Original Article

Effect of injectable platelet-rich fibrin (i-PRF) on the rate of tooth movement:
A randomized clinical trial

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ABSTRACT

Objectives: To evaluate the efficiency of injectable platelet-rich fibrin (i-PRF) in accelerating canine tooth movement and to examine levels of the matrix metalloproteinase-8 (MMP-8), interleukin-1β (IL-1β), receptor activator of nuclear factor kappa-light-chain-enhancer of activated B cells ligand (RANKL), and osteoprotegerin (OPG) in the gingival crevicular fluid during orthodontic treatment.

Materials and Methods: Twenty patients (mean age = 21.4 ± 2.9 years) with Class II Division 1 malocclusion were included in a split-mouth study. The treatment plan for all patients was extraction of maxillary first premolars followed by canine distalization with closed-coil springs using 150 g of force on each side. The study group received i-PRF two times, with a 2-week interval, on one side of the maxilla. The contralateral side served as the control and did not receive i-PRF. Maxillary canine tooth movement was measured at five time points (T1–T5) on each side. Also, the activity of inflammatory cytokines was evaluated at three time points in the gingival crevicular fluid samples.

Results: There was a significant difference in canine tooth movement between the two groups ($P <$ .001). i-PRF significantly increased the rate of tooth movement, and stimulation in the levels of inflammatory cytokines supported this result ($P <$ .001). The levels of cytokines changed in both groups between T1 and T2. The IL-1β, MMP8, and RANKL values were significantly increased in the study group compared with the control group, while the OPG values were significantly decreased.

Conclusions: i-PRF-facilitated orthodontics is an effective and safe treatment modality to accelerate tooth movement, and this method can help shorten orthodontic treatment duration. (*Angle Orthod.* 2021;91:285–292.)

KEY WORDS: i-PRF; Injectable platelet-rich fibrin; Rate of tooth movement

INTRODUCTION

It is generally accepted that movement of the teeth with orthodontic forces depends on the bone remodeling phase, which is associated with the activity of inflammatory markers, quality and quantity of bone turnover, and the balance between osteoclastic and osteoblastic activity.[1–5] Osteoclastic activity is stimulated by changes in tooth-supporting tissue biomarkers of receptor activator of nuclear factor kappa-light-chain-enhancer of activated B cells (RANK), RANK ligand (RANKL), and osteoprotegerin (OPG) during tooth movement.[6,7] RANKL is a membrane-residing protein on osteoblasts and their precursors, which recognizes its receptor RANK on macrophages, promoting them to assume the osteoclast phenotype.[6–8] RANKL mediates osteoclastogenesis and tooth movement, and its actions are antagonized by OPG. The matrix metalloproteinase (MMP) family plays an important role in the remodeling of bone as well as in response to forces during tooth movement.[7,8]

Many experimental and clinical studies have aimed to shorten the duration of orthodontic treatment with different methods including surgical, pharmaceutical,

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laser, electromagnetic, or other procedures.[3,7,9–14] However, none of these procedures have yet become a gold standard method. Platelet-based preparations from the patient's blood provide a safe alternative to commercially available bioactive materials.[15–19] A liquid injectable platelet-rich fibrin (i-PRF) was developed by modifying spin centrifugation forces. i-PRF is a rich source of platelets during bone healing and provides an increased concentration of gingival crevicular fluid (GCF).[18] Wang et al.[18] reported that i-PRF affected osteoblastic behavior remarkably by influencing its migration, proliferation, and differentiation. This promotes cellular activity and accelerates bone turnover and healing.

Several animal research investigations and limited clinical studies have shown the effectiveness of platelet-based preparations for accelerating tooth movement.[4,20–24] The purpose of this study was to investigate the efficiency of i-PRF in accelerating tooth movement. We also evaluated the effect of i-PRF on stimulating the expression of inflammatory cytokines in GCF samples.

MATERIALS AND METHODS

A prospective, randomized, single-center, split-mouth study was approved by the ethical committee of the Ministry of Health of Turkey (Permit number 56733164/203). The study was performed in the Department of Orthodontics of the Necmettin Erbakan University between March and June 2019. The sample size for the groups was calculated by G*Power (version 3.1.9.4, Franz Faul Universität, Kiel, Germany). Based on a 1:1 ratio between the groups, at a significance level of .05 and a sample size of 20 in each group, power of more than 80% (actual power = 0.817) was determined to be adequate to detect significant differences. The sample consisted of 20 adult patients (8 men, 12 women; mean age = 21.4 ± 2.9 years).

