Original Article

Effect of platelet-rich plasma on the rate of orthodontic tooth movement: *A split-mouth randomized trial*

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ABSTRACT

Objective: To investigate the effect of local injection of platelet-rich plasma (PRP) on the rate of orthodontic tooth movement.

Materials and Methods: Sixteen female patients were randomly allocated in a split-mouth study design to receive PRP injections with $CaCl_2$ activating solution on one side (intervention side) while the other side received $CaCl_2$ injection only (control side). Canine retraction was performed on 0.017 × 0.025-inch stainless steel archwire applying 1.5 N retraction force. PRP and $CaCl_2$ injections were done at 0, 3, and 6 weeks. The duration of the study was 4 months. Data were collected from digitized models. Assessment of pain accompanying the procedure was done using a visual analogue scale.

Results: The rate of canine retraction was faster on the intervention side in the first 2 months, with a statistically significant difference in the first month ($P = .049$). On the other hand, the rate was statistically significantly slower on the intervention side in the third month following cessation of PRP injections ($P = .02$). Pain increased following injections on both sides.

Conclusions: PRP showed a positive potential to accelerate the rate of tooth movement when injected in the first 2 months. Repeated injections of PRP to maintain a steady rate of accelerated tooth movement warrant further investigation. (*Angle Orthod.* 2020;90:354–361.)

KEY WORDS: Platelet-rich plasma; Acceleration; Tooth movement; Pharmacological approaches; Canine retraction; Digital models

INTRODUCTION

Orthodontic tooth movement is the product of a biological response to an interference in the physiological equilibrium in the dentofacial complex by an externally applied force.[1] Various approaches have been attempted to accelerate the rate of orthodontic tooth movement. Although each approach has claimed to be superior to the others in different studies, conflicting evidence concerning each technique still exists.[2,3] Pharmacologic approaches to accelerate the rate of orthodontic tooth movement have been investigated in humans since the 1980s.[4] If proven clinically efficient, pharmacologic approaches might surpass other approaches as they are less invasive, less costly, and more controlled. The problem that remains is their concomitant side effects that might occur especially in association with systemic administration.

One of the recently used local agents to accelerate the rate of orthodontic tooth movement is platelet-rich plasma (PRP).[5] PRP is defined as an autologous concentration of platelets in a minute volume of plasma.[6] The alpha granules in the platelets are the most abundant secretory granules. They contain numerous proteins, including growth factors and chemokines, which are crucial for primary hemostasis and wound healing.[7,8] Research concerning PRP has focused on its applications in regenerative medicine.[9] The relationship between PRP and orthodontic tooth

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Table 1. Eligibility Criteria for Patients Included in the Study

Inclusion Criteria	Exclusion Criteria
Female patients	Systemic disease or syndrome
Age 18 ± 3 y	Abnormalities in teeth size and/or shape
Full permanent dentition	Vertical, transverse, or anteroposterior skeletal discrepancies
Good general and oral health	History of previous orthodontic treatment
Severe crowding or protrusion requiring first premolars extractions	Anti-inflammatory medication

movement has drawn some attention lately. In two recently published animal studies, Rashid et al.[5] and Gülec et al.[10] evaluated the effects of PRP on tooth movement. Both studies showed a positive correlation between local injection of PRP and acceleration of orthodontic tooth movement. On the other hand, Akbulut et al.[11] reported no beneficial effects of PRP injections on tooth movement, yet they recommended that further studies be conducted.

The aim of the current study was to investigate the effect of local injection of PRP on the rate of orthodontic tooth movement clinically and also to report any associated pain.

MATERIALS AND METHODS

Subjects

The current study was a split-mouth randomized controlled clinical trial with a 1:1 allocation following the CONSORT statement reporting guidelines. The study was performed at Cairo University and approved by the Faculty of Dentistry Ethical Committee (No. 1522015). No changes were reported after commencement of the study.

The sample requirement for this study was calculated to be 10 female patients using Minitab software based on the results of Abou Ela et al.,[12] who implemented a comparable split-mouth study design. Six additional patients were included to consider sample attrition. A computer-generated random list was created (https://www.random.org/), and allocation concealment was achieved with opaque sealed envelopes. Patient eligibility criteria are presented in Table 1. Consent was obtained from the patients and/or their legal guardian before recruitment.

