Experimental investigation of effects of platelet-rich plasma on early phases of orthodontic tooth movement

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Introduction: The aim of this study was to evaluate the effects of platelet-rich plasma on orthodontic tooth movement in rats. **Methods:** We divided 48 Wistar male albino rats into 3 groups: control group, platelet-rich plasma group, and platelet-poor plasma group. The rats in all study groups had orthodontic tooth movement of their maxillary right first molars. Either platelet-rich plasma or platelet-poor plasma was injected into the animals in the platelet-rich plasma and platelet-poor plasma groups, respectively; the rats in the control group had no injection. Distances between the maxillary molar and incisor were measured on days 0, 1, 3, 7, and 14. Active osteoblast numbers in tension sites and osteoclast numbers in compression sites were examined histologically. Immunohistochemical evaluations of tartrate-resistant acid phosphatase (TRAP), transforming growth factor-β (TGF-β), and alkaline phosphatase (ALP) expressions were also performed. **Results:** The rats in the platelet-rich plasma group showed less tooth movement than those in the control group at day 3. At day 14, maximum tooth movement was observed in all groups. However, there was no statistical significance among the groups at day 14. In terms of osteoclast and osteoblast cells, no significant differences were observed in any group or at any time. Also, there were no significant differences in TRAP, ALP, and TGF-β expressions in the groups. **Conclusions:** The application of platelet-rich plasma was not beneficial as an adjunct to orthodontic treatment. (Am J Orthod Dentofacial Orthop 2019;155:71-9)

Orthodontic treatment provides optimal esthetics and functions along with correction of malocclusions. Targeted tooth movement with orthodontic treatment takes a long time because of the remodeling process of the bone, and the treatment usually lasts several years. The duration of orthodontic treatment might be an undesirable or even a dissuasive factor for patients. Different treatment modalities are available to shorten the treatment period, but there is no clinically accepted treatment option for accelerating tooth movement. Therefore, easy, tolerable, and noninvasive methods for accelerating orthodontic tooth movement are sought.

Numerous authors have studied accelerated orthodontic tooth movement. Recently, prostaglandin E2 and thyroid hormone were shown to increase orthodontic tooth movement in rats.[1] In addition to prostaglandins, corticosteroids, especially triamcinolone acetonide, were also found to be effective in shortening orthodontic treatment.[2] Other than these, nonsteroidal anti-inflammatory drugs, such as potassium diclofenac and dexamethasone, prevented bone resorption in the early phases of orthodontic movement.[3] Growth factors were also effective in accelerating tooth movement. Basic fibroblast growth factors increased the rate of tooth movement in a dose-dependent manner.[4] Zhang et al[5] reported that combined platelet-derived growth factor and transforming growth factor increased the velocity of tooth movement by up-regulating osteoclastic focal adhesion kinase expression and thus inducing osteoclastic proliferation, differentiation, and bone resorption in compression sites. Based on these studies, biochemical applications might help to reduce the time required for orthodontic treatment.

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However, such biochemical agents might not be practical in routine clinical practice due to their high costs.

Platelet-rich plasma (PRP) is an autogenous platelet concentrate, prepared by partitioning the blood into cellular components. Highly concentrated platelet fractions enhance the efficiency of platelets in physiologic processes such as hemostasis, inflammation, angiogenesis, and wound healing. Platelets contain inactive growth factors stored in alpha granules. Recently, it was demonstrated that PRP had equal efficacy to bone morphogenetic protein in terms of increasing bone regeneration.[6] Additionally, PRP was shown to increase proliferation, viability, and migration of mesenchymal stem cells, and promote angiogenesis, osteogenesis, and bone regeneration.[7] Regarding orthodontic treatment, Rashid et al[8] demonstrated that 250 μL of PRP provides significant improvement in orthodontic tooth movement in dogs. Gulec et al[9] also showed that PRP at a dose of 10 μL accelerated orthodontic movement by increasing osteoclastic activity and decreasing bone density in rats.

Evidence suggests that PRP might be beneficial in orthodontic treatment, but the mechanism of its efficiency in tooth movement is not well understood. Therefore, the aim of this study was to evaluate the effects of PRP on early tooth movement by determining tartrate-resistant acid phosphatase (TRAP), alkaline phosphatase (ALP), and transforming growth factor-β (TGF-β) expressions in rats.