Subject inclusion criteria were as follows: age ≥18, systemically healthy condition, Class II Division 1 malocclusion requiring extraction of maxillary first premolars, permanent dentition, no bleeding on probing, plaque index <1 mm, probing depth values <3 mm, no previous orthodontic treatment, and no smoking. The treatment protocol was explained in detail to all patients. Patients who met the selection criteria and completed an informed consent form were included in the study. In this split-mouth study, i-PRF was applied on a random basis (coin toss) on one side of the maxilla, either left or right as the study group, and the contralateral side served as a control and received only a sham injection.

All periodontal and radiographic records were taken before orthodontic treatment. The treatments were performed by the same orthodontist. In the initial phase, leveling and alignment were completed with a straight wire, 0.022" slot MBT appliance (Dentaurum, Ispringen, Germany). After alignment, miniscrews (Tomas-pin; Dentaurum) were placed bilaterally between the maxillary second premolar and the first molar before canine distalization. Then, patients were referred for extraction of maxillary first premolars, and a 0.017" × 0.025" stainless steel wire was tied back immediately. Canine distalization was conducted using calibrated 150 g Ni-Ti closed-coil springs connected from a miniscrew to a hook placed in front of the canine bracket. The force produced by the coil was calibrated with a gauge and readjusted at each visit. The total follow-up period started with premolar extraction and was concluded at the 12th week of canine distalization. Patients continued with treatment, and routine records were repeated at the end of treatment.

Preparation and Application of i-PRF

A venous blood sample was taken for each patient using a 30-mL injection syringe into 10-mL i-PRF tubes without anticoagulant and was immediately centrifuged at 700 rpm for 3 minutes at room temperature with Choukroun PRF Duo Centrifuge (Process for PRF, Nice, France). The i-PRF obtained from the upper liquid layer was placed in dental injectors. The amount of i-PRF was standardized as 4 mL and was injected intraligamentally into the distobuccal and distopalatal side of the canine tooth (2 mL for each side). Before the injection of platelet-rich fibrin (PRF), local anesthesia was applied for pain control. The study group received i-PRF two times: just after premolar extraction and at the second week of distalization. The contralateral side served as a control and received only a sham injection.

Collection of GCF

GCF samples were collected from the mesiobuccal and distobuccal sides of the canine tooth just before premolar extraction (T0), at the first week (T1), and at the fourth week (T2) of canine distalization for a total of three times. While collecting GCF samples, the supragingival plaque was removed if present. The site was isolated with cotton rolls, and filter-paper strips (Periopapers, Interstate Drug Exchange, Amityville, NY) were gently inserted 1 mm into the gingival margin for 10 seconds. Samples were immediately placed in Eppendorf tubes and stored at −80°C. The sample volume was assessed with Periotron 8000 (Oraflow, Inc, New York, NY) according to the manufacturer's instructions. Approximately 1mL of GCF was collected

Table 1. Comparisons of Canine Movements in Both Groups at Each Time Point

Group	Time Point	Mean ± SD	P Value[a]
Control	T0–T1	0.35 ± 0.08	(T0–T1) <.001
	T1–T2	1.08 ± 0.1	(T1–T2) <.001
	T2–T3	1.23 ± 0.12	(T2–T3) <.001
	T3–T4	1.23 ± 0.13	(T3–T4) <.001
	Total (T0–T4)	3.89 ± 0.34	(Total) <.001
Study	T0–T1	0.73 ± 0.11	
	T1–T2	1.56 ± 0.08	
	T2–T3	1.90 ± 0.1	
	T3–T4	1.88 ± 0.11	
	Total (T0–T4)	6.06 ± 0.29	
Differences	D1	0.38 ± 0.09^x	P Value[b]
	D2	0.48 ± 0.1^y	<.001
	D3	0.67 ± 0.13^z	
	D4	0.65 ± 0.11^z	

[a] Student *t*-test results for comparison of canine tooth movement in both groups between time points.

[b] One-way analysis of variance results for time-point differences between the study and control groups. Differences: D1 = T0–T1; D2 = T1–T2; D3 = T2–T3; D4 = T3–T4.

^{x,y,z} Different small letters in each row indicated that statistically significant difference between the groups.

from both regions and diluted to obtain the sample volume of 50–100 mL required for analysis using a glass slide-based protein array. Commercial enzyme-linked immunosorbent assay kits were obtained for measuring IL-1β, MMP-8, OPG, and RANKL, and assays were carried out according to the manufacturer's recommendations (Elabscience-Biotechnology Co. Ltd, Wuhan, China).