METHODS

Full preoperative records were obtained, and Roth 0.022-inch brackets (American Orthodontics, Sheboygan, Wis) were bonded. Leveling and alignment were accomplished until 0.017 × 0.025-inch stainless steel archwire was reached. Two mini-screws (1.6 × 8 mm, bracket head design; Dual Top Anchor System, Jeil Medical Corporation, Seoul, Korea) were inserted in the interradicular region between the upper second premolars and upper first molars on each side at the level of the junction between the attached and nonkeratinized gingiva. First molars were anchored to the miniscrew using a 0.019 × 0.025-inch stainless steel wire. NiTi closed-coil springs delivering a retraction force of 1.5 N[12] per side were attached to the right and left canine hooks following the injection of the PRP on the intervention side (Figure 1).

PRP Preparation and Injection

PRP was prepared by the double-spin technique as described by Marx and Garg[13] and Rashid et al.[5] The intervention side was anesthetized with 2% mepivacaine with vasoconstrictor and left for 15 minutes. Then, 25 units (0.25 mL) of PRP was injected intraligamentally in the middle, distobuccal, and distopalatal areas of the distal surface of the canines (5 units each area) together with submucosal injections buccally and palatally (5 units each area). Immediately following PRP injection, the same volume of 10% $CaCl_2$ solution was injected for activation of PRP. The intervention side was injected at the following intervals: 0, 21, and 42 days. The control side was anesthetized and injected with 25 units of 10% $CaCl_2$ following the same protocol and frequency as the intervention side (Figures 2–4).

Alginate impressions for the upper arches were made before canine retraction and monthly until the fourth month (T0–T4). Stone models were scanned

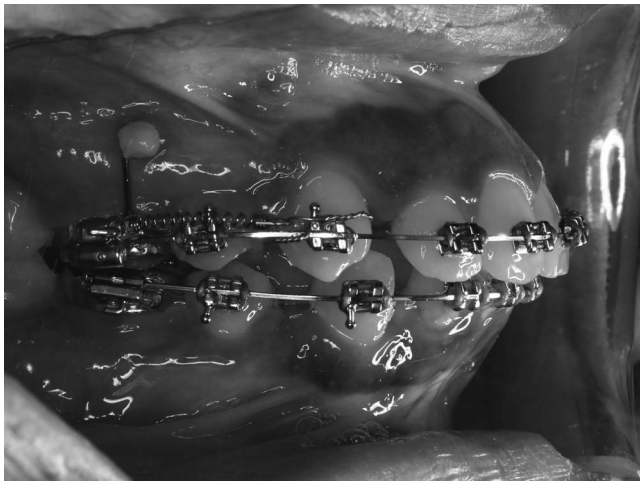

Figure 1. Fixed appliance setup during canine retraction.

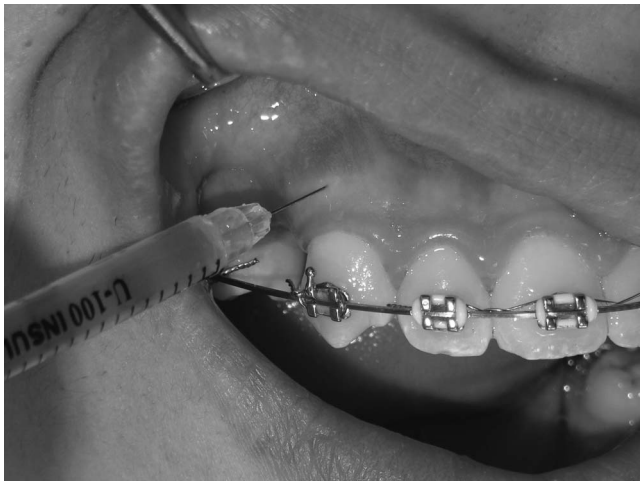

Figure 2. Submucosal injection of 5 units of platelet-rich plasma at the buccal surface on the intervention side.