MATERIAL AND METHODS

We used 48 Wistar male albino rats (6-8 weeks old; weight, 150-200 g) in this study. Experiments were carried out in accordance with the guidelines of the National Institutes of Health of the United States for the care and use of animals for experimental procedures or the European Communities Council Directive of November 24, 1986 (86/609/EEC), and in accordance with the guidelines of the animal ethics committee of the Faculty of Medicine, Erciyes University, Kayseri, Turkey. The rats were housed in a room with a 12-hour light and dark cycle and temperature between 22°C and 24°C; they were fed ad libitum with a standard laboratory diet and tap water. All necessary precautions were taken to minimize their discomfort or pain during the study.

The rats were randomly divided into 3 study groups: control group (C; n = 16), PRP group (n = 16), and platelet-poor plasma group (PPP; n = 16).

Each group was divided into 4 subgroups, and the rats were killed on days 1, 3, 7, and 14 by applying high doses of anesthetic agent.

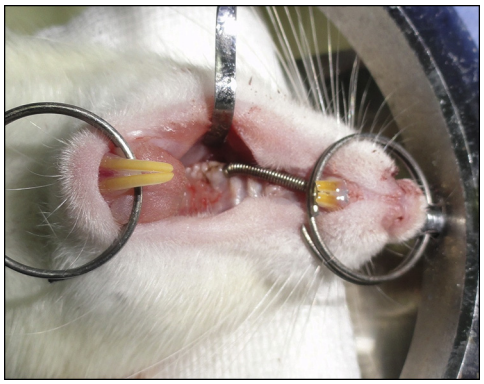

Fig 1. Nickel-titanium coil spring between the maxillary first molar and incisors.

Six additional rats were used to obtain the necessary blood to prepare the PRP. Under general anesthesia obtained by injection of a mixture of ketamine and hydrochloric acid (Alfamine; Alfasan International B.V., Woerden, Nederland) and xylazine hydrochloric acid (Rompun; Bayer, Berlin, Germany), whole blood was taken from these animals intracardially using 10-mL syringes containing 2 mL of anticoagulant (CPD solution; Baxter Healthcare, Deerfield, Ill). The CPD solution contained 26 mg per milliliter of sodium citrate dihydrate, 25 mg per milliliter of dextrose monohydrate, 2.9 mg per milliliter of citric acid, and 2.2 mg per milliliter of monobasic sodium phosphate monohydrate. The collected blood was centrifuged for 20 minutes at 220 g, at a temperature of 22°C to separate the plasma from the red blood cells. The red blood cells precipitated as a result of centrifugation. The supernatants were collected in a separate tube and subjected to a second centrifugation for 20 minutes at 480 g. The upper plasma was reserved for use as PPP. Resuspended platelets were diluted with some plasma to obtain PRP. When cells were counted, the platelet concentrations were $3617 \times 10^3/\mu L$ in the PRP and $23 \times 10^3/\mu L$ in the PPP, and the whole blood platelet concentration was $793 \times 10^3/\mu L$. It was calculated that the PRP contained 4.5-fold more platelets than at baseline.

Nickel-titanium closed-coil springs (International Orthodontic Services, Houston, Tex) were used for orthodontic tooth movement. The closed-coil springs were ligated to the maxillary incisors and first molars with stainless steel ligature wires (0.010 in; G&H Wire, Franklin, Ind) (Fig 1). A constant force of 50 g was applied, and no reactivation was performed during the experimental period. To prevent removal of the appliance by the animals, a notch was made at the cementoenamel junction level on the distal surface of the incisors with a

diamond flame bur for seating the ligature wire. Also, the ligature wires were fixed to the incisors with a flowable composite. Orthodontic tooth movement was demonstrated on the right side of the rats in all groups.

The injections were performed submucosally from the buccal vestibular mucosa next to the distal root of the maxillary right first molars via a 30-gauge insulin injector. The rats in the group C received no injections, those in the PRP group received 100 μL of PRP, and those in the PPP group received 100 μL of PPP. The injections were administered as 1 dose on the day of orthodontic force application.

The distance between the incisor (lingual side, gingival level) and the first molar (most convex point of the mesial surface) was measured with a digital caliper with accuracy of 0.01 mm. Measurements were performed at T0 (before orthodontic force application) and at every observational time point (T1, T2, T3, T4) under general anesthesia. Tooth movement at every time point were calculated by subtracting the incisor-to-molar distance from the incisor-to-molar distance at T0. All measurements were repeated 3 times, and mean values were used.

For the histologic examinations, the cervical halves of the distal roots of the maxillary first molars were used. Only the cervical half of the distal root was used for histologic examination because different pressure-tension zones were seen at the cervical and apical halves of the root as a result of the tipping movement of the first molars.