Measuring Distalization Rate

Movement of the canine was evaluated by measuring the distance between the midpoints of the vertical lines drawn from the incisal edge to the cervical line over the marginal ridge of the lateral and canine teeth on the dental cast. All cast measurements were made using a digital caliper. Dental casts were obtained at five time points: before tooth extraction (T0) and in the first week (T1), fourth week (T2), eighth week (T3), and 12th week (T4) from the beginning of distalization. The casts were labeled with the patient's name and date, and then stored.

Statistical Analysis

To assess the method error and intraobserver reliability, 10 randomly selected dental casts were remeasured at a 2-week interval by the same investigator. For the interobserver error, a second investigator measured the same set of models twice, and the mean values of the two measurements by each investigator were compared. The random and systematic errors were calculated using a formula described by Dahlberg[25] and Houston.[26] Both the
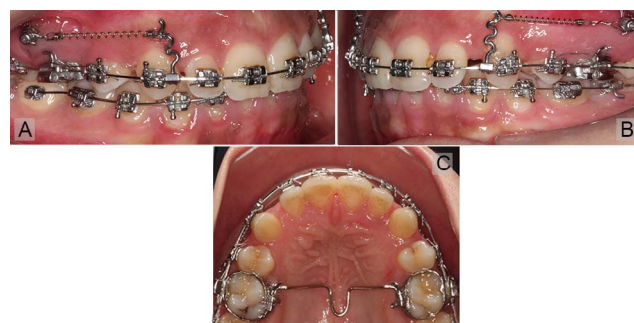
Figure 1. Effect of i-PRF on canine retraction. (A) Intraoral view 6 weeks after the first application of i-PRF and initiating canine retraction (left side). (B) The contralateral side was exposed to the same force but did not receive any i-PRF (right side). (C) Occlusal view at the sixth week after initiation of canine retraction. The left side, which received i-PRF, shows significant retraction compared with the right side, which did not receive any i-PRF.

random and systematic errors were found to be insignificant, confirming reliability.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS version 21.0, Chicago, IL). All of the data were found to be normally distributed with a homogeneous variance; therefore, parametric tests were used. The rate of canine movement was evaluated by the Student *t*-test for within and between comparisons, and one-way analysis of variance (ANOVA) was performed to determine time-interval differences between the groups. A repeated-measures ANOVA was performed to determine the mean cytokine values at different time points. Pairwise multiple comparison analysis was performed with the Tukey post hoc test. A Pearson correlation coefficient test was performed to evaluate the correlation between the tooth movement and cytokine levels. Statistical significance was set as $P < .05$.

RESULTS

The results of the Student *t*-test showed that the rate of canine tooth movement was higher in the study group than the control group at all time points, and the total movement was significantly higher in the study group (6.06 ± 0.29) than the control group (3.89 ± 0.34) ($P < .001$). The results of the ANOVA showed that the mean movement increased significantly in weeks that the i-PRF was applied ($P < .001$) (Table 1; Figure 1).

According to the within-group comparison, none of the mean cytokine values showed any significant differences between the distal and mesial sides of the teeth, in both groups and at all time points ($P > .05$). A repeated-measures ANOVA was performed to compare the mean cytokine values among the three time points according to tooth and surface, and significant differences were found (Tables 2 through

Table 2. Comparison of IL-1β Levels in GCF Samples at Each Time Point[a]

Inflammatory Marker: IL-1β	Time Points			P Value[b]
	T0, Mean ± SD	T1, Mean ± SD	T2, Mean ± SD	
Study group mesial (n = 20)	20.33 ± 7.72[v]	92.85 ± 14.54[w]	60.71 ± 22.69[y]	<.001
Study group distal (n = 20)	20.20 ± 7.54[v]	93.02 ± 14.73[w]	61.35 ± 21.68[y]	<.001
P value[c]	NS	NS	NS	
Control group mesial (n = 20)	20.98 ± 8.00[v]	39.79 ± 15.32[x]	30.50 ± 12.31[z]	<.001
Control group distal (n = 20)	20.86 ± 7.80[v]	40.11 ± 14.14[x]	31.02 ± 11.95[z]	<.001
P value[c]	NS	NS	NS	
P value[d]	NS	<.001	<.001	
P value[e]	NS	<.001	<.001	

[a] GCFindicates gingival crevicular fluid; IL-1β, interleukin-1β; NS; not significant; SD; standard deviation.
[b] A repeated measure analysis of variance according to each tooth and surface between the time points.
[c] Student t-test results for comparison of mesial and distal surfaces at each time point.
[d] Student t-test results for comparison of tooth 13 and tooth 23 according to mesial surfaces at each time point.
[e] Student t-test results for comparison of tooth 13 and tooth 23 according to distal surfaces at each time point.
[v,w,x,y,z] Different small letters in each row indicate statistically significant difference between the groups.