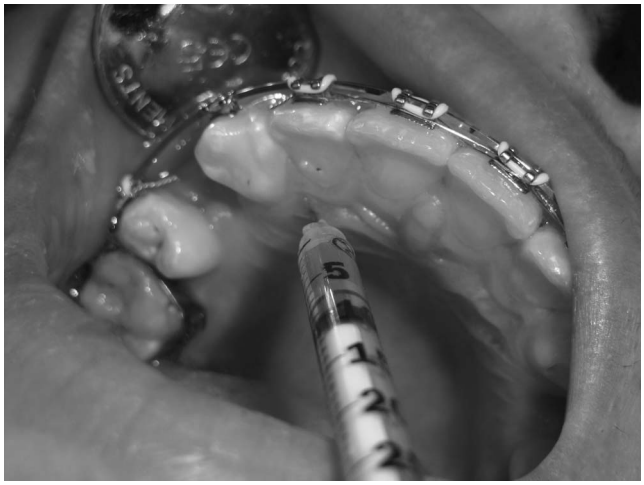

Figure 4. Submucosal injection of 5 units of platelet-rich plasma on the palatal aspect of the intervention side.

using a 3-Shape scanner (R500, 3shape, Copenhagen, Denmark). The five consecutive digital models were superimposed using 3-Shape analyzer software[14] (3shape, Copenhagen, Denmark). Color-coded superimposition was done to verify the accuracy of the superimposed models[15] (Figure 5). The change in the canine position in the superimposed models was measured to detect the rate of canine retraction per month (Figure 6). The rate of canine retraction was calculated from the difference in the canine position in the consecutive models (Figure 7). In addition, the mesial and distal contact points of the canines were used to form a horizontal line that formed an angle with the median palatine raphe (Figure 8). The change in that angle between the initial and final models indicated the amount of canine rotation. Blinding of measurements was performed only during outcome assessment, which was carried out by two assessors not involved in the clinical procedures.

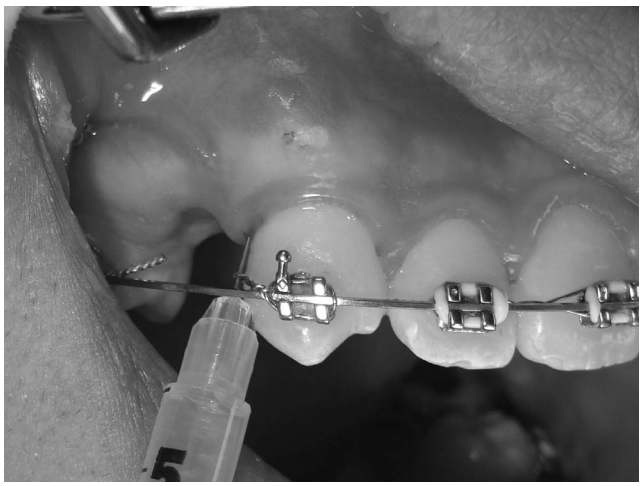

Figure 3. Intraligamental injection of 5 units of platelet-rich plasma in the distobuccal area of the distal surface of the canine on the intervention side.

Pain was assessed using a visual analogue scale questionnaire that was completed by the patient starting from the day following PRP injection and repeated every week until the seventh week. The format of the questionnaire was a 10-cm line, and the patients were requested to mark a location on the line corresponding to the amount of pain they experienced, with 0 indicating no pain and 10 indicating unbearable pain.[16] The patients were instructed not to use any additional analgesics.

Statistical Analysis

Analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 22.0 (SPSS Inc., Chicago, Ill) for Windows. Shapiro-Wilk tests of normality were used to test normality of all quantitative variable distributions. A paired *t*-test was used to determine the statistical significance of differences between the experimental and control sides for preoperative and postoperative measurements.

The significance level was set at $P \leq .05$. For inter- and intraobserver reliability, concordance correlation coefficients including 95% confidence limits were used.

RESULTS

Numbers Analyzed for Each Outcome

Of the 16 recruited patients, one patient discontinued the trial due to traveling. For the remaining 15 patients, the rate of canine retraction and rotation together with concomitant pain assessment were evaluated.