On the histologic images obtained, active osteoblast numbers in tension sites and osteoclast numbers in compression sites were examined. Osteoblastic activity was determined with ALP immunostaining, and osteoclastic activity was determined with TRAP immunostaining. Evaluation of ALP was performed in the tension sites of the periodontal ligament (PDL), and TRAP evaluation was performed in the pressure sites of the PDL.

The right mandibles were immersed in 10% neutral buffered formalin for 48 hours. After fixation, decalcification of the mandibles was performed with a solution of 12.5% ethylenediaminetetraacetic acid and a fixative agent for 10 weeks. Decalcification solutions were stirred 10 times a day and changed twice a week until decalcification was completed. After decalcification, all samples were dehydrated through ethanol series and embedded in paraffin. One examiner (A.H.Y.) who was unaware of the identity of the samples performed all histologic evaluations. Continuous sections of 5 μm were prepared, and 5 sections from each animal were stained with Masson's trichrome. The histomorphometric analysis was carried out, and osteoblast cells were counted. Cubic shaped osteoblast cells adjacent to the periodontal ligament and surrounded by osteoid were considered to be active osteoblast cells and counted in an area of 10,000 μm^2. Osteoblasts were counted in 3 areas in the coronal region of the distal side of the distal root, and mean osteoblast counts were recorded. Cells were counted with a digitized program (NIS-Elements Basic Research; Nikon Instruments Europe, Amsterdam, the Netherlands).

TRAP, ALP, and TGF-β immunohistochemistry evaluations were performed. After deparaffinization and dehydration of the sections, antigen retrieval was performed using 10 mmol/L of sodium citrate buffer (pH 6.0) for 2 hours at 70°C. Then the sections were treated with 3% hydrogen peroxide to quench endogenous peroxidase activity. After incubation with normal rabbit serum for 30 minutes, the samples were incubated with primary antibodies overnight. The antibodies and conditions were as follows: goat polyclonal anti-TRAP antibody (Abcam, Cambridge, United Kingdom; 1:500), anti-ALP antibody (Abcam; 1:750), and anti-TGF-β antibody (Abcam; 1:100). After washing 5 times with phosphate buffered saline solution, the sections were incubated with biotinylated immunoglobulin G for 30 minutes, washed several times with phosphate-buffered saline solution, and reacted with streptavidin-horseradish peroxidase conjugated reagent for 30 minutes. After 5-minute washes (3 times) with phosphate-buffered saline solution to make immunoreactivity visible, the sections were incubated with 3, 3′-diaminobenzidine chromogen (Thermo Fisher Scientific, Waltham, Mass). Then counterstaining was performed with hematoxylin, and the sections were analyzed with light microscopy (Eclipse, E 600; Nikon, Tokyo, Japan).

PDL areas surrounding the roots of the first molars were examined and evaluated by measuring the stained areas of the bone and PDL surrounding the teeth. Five areas were selected randomly from the sections of each animal to be examined under a light microscope with 400-times magnification. Categorical enumeration of the cells in these areas was made according to their immune-staining intensity. The average of the results of a blind study was taken. During these counts, both the number of cells showing positive immunoreactivity and the immunoreactive intensity degrees of these cells and all cells that were stained and not stained were considered. A staining score was created for all parameters.[10-12]

Statistical analysis

The normal distribution of the data was evaluated using the Shapiro-Wilk normality test and Q-Q graphs. The intraclass correlation coefficient was used to evaluate the reliability of the measurements.

Table I. Comparison of molar mesialization values between groups (mm)

	C	PRP	PPP	P
Day 1 (T0-T1)	0.462 ± 0.094	0.287 ± 0.122	0.335 ± 0.081	>0.05
Day 3 (T0-T2)	0.625 ± 0.028a	0.287 ± 0.176b	0.482 ± 0.128ab	0.01*
Day 7 (T0-T3)	0.550 ± 0.240	0.282 ± 0.423	0.467 ± 0.182	>0.05
Day 14 (T0-T4)	0.715 ± 0.298	0.292 ± 0.128	0.487 ± 0.113	>0.05

Common letters show similarity; those without common letters express statistical difference, *$P < 0.05$.