5; Figure 2). Pairwise comparisons showed that the mean IL-1β, MMP-8, and RANKL values were significantly higher at T1 and T2 than T0; the mean values were also significantly higher at T1 than T2 in both groups ($P < .001$; Tables 2 through 4). The mean OPG values were significantly lower at T1 and T2 than T0, and the mean values were significantly lower at T1 than T2 in both groups ($P < .001$; Table 5). According to the between-group comparison, none of the mean cytokine values showed any significant differences at T0 ($P>.05$; Tables 2 through 5). In the study group, the mean IL-1β, MMP-8, and RANKL values were significantly higher ($P < .001$), while the mean OPG values were significantly lower ($P < .05$) at T1 and T2. A Pearson correlation coefficient test showed a positive correlation between cytokine levels and acceleration of orthodontic tooth movement ($P < .0001$; Table 6).

DISCUSSION

In this split-mouth study, i-PRF was applied in the study groups to shorten the duration of treatment in patients treated with extractions. Analysis of the results demonstrated that i-PRF stimulated the expression of inflammatory cytokines, which indicated osteoclastic activity and an increased rate of tooth movement. During the total follow-up period, the canine experienced nearly twice as much movement on the study side than the control side.

To reduce treatment time, many techniques have been described in the literature to accelerate tooth movement based on the regional acceleratory phenomenon.[3,4,7,9–14,20–24,27,28] Surgically assisted approaches have been found most effective, but these procedures are invasive, are uncomfortable for the patient, can have consequent side effects (alveolar bone loss can occur in the target teeth), require the intervention of another specialist, and have higher costs.[3,7,13,14,27,28] Therefore, none are used routinely in orthodontic practices.

The use of platelet concentrations that secrete a wide variety of proteins and growth factors has increased to accelerate tissue healing and regeneration in different fields of medicine and dentistry.[15–19]

Table 3. Comparison of MMP-8 Levels in GCF Samples at Each Time Point[a]

Inflammatory Marker: MMP-8	Time Points			P Value[b]
	T0, Mean ± SD	T1, Mean ± SD	T2, Mean ± SD	
Study group mesial (n = 20)	13.03 ± 4.41[v]	70.88 ± 15.56[w]	54.69 ± 26.20[y]	<.001
Study group distal (n = 20)	12.89 ± 4.20[v]	70.58 ± 15.45[w]	55.43 ± 26.63[y]	<.001
P value[c]	NS	NS	NS	
Control group mesial (n = 20)	13.03 ± 4.57[v]	40.78 ± 22.97[x]	32.51 ± 20.64[z]	<.001
Control group distal (n = 20)	13.09 ± 4.51[v]	40.29 ± 21.25[x]	33.19 ± 20.39[z]	<.001
P value[c]	NS	NS	NS	
P value[d]	NS	<.001	.005	
P value[e]	NS	<.001	.005	