The rate of canine retraction showed a statistically significant difference between the two sides in the first

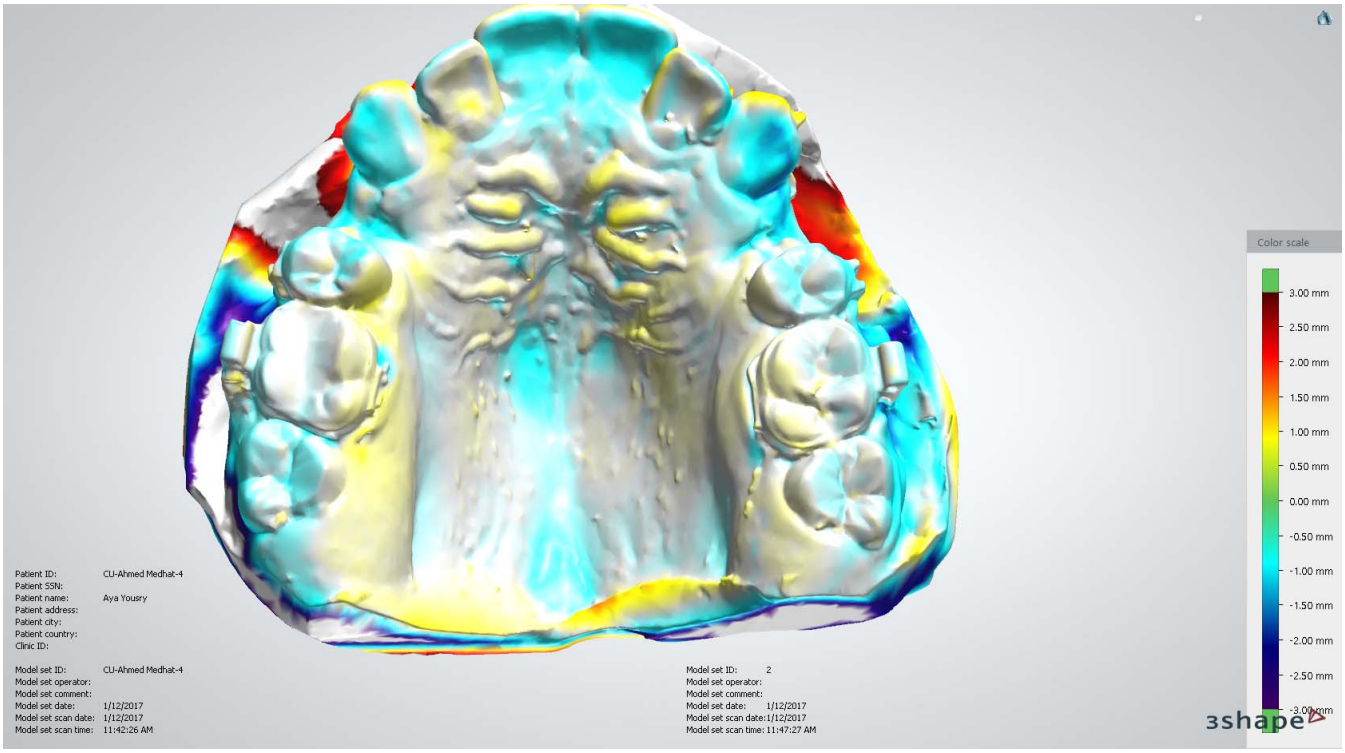

Figure 5. Color-coded verification of the superimposition of the digital models.