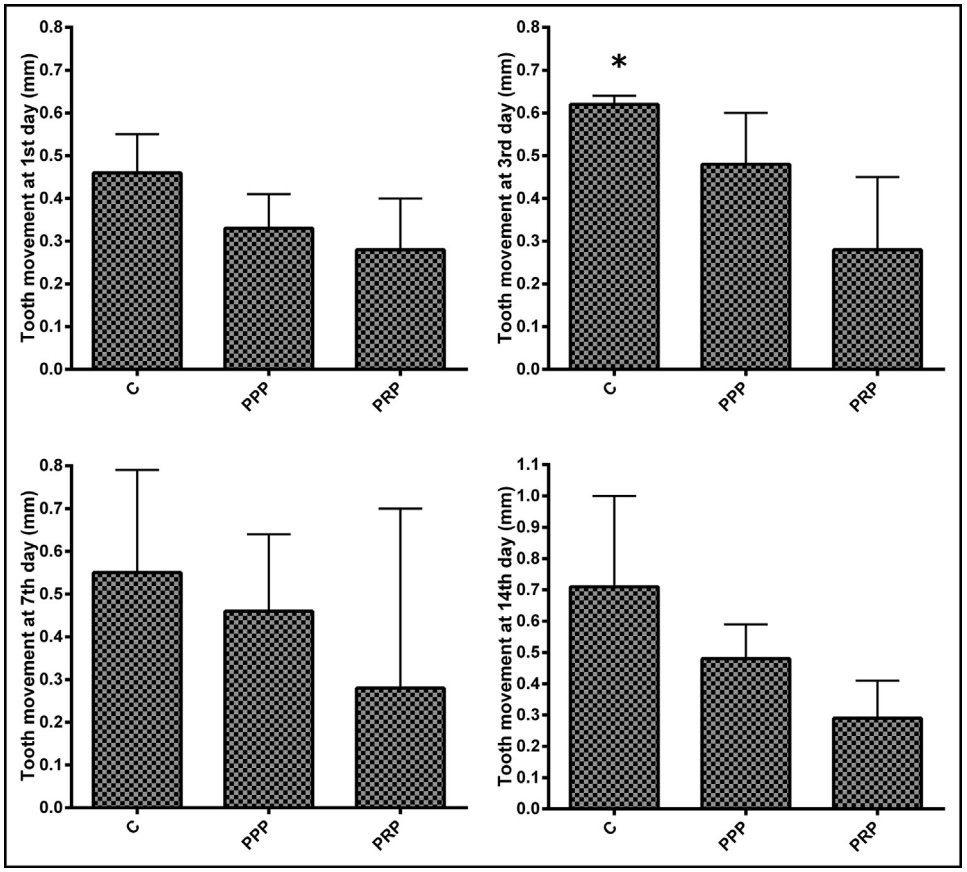

Fig 2. Graphic representation of amounts of mesialization at every time point (T0-T1, T0-T2, T0-T3, and T0-T4). *Significant difference from the PRP group.

For normally distributed variables, the homogeneity of the groups was evaluated with the Levene test; comparisons between groups were performed by 1-way analysis of variance. The Student-Newman-Keuls test was used as the multiple comparison test in the groups that had differences. The Kruskal-Wallis analysis was used for comparison of not normally distributed groups.

RESULTS

In all groups, statistically significant weight losses were observed 24 hours after the application of the appliances, and regular weight gains were observed in the following days in all groups.

The intraclass reliability coefficient for repeated measurements was 0.95. The amount of molar mesialization was significantly less in the PRP group on day 3 than in the C group ($P < 0.05$). No other significant difference was observed among the groups on days 1, 7, or 14 ($P > 0.05$). The amounts of molar mesialization in the C, PRP, and PPP groups were 0.625 ± 0.028, 0.287 ± 0.176, and 0.482 ± 0.128 mm at day 3, respectively. Mean tooth movement values are shown in Table I, and graphic representations of molar

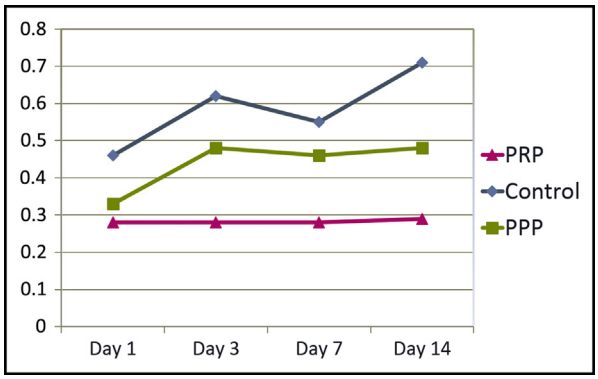

Fig 3. Tooth movement curves of the groups.