[a] GCFindicates gingival crevicular fluid; MMP-8, matrix metalloproteinase-8; NS; not significant; SD; standard deviation.
[b] A repeated measure analysis of variance according to each tooth and surface between the time points.
[c] Student t-test results for comparison of mesial and distal surfaces at each time point.
[d] Student t-test results for comparison of tooth 13 and tooth 23 according to mesial surfaces at each time point.
[e] Student t-test results for comparison of tooth 13 and tooth 23 according to distal surfaces at each time point.
[v,w,x,y,z] Different small letters in each row indicate statistically significant difference between the groups.
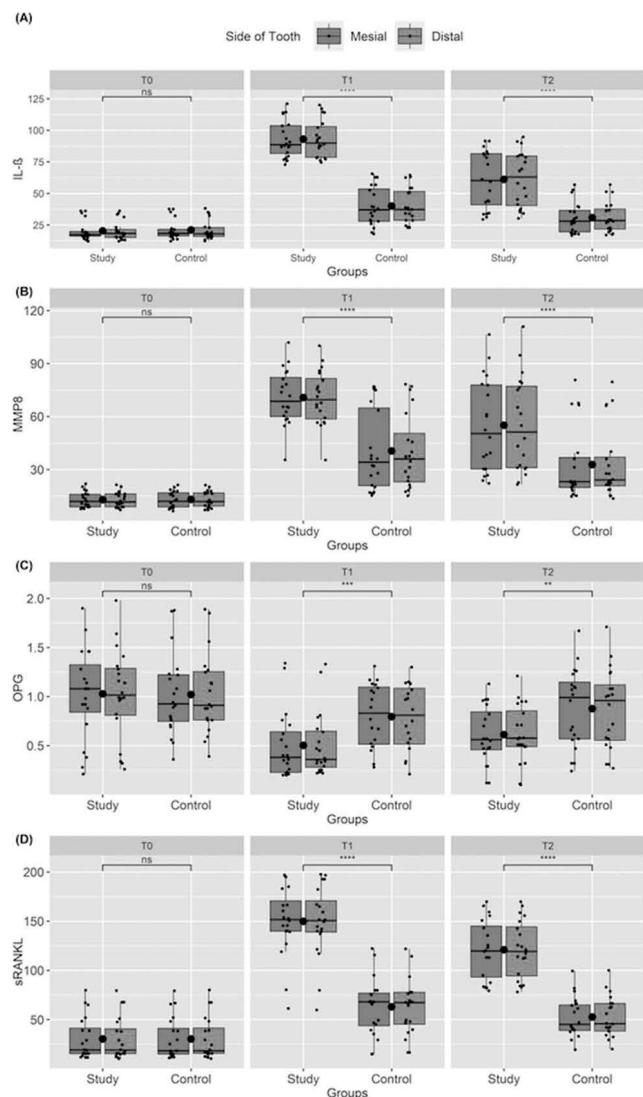
Figure 2. Box-plot representation of cytokine-level comparisons in GCF samples at each time point for the study and control groups. The samples were collected from the mesiobuccal and distobuccal side of the canine just before premolar extraction (T0), at the first week (T1), and at the fourth week (T2) of canine distalization, for a total of three times. According to the within-group comparison, none of the mean cytokine values showed any significant differences between the distal and mesial sides of the teeth, in either group and at all time points ($P > .05$). (A) Comparison of IL-1β levels. (B) Comparison of MMP-8 levels. (C) Comparison of OPG levels. (D) Comparison of RANKL levels.

Platelet-rich plasma (PRP) and PRF are the two main autologous platelet concentrations, and they differ according to their contents and methods. PRF, a completely autologous fibrin matrix, was developed as a second-generation platelet concentrate without the addition of anticoagulant and additives at lower centrifugation speeds.[17–19] Researchers have reported that higher leukocyte proportions were obtained in the upper layer of the tubes where i-PRF is collected with lower centrifugation speeds, thereby stimulating the growth factor release.[29,30] Applying i-PRF is an easy, minimally invasive, repeatable, autogenous, low-cost, and complication-avoiding procedure.[18,19,24,31] Recently, an in vivo study showed that a new formulation of PRF (A-PRF, i-PRF) had a gradual release of growth factors, up to about 1 weeks, and stimulated significantly higher growth factor release over time.[32] For these reasons, in this study we preferred to apply i-PRF to shorten treatment time, through an increase in tooth movement.

Regarding orthodontic treatment, although some experimental and clinical studies have pointed to the positive effects of PRP,[4,20,21,24] others did not report any positive effect.[22,33] Animal-based studies[4,20,21] showed that different concentrations of PRP accelerated orthodontic tooth movement. In a clinical study, Tehranchi et al.[24] demonstrated that PRF (membrane form) accelerated orthodontic tooth movement. In contrast, Akbulut et al.[22] reported no effect of PRP on orthodontic tooth movement in an animal-based study. In the current study, i-PRF demonstrated a significant increase in the rate of canine tooth movement. The positive effect of i-PRF on the rate of tooth movement started in the first week and was seen throughout the follow-up period.

Bone density can play a significant role in the rate of tooth movement. Alikhani et al.[3] reported that bone density was related to patient age, rate of osteoclast recruitment, or activation. To eliminate the effect of age on the rate of tooth movement, only adults between 18 and 24 years old were selected for the current study. Also, a split-mouth design was used to limit the effect of individual variations in response to i-PRF. Extraction of the teeth can increase the activity of inflammatory markers, which could obscure the effect of i-PRF. To minimize this possibility, tooth extractions were performed at the same time in the study and control groups.