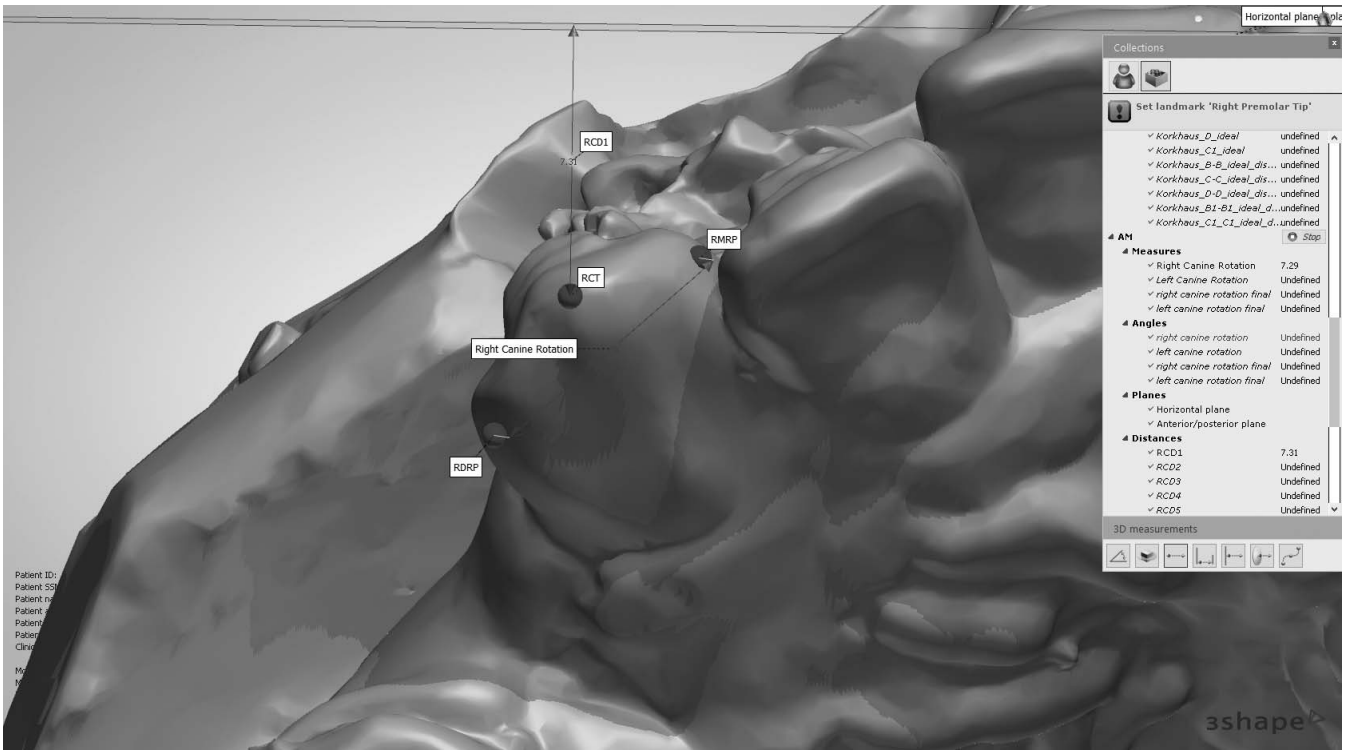

Figure 6. Point localization of the canine. RCT indicates the most incisal point on the right canine tip; RMRP, mesial contact point of the maxillary right canine; LDMRP, distal contact point of the maxillary right canine; RCD1, perpendicular distance from RCT to the median palatine raphe.

