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## Research Article

### Effect of Submucosal Platelet Rich Plasma Injection on the Rate of Orthodontic Tooth Movement: A Randomized Split Mouth Trial

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## Abstract

**Background:** Platelet Rich Plasma (PRP) is one of the recent modalities introduced to accelerate orthodontic tooth movement (OTM). The aim of this split-mouth trial was to investigate the effect of PRP injection on the rate of OTM.

**Methods:** Fourteen patients requiring bilateral first premolar extraction and upper canine retraction with maximum anchorage were included. A split mouth design was adopted in the study. Submucosal PRP injection (70 units) was randomly assigned to one side of the maxillary arch (experimental side), while the other side served as control. PRP injected disto-buccal and disto-palatal to the maxillary canine. Digital models were used to evaluate the monthly rate of canine retraction and anchorage loss.

**Results:** Three patients dropped out, and eleven were analyzed. The mean rate of canine retraction was significantly higher in the experimental side compared to control side in the first month ( $P \leq 0.05$ ), with no significant differences in the remaining months.

**Conclusions:** Submucosal PRP injection can be effective and safe method for acceleration of orthodontic tooth movement on short term.

## Keywords :

Platelet rich plasma, Accelerated orthodontics, Tooth movement, Canine retraction, Digital models.

## Declaration of Conflicting Interest

The authors declare that they have no conflict of interest

## Introduction:

Lengthy treatment is one of the main challenges in orthodontics. Prolonged treatment duration could be very disappointing for our patients, particularly for older age categories, and usually associated with other negative sequelae as increased risk for root resorption and dental caries [1-4]. Pharmacological agents like prostaglandin or hormones like parathyroid hormone have been attempted [5,6]. However, undue systemic effects, pain, and root resorption have been reported with these biochemical agents [7-9]. Several surgical approaches including corticotomy, corticision, piezocision, dento-alveolar or periodontal distraction, and interseptal bone reduction have been tried in order to accelerate tooth movement. However, due to their invasive nature they may not be acceptable to most patients [10].

One of the recently used local agents to accelerate the rate of OTM is PRP. PRP is an autologous concentration of platelets in a small volume of plasma after centrifugation. About: 1,000,000 platelets/ $\mu$ L is present in PRP [11]. PRP was first introduced to the dental literature in 1998 in combination with autogenous bone grafts for the reconstruction of mandibular defects, reporting that the addition of PRP to bone grafts resulted in a faster radiographic maturation rate than bone grafts alone. Since 1998, PRP is increasingly used in dentistry, mainly in periodontal defects, extraction sockets, during

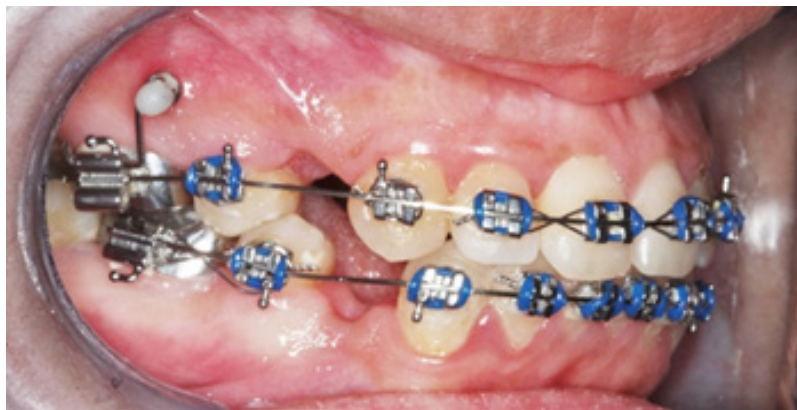
implant placement, and in guided bone regeneration procedures around implants <sup>[12,13]</sup>. Liou <sup>[14]</sup> in 2016 introduced the submucosal PRP injection for acceleration of OTM. Later, Güleç et al., <sup>[15]</sup> and Rashid et al., <sup>[16]</sup> conducted experimental studies that showed its acceleratory effect. Akbulut et al., <sup>[17]</sup> concluded that PRP was not beneficial as an adjunct to orthodontic treatment. El-Timamy et al., <sup>[18]</sup> conducted the first human trial and concluded that PRP have a positive potential to accelerate OTM when injected in the first 2 months. The effectiveness of PRP injection on acceleration of OTM remains debatable. Accordingly, the current study was designed to determine the effect of submucosal PRP injection on rate of OTM.