The inflammatory marker findings of the study demonstrated that the level of cytokines changed in both groups 1 week after the first application of i-PRF and 2 weeks after the second application of i-PRF. IL-1β, MMP8, and RANKL values increased significantly in the study group compared with the control group, while the OPG values decreased significantly. OPG inhibits osteoclast differentiation by binding to RANKL. These cytokines play significant roles in reinforcing and activating osteoclast precursor cells. Increased release of these factors is accompanied by higher osteoclast activation and therefore a higher rate of tooth movement.[3,7] Periodontal ligament cells can regulate osteoclastogenesis by reverse mechanisms with stimulation of resorptive activity by RANKL and inhibition by OPG. Kanzaki et al.[34,35] demonstrated that compressive force increased the production of RANKL and decreased that of OPG in human periodontal ligament cells. Addition-

Table 4. Comparison of RANKL Levels in GCF Samples at Each Time Point[a]

Inflammatory Marker; RANKL	Time Points			P Value[b]
	T0, Mean ± SD	T1, Mean ± SD	T2, Mean ± SD	
Study group mesial (n = 20)	30.49 ± 21.34[v]	150.23 ± 35.46[w]	120.93 ± 29.68[y]	<.001
Study group distal (n = 20)	30.30 ± 21.60[v]	149.40 ± 36.42[w]	121.06 ± 29.34[y]	<.001
P value[c]	NS	NS	NS	
Control group mesial (n = 20)	30.28 ± 21.41[v]	62.90 ± 29.13[x]	52.23 ± 20.65[z]	<.001
Control group distal (n = 20)	30.46 ± 21.70[v]	63.02 ± 28.37[x]	53.01 ± 20.56[z]	<.001
P value[c]	NS	NS	NS	
P value[d]	NS	<.001	<.001	
P value[e]	NS	<.001	<.001	

[a] GCFindicates gingival crevicular fluid; NS; not significant; RANKL, receptor activator of nuclear factor kappa-light-chain-enhancer of activated B cells ligand; SD; standard deviation.
[b] A repeated measure analysis of variance according to each tooth and surface between the time points.
[c] Student t-test results for comparison of mesial and distal surfaces at each time point.
[d] Student t-test results for comparison of tooth 13 and tooth 23 according to mesial surfaces at each time point.
[e] Student t-test results for comparison of tooth 13 and tooth 23 according to distal surfaces at each time point.
[v,w,x,y,z] Different small letters in each row indicate statistically significant difference between the groups.

Table 5. Comparison of OPG levels in GCF samples at each time point

Inflammatory Marker: OPG	Time Points			P Value[b]
	T0, Mean ± SD	T1, Mean ± SD	T2, Mean ± SD	
Study group mesial (n = 20)	1.03 ± 0.46[v]	0.50 ± 0.34[w]	0.61 ± 0.29[y]	<.001
Study group distal (n = 20)	1.03 ± 0.46[v]	0.51 ± 0.33[w]	0.62 ± 0.29[y]	<.001
P value[c]	NS	NS	NS	
Control group mesial (n = 20)	1.02 ± 0.42[v]	0.80 ± 0.33[x]	0.88 ± 0.40[z]	<.001
Control group distal (n = 20)	1.03 ± 0.41[v]	0.79 ± 0.33[x]	0.87 ± 0.41[z]	<.001
P value[c]	NS	NS	NS	
P value[d]	NS	.007	.018	
P value[e]	NS	.010	.029	

[a] GCFindicates gingival crevicular fluid; OPG< osteoprotegerin; NS; not significant; SD; standard deviation.
[b] A repeated measure analysis of variance according to each tooth and surface between the time points.
[c] Student t-test results for comparison of mesial and distal surfaces at each time point.
[d] Student t-test results for comparison of tooth 13 and tooth 23 according to mesial surfaces at each time point.
[e] Student t-test results for comparison of tooth 13 and tooth 23 according to distal surfaces at each time point.
[v,w,x,y,z] Different small letters in each row indicate statistically significant difference between the groups.

ally, they reported in another study that OPG gene transfer to periodontal tissue inhibited RANKL-mediated osteoclastogenesis and inhibited tooth movement. Similarly, in the current study, a low OPG level may be related to rapid orthodontic tooth movement.