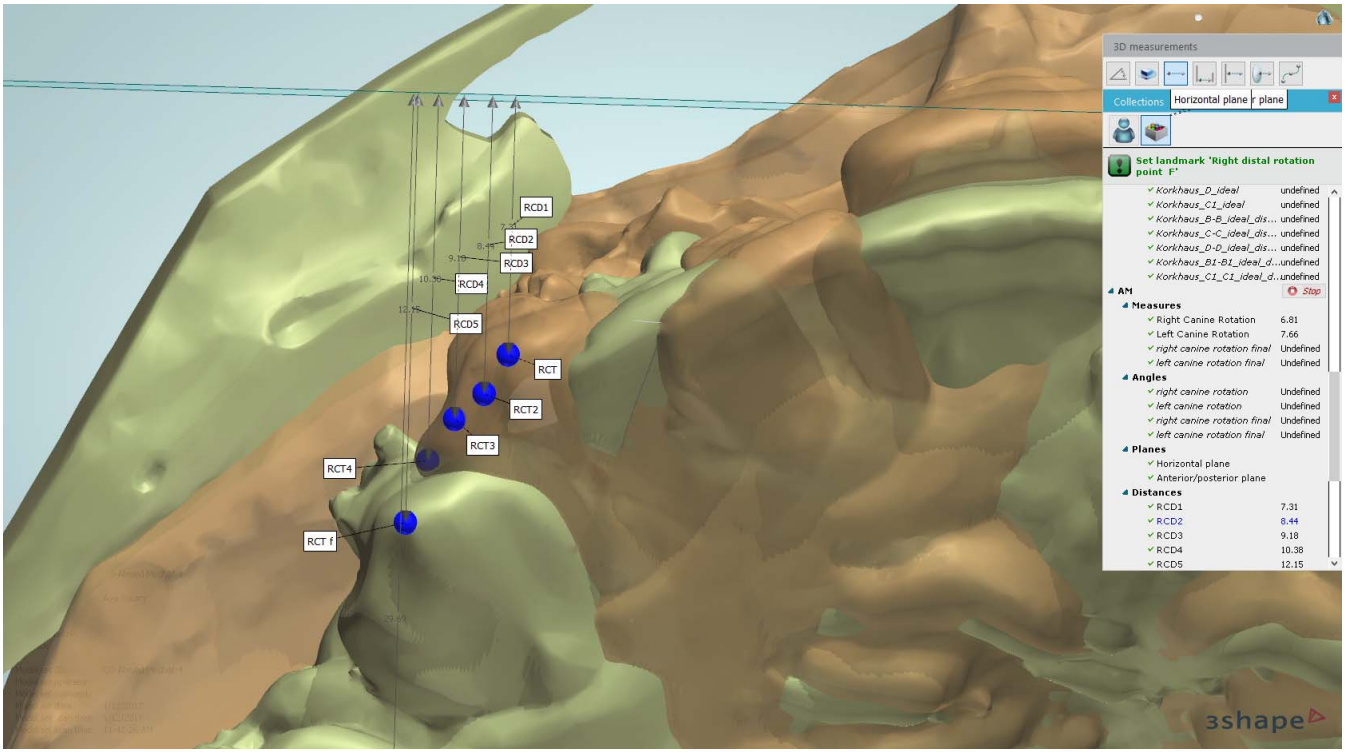

Figure 7. The canine tip localized on the five consecutively superimposed digital models.

