necrosis factor-α
L-PRF	Leucocyte- and platelet-rich fibrin
A-PRF	Advanced platelet-rich fibrin

Acknowledgements

The authors thank Ayça Ölmez for her assistance in performing the statistical analysis and Şadiye Günpınar and Tuğçe Paksoy for their contributions in interpreting the data.

Author contributions
This study was designed by B.M.Y and T.Ç.G. T.Ç. G was responsible for data acquisition. B.M.Y. performed the statistical analysis. The manuscript was drafted by T.Ç.G and edited by B.M.Y.

Funding
The authors declare that no funds, grants, or other support was received during the preparation of this manuscript.

Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of the School of Medicine, Bolu Abant Izzet Baysal University (decision number: 2023/201). All participants were verbally informed about the study protocol, and written informed consent was obtained. The study protocol was conducted in accordance with the Helsinki Declaration 2013.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 3 February 2025 / Accepted: 16 April 2025
Published online: 23 April 2025

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