Table II. Comparison of osteoblast numbers in the tension-side PDL region between groups (n)

Group	*C*	*PRP*	*PPP*
Day 1	28.75 ± 7.13	21.75 ± 8.53	30.25 ± 9.46
Day 3	44.75 ± 20.59	34.33 ± 16.50	29.25 ± 21.09
Day 7	39.25 ± 19.25	33.75 ± 11.92	29.25 ± 11.08
Day 14	34.00 ± 11.10	33.33 ± 8.02	38.75 ± 8.99

No significant difference was observed ($P > 0.05$).

Table III. Comparison of osteoclast numbers in the pressure-side PDL region between groups (n)

	C	*PRP*	*PPP*
Group	*Median (25%-75%)*	*Median (25%-75%)*	*Median (25%-75%)*
Day 1	0.00 (0.00-0.50)	0.50 (0.00-1.50)	1.00 (0.50-2.00)
Day 3	2.50 (2.00-4.50)	3.00 (0.00-7.00)	1.50 (0.50-3.50)
Day 7	1.00 (0.00-2.50)	3.50 (1.50-5.50)	1.50 (0.50-3.00)
Day 14	1.00 (0.00-3.50)	1.50 (0.50-2.50)	0.00 (0.00-1.00)

No significant difference was observed ($P > 0.05$).

mesialization are given in Figures 2 and 3. Characteristic tooth movement phases including the lag phase between days 3 and 7 can be seen in Figure 3. Maximum tooth movements were observed in the C, PPP, and PRP groups.

Osteoblast cell counts were similar on days 1, 3, 7, and 14 in the groups ($P > 0.05$). There was no statistically significant difference between groups in osteoclast numbers at any time ($P > 0.05$). The mean osteoblast and osteoclast cell counts for all time points are given in Tables II and III. Representative histologic images of the osteoblast and osteoclast cells are shown in Figure 4.

Mean immunohistochemistry scores of the study groups are shown in Tables IV,V, and VI. No significant differences were observed in the groups in terms of ALP, TRAP, and TGF-β immunostaining at any time ($P > 0.05$). Representative immunostaining images of the groups are shown in Figure 5.

DISCUSSION

This is one of the first studies to evaluate any beneficial effects of PRP on the early phases of experimental tooth movement. The results showed that 100 μL of PRP (approximately 360×10^6 platelets), in a concentration 4.5-fold higher than baseline levels, was not effective in accelerating tooth movement in a rat model. Osteoblast and osteoclast cell counts remained unchanged. Likewise, TRAP, ALP, and TGF-β expressions were not changed.

Orthodontic tooth movement requires a certain degree of mechanical stress that could direct osteoblastic and osteoclastic activities and modify bone metabolism. Bone metabolism could also be regulated by any factor regulating osteoblastic or osteoclastic activity, such as hormones, growth factors, and inflammatory or proinflammatory cytokines. In terms of growth factor, PRP is known to contain many growth factors: PDGF, PDEGF, EGF, IGF, VEGF, and TGF-β. Due to the growth factors in PRP, it modifies bone remodeling in favor of bone formation.[13,14] In early studies, Marx et al[15] found that PRP added to cancellous bone grafts showed increased bone maturation and bone density. Otero et al[16] suggested that PRP added to PDL stem-cell culture induces osteogenic differentiation by increasing mineralization and expression of ALP, runt-related transcription factor, osteoprotegerin, and osteopontin, and production of type-1 collagen. The bone promotive effect of PRP has also been shown in clinical studies. Recently, Acosta-Olivo et al[17] demonstrated that PRP application with an autogenous graft promoted bone consolidation in patients with humeral shaft fractures. Furthermore, Hakimi et al[18] suggested that PRP added to bone marrow concentrate increased new bone formation and even provided equal bone formation as observed with autogenous bone grafts. All these studies confirm the effect of PRP on bone metabolism.