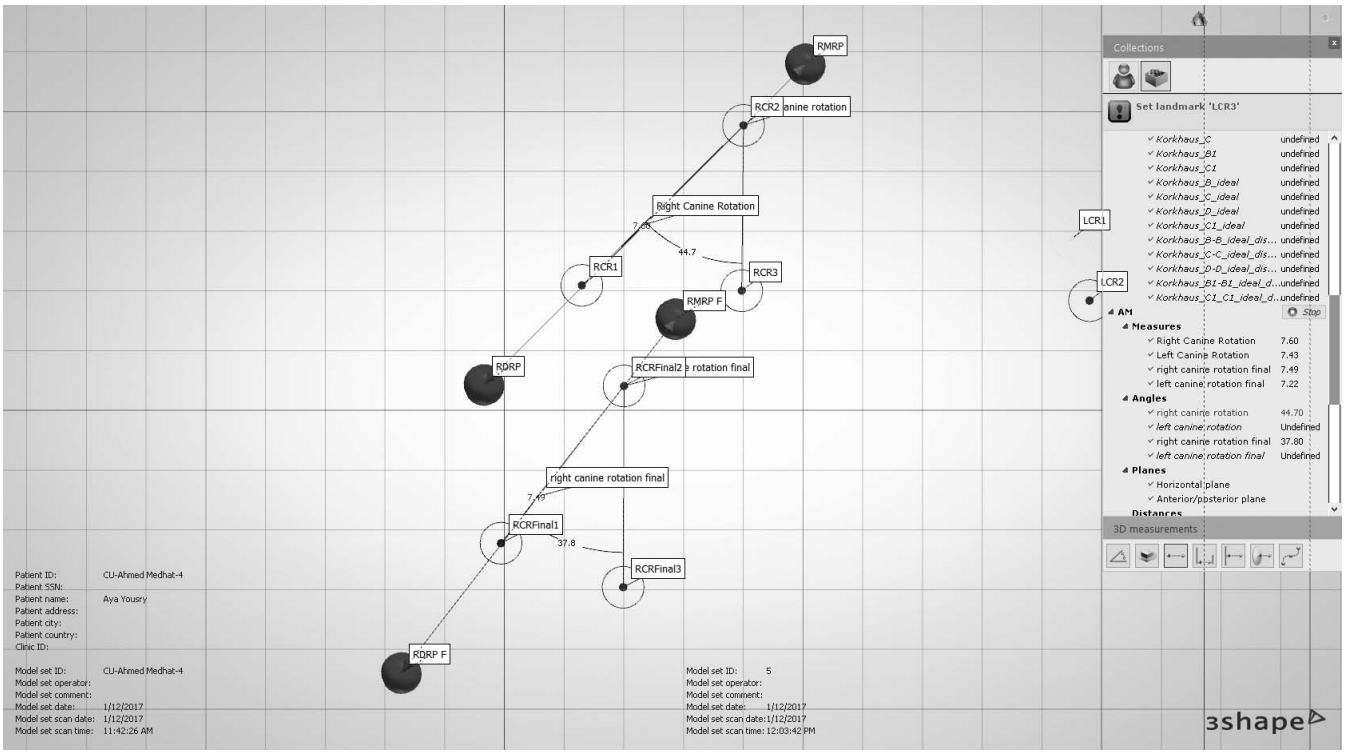

Figure 8. Measurements of canine rotation after removing images of the digital models for clarity. RMRP and RMRP f indicate the mesial contact point of the maxillary right canine at T0 and T4, respectively; LDMRP and LDMRP f, distal contact point of the maxillary right canine at T0 and T4, respectively; RMRP 1, RMRP 2, and RMRP 3, angle between the right canine and the median palatine raphe at T0; RMRP final 1, RMRP final 2, and RMRP final 3, the same angle at T4.

Table 2. Mean Values for the Rate of Canine Retraction in Both Groups (mm)

Measurement	Group	Min	Max	Mean	SD
First month (T0–T1)	Control	0.57	2.60	1.35	0.62
	Intervention	0.39	2.92	1.55	0.63
Second month (T1–T2)	Control	0.76	1.99	1.27	0.40
	Intervention	0.07	2.73	1.33	0.87
Third month (T2–T3)	Control	−0.41	1.96	1.01	0.63
	Intervention	−1.39	2.08	0.59	0.96
Fourth month (T3–T4)	Control	0.09	2.08	0.90	0.50
	Intervention	0.26	2.29	1.10	0.58

month ($P = .049$), with a mean value of 1.35 ± 0.62 mm/mo for the control side compared with 1.55 ± 0.63 mm/mo for the intervention side, reflecting acceleration of tooth movement with PRP injection. Surprisingly, at the third month, a statistically significant difference between the two sides ($P = .020$) was reported, but this time it was greater on the control side, with a mean value of 1.01 ± 0.63 mm/mo compared with 0.59 ± 0.96 mm/mo for the intervention side, reflecting a deceleration in the rate of tooth movement on the intervention side following cessation of PRP injections. The total distance traveled by the canine following retraction was similar in both groups during the 4 months of the study period, with a mean of 4.53 ± 1.12 mm for the control side and 4.57 ± 1.32 mm for the intervention side (Tables 2 and 3; Figure 9). Canine distal-in rotation was comparable in both groups, with a mean difference of 1.036° (Table 4).

All patients returned their pain questionnaires, and none reported using any analgesics. An increase in pain scores was reported in the first, fourth, and seventh weeks following each injection on both the intervention and control sides.

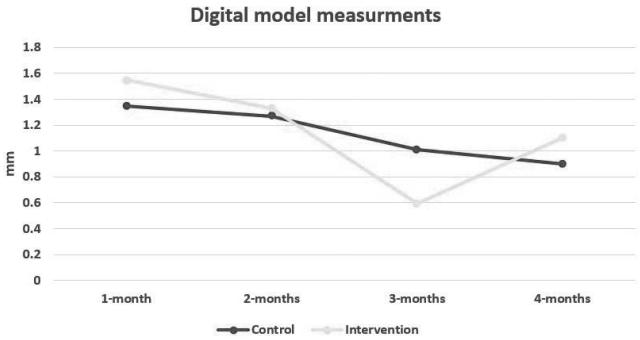

Figure 9. Line chart showing the rate of canine retraction on the intervention vs control sides.

DISCUSSION

PRP has been used extensively in various fields of dentistry, showing vast advantages and applications.[13,17] Previous literature revealed that methods of PRP preparation have evolved in many techniques,[18] all aiming at standardization of the procedure for PRP preparation. First attempts of PRP preparation reported the use of a mixture of 10 mL of 10% calcium chloride combined with 10,000 units of bovine thrombin for PRP activation.[19] Activation with bovine thrombin is no longer recommended, as this was reported to cause coagulopathy resulting from cross-reactivity of anti–bovine factor V antibodies with human factor V.[20] Hence, suggestions to use autologous thrombin[21] or calcium chloride alone were recommended.[20] Textor and Tablin[21] showed that calcium chloride activation might be the most inexpensive and effective method, although it might need 20 minutes for activation of PRP.[20]