### Methods:

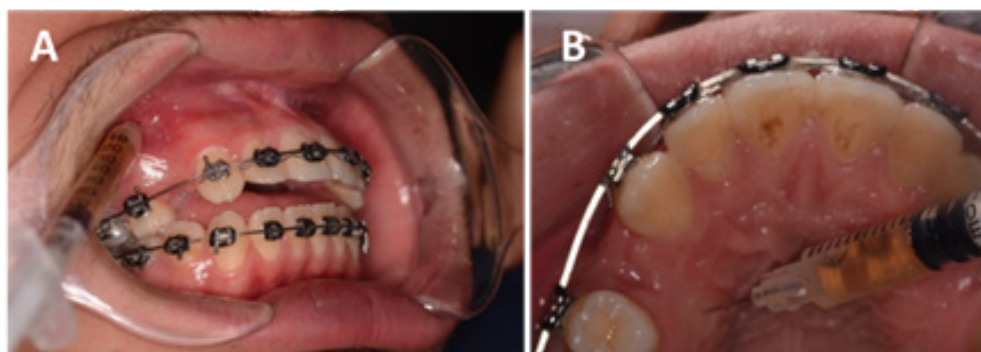
This study was split-mouth randomized controlled clinical trial with a 1:1 allocation ratio. The purpose of the study was explained to the patients and informed consents were obtained from them according to the guidelines on human research adopted by the Research Ethics Committee of the Faculty of Dentistry, Tanta University. The sample consisted of 14 patients seeking orthodontic treatment with the following inclusion criteria: age 16 to 22 years old; malocclusion that requires extraction of the maxillary first premolars and canine retraction (e.g. class I bimaxillary dentoalveolar protrusion and class II div 1 malocclusion); maximum anchorage needed for the maxillary arch; good oral hygiene and periodontal condition. Patients with the following criteria were excluded: medically compromised patients, chronic use of medications affecting OTM, and previous orthodontic treatment.

All patients received fixed orthodontic appliance (MBT, Leone 0.022 inch slot). Extraction of the maxillary first premolars followed by leveling and alignment until insertion of 0.016x0.022-inch stainless steel arch wire. Miniscrew (8 x 1.6 mm 3S screw, World Bio Tech Co. Korea) with bracket head design inserted between the maxillary first molar and maxillary second premolar at the level of mucogingival junction on both sides. L-shaped 0.019 x 0.025-inch stainless steel wire connecting the miniscrew to the auxiliary tube of the upper first molar band, cinched back, and fixed with a composite ball was used to obtain indirect anchorage (Figure 1). Before canine retraction, submucosal PRP injection was randomly assigned to one side of the maxillary arch (experimental side), while the contralateral side served as control.

PRP was prepared using double spin technique using a table-top centrifuge, and (0.7 ml = 70 units) was injected submucosal disto-buccal and disto-palatal to the maxillary canine like the local anesthesia injection in the experimental sides (Figure 2) <sup>[14]</sup>.



**Figure 1:** Miniscrew indirect anchorage.



**Figure 2:** Submucosal injection of PRP **A:** disto-buccal and **B:** disto-palatal to the maxillary canine.

Immediately after PRP injection, canine retraction was commenced using NiTi coil spring with a force of (150 g=1.5 N) extending from canine bracket to hook on the first molar band. Every appointment, the coil spring was checked using tension gauge to maintain a constant force. Also, bite raising was done on the mandibular molars if interferences were detected. Pain killers were restricted to paracetamol.