PRP-related studies have reported conflicting results in terms of bone remodeling. In contrast to the aforementioned results, Comert Kilic et al[19] found that PRP did not affect bone formation in sinus floor elevation. Okuda et al[20] also demonstrated that PRP inhibited ALP expressions. In addition, a decrease in osteoblast proliferation was reported in in-vitro studies.[21,22] One possible reason for the inhibitory effect of PRP on bone formation could be TGF-β. Studies have reported that high concentrations of TGF-β inhibit osteoblastic activity and bone formation.[23] On the other hand,

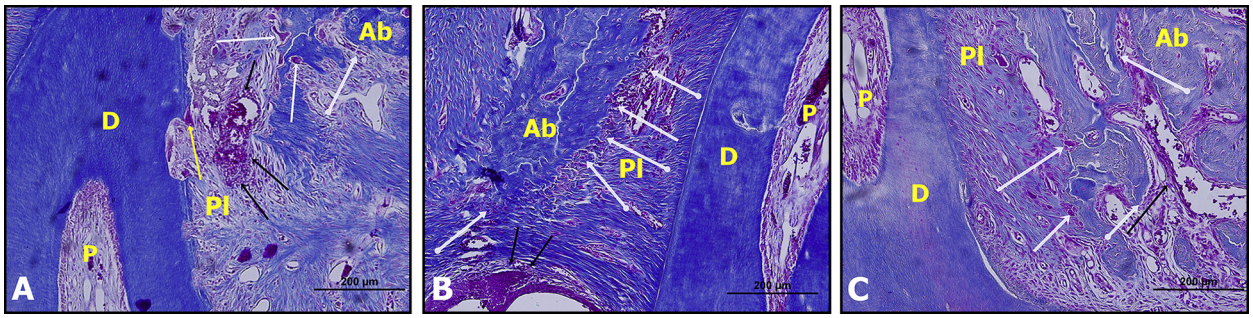

Fig 4. Representative images of Masson's trichrome staining at day 14: **A**: C group; **B,** PPP group; **C,** PRP group. *Straight yellow arrow*, cementoclastic cell; *straight black arrows*, inflamatory cells; *white arrows*, osteoclast cells; *white arrows with round ends*, osteoblast cells. *Ab*, Alveoler bone; *D*, dentin; *P*, pulp; *Pl*, PDL.

Table IV. Comparison of mean ALP immunostaining scores between groups

Group	*C*	*PRP*	*PPP*
Day 1	1.5 ± 0.5	1.5 ± 0.5	1.0 ± 0.5
Day 3	1.0 ± 1.0	1.0 ± 1.0	1.5 ± 0.5
Day 7	1.5 ± 0.5	1.5 ± 1.0	1.0 ± 0.5
Day 14	1.0 ± 1.0	1.5 ± 1.0	1.0 ± 1.0

No significant difference was observed ($P > 0.05$).

Table V. Comparison of mean TRAP immunostaining scores between groups

Group	*C*	*PRP*	*PPP*
Day 1	0.5 ± 0.5	0.5 ± 0.5	0.5 ± 0.5
Day 3	1.0 ± 0.5	0.5 ± 0.5	0.5 ± 0.5
Day 7	1.0 ± 0.0	1.0 ± 0.5	1.0 ± 0.5
Day 14	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.5

No significant difference was observed ($P > 0.05$).

Table VI. Comparison of mean TGF-β immunostaining scores between groups

Group	*C*	*PRP*	*PPP*
Day 1	1.5 ± 1.0	1.5 ± 1.0	1.5 ± 0.5
Day 3	1.5 ± 1.0	1.5 ± 1.5	1.5 ± 0.5
Day 7	2.0 ± 0.5	2.0 ± 1.0	1.5 ± 1.0
Day 14	2.0 ± 1.0	2.0 ± 0.5	2.0 ± 0.0

No significant difference was observed ($P > 0.05$).

TGF-β can stimulate almost every type of cell in the body and is especially important in chemotaxis and mitogenesis of preosteoblast cells.[15] TGF-β is also related to bone remodeling via stimulating synthesis of collagen and osteoprotegerin, which is an indicator of inhibition of bone resorption.[24,25] Increased TGF-β levels were also observed in tension sites in experimental tooth movement in rats.[26] Therefore, TGF-β might be an important marker in bone remodeling. We evaluated the effect of PRP on bone metabolism along with osteoblast and osteoclast cell counts, and ALP, TRAP, and TGF-β expressions in an experimental orthodontic tooth movement model in Wistar rats. However, our results showed no significant differences in ALP, TRAP, and TGF-β expressions. The differences in osteoblast and osteoclast cell counts were also insignificant. Therefore, no effect of PRP was observed in the histologic bone slides around the first molars.