The injection technique in five different areas around the retracted canine followed the same protocol reported by Rashid et al.[5] This may be compared with the findings of Gülec et al.,[10] who injected the PRP only at the buccal vestibular mucosa adjacent to the mesial root of the first molar. Intraligamentary injection at the distobuccal and distopalatal surfaces of the canine root was advocated in this study based on the work by Von Böhl et al.,[22,23] who reported that, as a consequence of local stress and shear concentrations, most hyalinized areas were not found in the area of the central plane but rather lingually and buccally from it. Rapid bone metabolism was required in these areas to accelerate

Table 3. Comparison of the Mean Differences in the Amount of Canine Retraction Between Groups for Each Month

Measurement	Group	Mean Difference	SD	SEM	95% Confidence Interval of Mean Difference		*t*	*df*	*P* Value
					Lower	Upper			
First month (T0–T1)	Control Intervention	−0.20133	0.44694	0.11540	−0.44884	0.04617	−1.75	14	.049*
Second month (T1–T2)	Control Intervention	−0.06067	0.79570	0.20545	−0.50131	0.37998	−0.295	14	.772
Third month (T2–T3)	Control Intervention	0.41600	0.61618	0.15910	0.07477	0.75723	2.62	14	.020*
Fourth month (T3–T4)	Control Intervention	−0.20133	0.67889	0.17529	−0.57729	0.17463	−1.15	14	.270

* Significant at $P \leq .05$.

Table 4. Comparison of the Mean Differences in the Total Amount of Canine Rotation and Retraction Between Groups

Measurement	Group	Mean	SD	Mean Difference	SD	SEM	95% Confidence Interval of Mean Difference		*t*	*df*	*P* Value
							Lower	Upper			
Canine rotation	Control	15.46	11.39	1.03600	10.56011	2.72661	−4.8120	6.88400	0.380	14	.710
	Intervention	14.42	9.70								
Total retraction (T0–T4)	Control	4.53	1.12	−0.04733	1.3703	0.35382	−0.80619	0.7115	−0.13	14	.895
	Intervention	4.57	1.32								

* Significant at $P \leq .05$.

orthodontic tooth movement.[24] Conversely, previous studies evaluating the effects of local pharmacologic agent injection to accelerate tooth movement reported only one or two submucosal or gingival injection sites.[4,10,25–27]

Injections were delivered every 3 weeks and repeated until the sixth week following the protocol reported by Rashid et al.[5] Although the study continued for 4 months, injections were not continued through the whole duration of the study in order to determine whether PRP injections were enough in the initial phases of tooth movement only, as compared with corticotomy[12] or low-level laser therapy applications.[3]

The results of the current study showed a faster rate of canine retraction on the intervention side in the first month by 15% and in the second month by 5%. Despite this increase being statistically significant in the first month ($P = .049$) and nonsignificant in the second month ($P = .772$), the results reflected a positive correlation between PRP injection and acceleration of orthodontic tooth movement. Unexpectedly, in the third month and following cessation of PRP injections, the rate of canine retraction on the intervention side was significantly ($P = .020$) slower than the control side by 40%. This might be related to a negative feedback mechanism in the growth factors' release, similar to hormonal negative feedback that occurs in association with elevated blood and/or tissue concentration. Hence, increasing the tissue concentration of growth factors incidental to local injection of PRP could have affected the normal production of growth factors during orthodontic tooth movement.[28–30] In the last month of the study period, results showed a nonsignificant difference in the rate of canine retraction between the two sides. The rate of canine retraction on the control side was slightly more than that reported by Aboul-Ela et al.[12] and less than that reported by Hayashi et al.[31] On the other hand, Gülec et al.[10] reported that PRP induced acceleration of orthodontic tooth movement by 1.4 to 1.7 times. Similarly, Rashid et al.[5] reported a higher value of acceleration (PRP:control rate = 2.13:1) compared with the present study. This could have been due to the difference in the nature of their studies being animal studies with a more controlled environment together with a possible difference in the PRP composition.

Pain scores showed no difference between the intervention and control sides. This could be related to the forceful intraligamental injection procedure itself rather than an effect related to the pharmacologic agent.

CONCLUSIONS

- Despite the statistically significant increase in the rate of canine retraction during the early stages of tooth movement concomitant with PRP injections, PRP did not exhibit long-term acceleration effects.
- The effect of repeated injections of PRP throughout the course of canine retraction to maintain a steady rate of accelerated tooth movement needs to be further investigated.

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