Alginate impressions for the upper arches were made before canine retraction and every month during canine retraction phase. The dental models were scanned with 1:1 proportion (Smartoptics scanner for lab work, Germany). The constructed 2d image was imported to the Facad software (Facad ortho tracing software version 3.10) where analysis was carried out. The anteroposterior crown tip movements of the canines and the molar anchorage loss were assessed with the method described by Ziegler and Ingervall<sup>[19]</sup>.

### Statistical Analysis

The collected data was statistically analyzed at the end of the study using the Statistical Package for the Social Sciences (SPSS) Version 21.0. Significant differences for all statistical tests were predetermined at  $p \leq 0.05$ . Independent sample t-test was used to compare the mean difference between the experimental and control sides.

### Method Error

Randomly selected models were measured twice within a 2-week interval, and the data subjected to the reliability coefficient (Cronbach alpha) and the interclass correlations coefficient (ICC) to test the intra-examiner reliability.

### Results:

Study sample consisted of 14 patients; 11 females and 3 males with one female, and 2 male patients dropped out due to COVID 19 pandemics. Eleven patients had successfully completed the study duration. The mean age of the patients included in the study was  $18.45 (\pm 1.71)$  years.

The rate of canine retraction showed a statistically significant difference between experimental and control sides in the 1st month, with a mean value of  $1.31 \pm 0.89$  mm/month for the experimental side compared with  $0.881 \pm 0.61$  mm/month for the control side, reflecting acceleration of tooth movement with PRP injection. Then the canine movement was comparable in the two sides with no significant difference in the remaining months (Table 1, Figure 3).

Results showed no statistically significant difference in the amount of anchorage loss between both the experimental and control sides (Table 2).

The reliability coefficient (Cronbach alpha) was 0.94, and the ICC was 0.89, which meant high reproducibility and excellent agreement of the measurements.

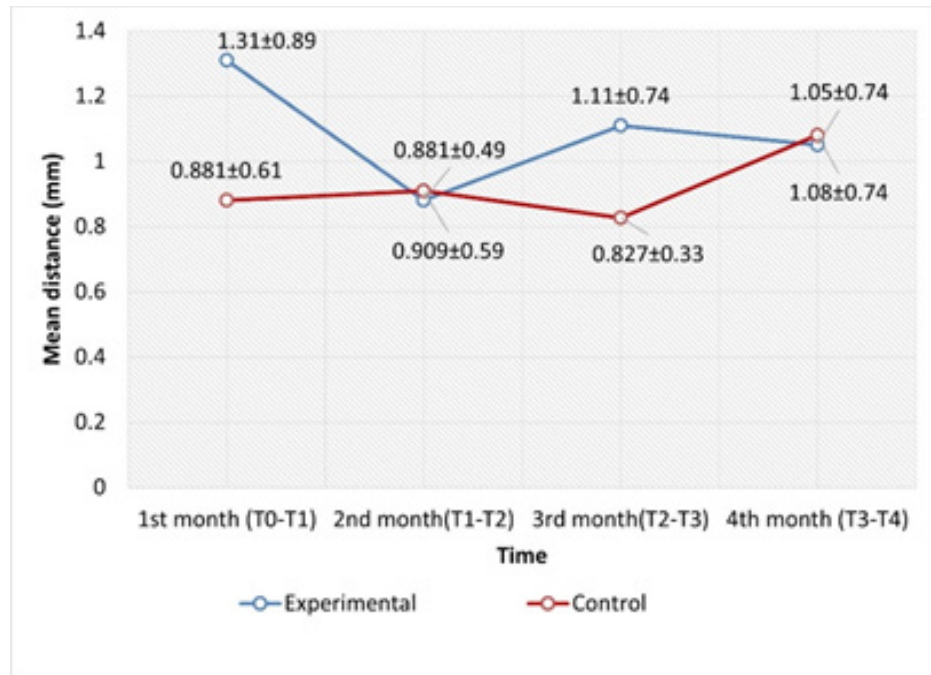
| Months            | Side         | Mean  | S.D  | Mean difference | St. Error difference | t     | p-value |
|-------------------|--------------|-------|------|-----------------|----------------------|-------|---------|
| 1st month (T0-T1) | experimental | 1.31  | 0.89 | 0.429           | 0.256                | 2.150 | 0.044*  |
|                   | control      | 0.881 | 0.61 |                 |                      |       |         |
| 2nd month (T1-T2) | experimental | 0.881 | 0.49 | 0.028           | 0.231                | 0.121 | 0.905   |
|                   | control      | 0.909 | 0.59 |                 |                      |       |         |
| 3rd month (T2-T3) | experimental | 1.11  | 0.74 | 0.283           | 0.244                | 1.158 | 0.260   |
|                   | control      | 0.827 | 0.33 |                 |                      |       |         |
| 4th month (T3-T4) | experimental | 1.05  | 0.74 | 0.030           | 0.316                | 0.095 | 0.925   |
|                   | control      | 1.08  | 0.74 |                 |                      |       |         |