Orthodontic tooth movement requires modification of bone metabolism. Osteoblastic activity is desired in tension sites, and osteoclastic activity is desired in pressure sites. Therefore, an experimental orthodontic tooth movement model is beneficial in observing the effect of PRP on both bone formation and bone resorption. Recently, PRP was found to accelerate tooth movement in dogs[8] and rats.[9] However, the mechanism of action was not shown. Rashid et al[8] reported increased osteoclast counts in compression sites at week 9, but early histologic findings were not presented. On the other hand, Gulec et al[9] reported that PRP accelerated tooth movement at days 7, 14, 21, and 60 despite decreased osteoclast cell counts in compression sites compared with the control group. We evaluated the early effects of PRP with immunohistochemical alterations in PDLs and alveolar bones on days 1,3, 7, and 14. A statistically significant difference between the groups was determined only on day 3. At day 14, all groups showed similar tooth movements. Biologic activity of growth factors was reported to last for 5 days, and 80% of the factor was reported to be released 24 hours after application and completed in 2 weeks.[23,27,28] Therefore, 14 days is enough to observe the early effects of PRP on tooth movement.[29]

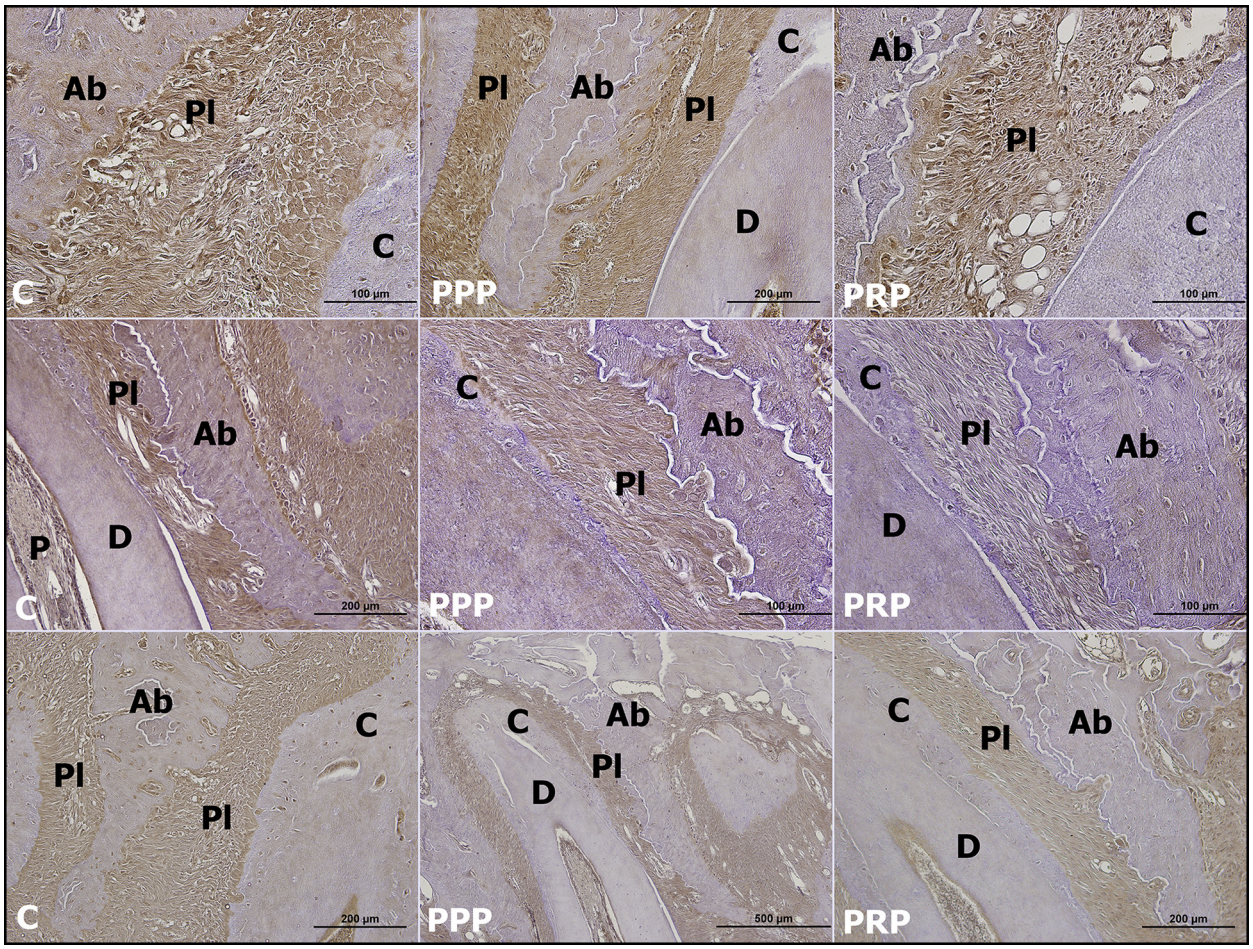

Fig 5. Representative images of ALP, TRAP, and TGF-β immunostaining in study groups at day 14: top row, ALP immunostaining images in each group; middle row, TRAP immunostaining images; bottom row, TGF-β immunostaining images. *Ab*, Alveoler bone; *C*, cementum; *D*, dentin; *P*, pulp; *Pl*, PDL.