Alikhani et al.[3] evaluated the effect of micro-osteoperforations(MOP) on the rate of tooth movement and the expression of inflammatory markers. They

Table 6. Correlation Between the Tooth Movement and Cytokine Levels in Both Groups at T0–T1[a]

Cytokine	Study Group (Tooth Movement)		Control Group (Tooth Movement)	
	r Value	P Value	r Value	P Value
IL-1β	0.987	<.0001	0.917	<.0001
MMP-8	0.988	<.0001	0.989	<.0001
OPG	−0.993	<.0001	−0.968	<.0001
RANKL	0.925	<.0001	0.962	<.0001

[a] IL-1β indicates interleukin-1β; MMP-8, matrix metalloproteinase-8; OPG, osteoprotegerin; RANKL, receptor activator of nuclear factor kappa-light-chain-enhancer of activated B cells ligand.
[b] Pearson correlation coefficient test.

reported that a higher level of inflammatory markers were found in the experimental group in response to MOPs. Baloul et al.[7] evaluated the effect of surgical alveolar decortication on the rate of tooth movement and bone resorption and formation. They reported that alveolar decortication stimulated the RANKL/OPG ratio where an increase in RANKL was associated with decreased OPG which was more rapid and simultaneous compared to conventional tooth movement. The current inflammatory marker findings were similar to Alikhani et al.[3] and Baloul et al.,[7] which demonstrated that higher cytokine levels stimulated osteoclastic activity. In other clinical platelet-based studies, the inflammatory markers were not examined for objective evaluation of the rate of tooth movement. According to the current results, i-PRF significantly stimulated the expression of cytokines and the rate of tooth movement. In this study, i-PRF was used for the first time to clinically accelerate tooth movement. For orthodontic purposes, i-PRF can be applied at all stages of orthodontic treatment and is minimally invasive.

CONCLUSIONS

- i-PRF-facilitated orthodontics is an effective alternative treatment method for shortening the treatment duration required for tooth movement by stimulating the expression of inflammatory cytokines.
- i-PRF is an easy, minimally invasive, repeatable, totally autogenous, and low-cost procedure to accelerate tooth movement.