The effect of PRP on bone remodeling was reported to be dose-dependent.[21,22,30] Gulec et al[9] studied moderate and high doses of PRP as 2.5-fold and 5-fold increases in platelet concentrations; 10 μL of each concentration (approximately 12×10^6 and 26×10^6 platelets) was applied. They reported that these doses promoted osteoclastic activity by increasing TRAP-positive osteoclast counts on day 3 and enhanced tooth movement in rats. In contrast, Graziani et al[21] stated that a 2.5-fold increase in platelet concentrations (approximately 28×10^6 platelets) elevated osteoblastic proliferation and activity that could prevent tooth movement in vivo. In addition, Slapnica et al[22] found that platelet concentrations from 0.38-fold to 2.86-fold increased inhibited osteoblast proliferation on days 1, 2, and 3, without indicating the baseline platelet concentration.

To properly discuss the dose-dependent effect of PRP, we must know the baseline platelet concentrations, increased platelet concentrations, and applied volume of the PRP. However, some studies provide insufficient information in this regard. The controversial effects of PRP in the literature might result from this fact. For instance, a recent study showed the effect of PRP even with the lowest dose reported,[9] whereas others reported no effect.[31] Rashid et al[8] reported that 250 μL of PRP increased both osteoblast and osteoclast counts, resulting in accelerated tooth movement. Seyhan et al[31] found no effect of PRP on bone regeneration even with high doses such as 500 μL. In contrast, Mansouri et al[32] recently demonstrated that 500 μL of PRP improved bone healing in a tibia defect in rabbits. Likewise, Wilson et al[33] suggested that 500 μL of PRP with a 4.0-fold increase of platelet concentration (containing

approximately 700 × 10^6 platelets) promoted bone healing in a rabbit model. In this study, 100 μL of PRP containing a 4.5-fold increase in platelets (approximately 400 × 10^6 platelets) was used. A dose of 100 μL of PRP could be considered moderate compared with similar studies.[8,9] Our study showed that 100 μL of PRP inhibited tooth movement on day 3, but tooth movement on day 14 was similar. This could be due to the short half-life of PRP and the growth factors in it. Tooth movement occurs parallel to osteoclastic activity, and the decrease in tooth movement in our study was not compatible with osteoclast and osteoblast cell counts. However, it might be observed because of the early bone promotive effect of PRP reported in the literature.[34,35]

PPP contains fewer platelet cells than PRP; rather, it contains serum proteins already present in blood. To evaluate the effect of platelet activation and platelet-derived factors on orthodontic tooth movement, PPP was also applied in a separate study group. PPP provided less tooth movement than in the control group but much less than in the PRP group. The observed effect of PPP results from the serum proteins, and the difference between PPP and PRP results from the platelet concentrations.

We evaluated the effect of PRP on experimental tooth movement and found that PRP does not affect osteoblast and osteoclast cell counts, and ALP, TRAP, and TGF-β expressions. Tooth movement was decreased on day 3 with PRP application; other than that, tooth movements were the same at all times and in all groups. There are certain limitations of this study. First, osteoblastic activity was evaluated via only ALP expression. Despite being an indicator of bone formation, ALP is not the strongest factor of bone formation. Additional factors such as bone morphogenetic proteins, osteocalcin, osteoprotegerin, and so on would be beneficial. Second, along with TRAP, the receptor activator of nuclear factor kappa B would be useful in evaluating osteoclastic activity. Third, a 4.5-fold increased platelet concentration was used in this study. Lower and higher doses would be beneficial in evaluatingthe dose-dependent effects of PRP on tooth movement.

CONCLUSIONS

The results of this study suggest that a 4.5-fold higher dose of PRP (100 μL of 3617 × 10^5/μL) is not beneficial as an adjunct to orthodontic treatment. Nevertheless, contradictory findings in the literature along with the limitations of this study demonstrate a need for further studies in this regard.

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