REFERENCES

1. Skidmore KJ, Brook KJ, Thomson WM, Harding WJ. Factors influencing treatment time in orthodontic patients. *Am J Orthod Dentofacial Orthop*. 2006;129:230–238.
2. Mavreas D, Athanasiou AE. Factors affecting the duration of orthodontic treatment: a systematic review. *Eur J Orthod,* 2008;30:386–395.
3. Alikhani M, Raptis M, Zoldan B, Sangsuwon C, Lee YB, Alyami B, et al. Effect of micro-osteoperforations on the rate of tooth movement. *Am J Orthod Dentofacial Orthop*. 2013; 144:639–648.
4. Güleç A, Bakkalbaşı BÇ, Cumbul A, Uslu Ü, Alev B, Yarat A. Effects of local platelet-rich plasma injection on the rate of orthodontic tooth movement in a rat model: a histomorphometric study. *Am J Orthod Dentofacial Orthop*. 2017;151:92–104.
5. Rody WJ Jr, King GJ, Gu G. Osteoclast recruitment to sites of compression in orthodontic tooth movement. *Am J Orthod Dentofacial Orthop*. 2001;120:477–489.
6. Teixeira CC, Khoo E, Tran J, Chartres I, Liu Y, Thant LM, et al. Cytokine expression and accelerated tooth movement. *J Dent Res*. 2010;89:1135–1141.
7. Baloul SS, Gerstenfeld LC, Morgan EF, Carvalho RS, Van Dyke TE, Kantarci A. Mechanism of action and morphologic changes in the alveolar bone in response to selective alveolar decortication-facilitated tooth movement. *Am J Orthod Dentofacial Orthop*. 2011;139:83–101.
8. Aubin JE, Bonnelye E. Osteoprotegrin and its ligand: a new paradigm for regulation of osteoclastogenesis and bone resorption. *Osteoporosis Int*. 2000;11:905–913.
9. Alhashimi N, Frithiof L, Brudvik P, Bakhiet M. Orthodontic tooth movement and de novo synthesis of proinflammatory cytokines. *Am J Orthod Dentofacial Orthop*. 2001;119:307–312.
10. Stark TM, Sinclair PM. Effect of pulsed electromagnetic fields on orthodontic tooth movement. *Am J Orthod Dentofacial Orthop*. 1987;91:91–104.
11. Kawasaki K, Shimizu N. Effects of low-energy laser irradiation on bone remodeling during experimental tooth movement in rats. *Lasers Surg Med*. 2000;26:282–291.
12. Liou EJW, Huang CS. Rapid canine retraction through distraction of the periodontal ligament. *Am J Orthod Dentofacial Orthop*. 1998;114:372–382.
13. Yu H, Jiao F, Wang B, Shen SG. Piezoelectric decortication applied in periodontally accelerated osteogenic orthodontics. *J Craniofac Surg*. 2013;24:1750–1752.
14. Kurt G, İşeri H, Kişnişçi R, Özkaynak Ö. Rate of tooth movement and dentoskeletal effects of rapid canine retraction by dentoalveolar distraction osteogenesis: a prospective study. *Am J Orthod Dentofacial Orthop*. 2017;152:204–213.
15. Dohan Ehrenfest DM, Del Corso M, Inchingolo F, Sammartino G, Charrier JB. Platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in human cell cultures: growth factor release and contradictory results. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2010;110:418–421.
16. Anitua E, Andia I, Ardanza B, Nurden P, Nurden AT. Autologous platelets as a source of proteins for healing and tissue regeneration. *Thromb Haemost*. 2004;91:4–15.
17. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: growth factor enhancement for bone grafts. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1998;85:638–646.
18. Wang X, Zhang Y, Choukroun J, Ghanaati S, Miron RJ. Effects of an injectable platelet-rich fibrin on osteoblast behavior and bone tissue formation in comparison to platelet-rich plasma. *Platelets*. 2018;29:48–55.
19. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part IV: clinical effects on tissue healing. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;101:56–60.
20. Nakornnoi T, Leethanakul C, Samruajbenjakun B. The influence of leukocyte-platelet-rich plasma on accelerated orthodontic tooth movement in rabbits. *Korean J Orthod*. 2019;49:372–380.
21. Rashid A, ElSharaby FA, Nassef EM, Mehanni S, Mostafa YA. Effect of platelet-rich plasma on orthodontic tooth movement in dogs. *Orthod Craniofac Res*. 2017;20:102–110.
22. Akbulut S, Yagci A, Yay AH, Yalcin B. Experimental investigation of effects of platelet-rich plasma on early phases of orthodontic tooth movement. *Am J Orthod Dentofacial Orthop*. 2019;155:71–79.
23. Sar C, Akdeniz SS, Arman Ozcirpici A, Helvacioglu F, Bacanlı D. Histological evaluation of combined platelet-rich fibrin membrane and piezo-incision application in orthodontic tooth movement. *Int J Oral Maxillofac Surg*. 2019;48:1380–1385.
24. Tehranchi A, Behnia H, Pourdanesh F, Behnia P, Pinto N, Younessian F. The effect of autologous leukocyte platelet rich fibrin on the rate of orthodontic tooth movement: a prospective randomized clinical trial. *Eur J Dent*. 2018;12:350–357.
25. Dahlberg G. Statistical methods for medical and biological students. New York: Interscience Publications; 1940.
26. Houston WJ. The analysis of errors in orthodontic measurements. *Am J Orthod*. 1983;83:382–390.
27. Yaffe A, Fine N, Binderman I. Regional accelerated phenomenon in the mandible following mucoperiosteal flap surgery. *J Periodontol*. 1994;65:79–83.
28. Iino S, Sakoda S, Ito G, Nishimori T, Ikeda T, Miyawaki S. Acceleration of orthodontic tooth movement by alveolar corticotomy in the dog. *Am J Orthod Dentofacial Orthop*. 2007;131:448.e1–8.
29. Ghanaati S, Booms P, Orlowska A, Kubesch A, Lorenz J, Rutkowski J, et al. Advanced platelet-rich fibrin: a new concept for cell-based tissue engineering by means of inflammatory cells. *J Oral Implantol*. 2014;40:679–689.
30. Fujioka-Kobayashi M, Miron RJ, Hernandez M, Kandalam U, Zhang Y, Choukroun J. Optimized platelet rich fibrin with the low speed concept: growth factor release, biocompatibility and cellular response. *J Periodontol*. 2017;88:112–121.
31. Gassling VL, Açil Y, Springer IN, Hubert N, Wiltfang J. Platelet-rich plasma and platelet-rich fibrin in human cell

culture. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2009;108:48–55.

32. Kobayashi E, Flückiger L, Fujioka-Kobayashi M, Sawada K, Sculean A, Schaller B, Miron RJ. Comparative release of growth factors from PRP, PRF, and advanced-PRF. *Clin Oral Invest.* 2016;20:2353–2360.

33. Aghaloo TL, Moy PK, Freymiller EG. Investigation of platelet-rich plasma in rabbit cranial defects: a pilot study. *J Oral Maxillofac Surg* 2002;60:1176–81.

34. Kanzaki H, Chiba M, Shimizu Y, Mitani H. Dual regulation of osteoclast differentiation by PDL cells through RANKL stimulation and OPG inhibition. *J Dent Res.* 2001;80:887–891.

35. Kanzaki H, Chiba M, Takahashi I, Haruyama N, Nishimura M, Mitani H. Local OPG gene transfer to periodontal tissue inhibits orthodontic tooth movement. *J Dent Res.* 2004;83:920–925.