$P > 0.05$  (non-significant) \* $P \leq 0.05$  (Significant)

**Table 1** Independent sample t-test comparing the mean difference in canine movement between sides in each month.

| Side         | Min   | Max  | Mean | S.D  | Independent t-test |         |
|--------------|-------|------|------|------|--------------------|---------|
|              |       |      |      |      | t                  | P-value |
| Experimental | 0.10  | 1.50 | 0.36 | 0.41 | 0.478              | 0.639   |
| Control      | -0.20 | 1.70 | 0.46 | 0.52 |                    |         |

**Table 2** Independent sample t-test comparing the total amount of anchorage loss between the experimental and control sides.



**Figure 3:** Timeline chart representing the mean distances (mm/month) travelled by maxillary canines in the experimental vs control sides.

### Discussion:

The PRP was widely used on humans with no evidence that local PRP injections have systemic effects. Due to its autologous nature, no immune reaction or allergy was reported<sup>[12,13,20,21]</sup>. In the current study, PRP was prepared using the double centrifugation technique which is the most widely used preparation protocol. According to Nagata et al.,<sup>[22]</sup> and Messori et al.,<sup>[23]</sup> double centrifugation protocol generated higher platelet concentration than single centrifugation protocol. PRP was not activated after preparation using aggregators as thrombin or CaCl<sub>2</sub>. Seddik et al.,<sup>[24]</sup> also injected PRP without activation, while Rashid et al.,<sup>[16]</sup> and El-Timamy et al.,<sup>[18]</sup> injected 10% CaCl<sub>2</sub> solution for activation of PRP. Recent studies found that the use of such aggregators is not necessary because at the time of administration, the platelets are automatically released and ready to exert their function<sup>[15,25,26]</sup>. PRP injection was done only one time at the beginning of canine retraction in order to determine how long the effect of this procedure lasts. In the present study, PRP was injected submucosal buccal and palatal distal to the maxillary canine in the experimental side. Rashid et al.,<sup>[16]</sup> and El-Timamy et al.,<sup>[18]</sup> injected PRP in five sites; intraligamentally in the middle, disto-buccal, and disto-palatal areas of the distal surface of the canines together with submucosal injections buccally and palatally. While Seddik et al.,<sup>[24]</sup> injected PRP in four sites; intraligamentally in the mesio-buccal, mesio-palatal, disto-buccal and disto-palatal area of the surface of the canines. Intraligamental injection was not adopted in our study as it would be very painful due to high pressure during injection.

The rate of canine movement was evaluated on digital models by using the rugae area as a fixed reference point<sup>[27,28]</sup>. The results showed statistically significant difference in the first month ( $P=0.044$ ) where the PRP side was 33% or 1.5 times faster than the control side, pointing out association between PRP injection and acceleration of OTM. In the remaining months, the retraction completed with insignificant difference between both sides. In the PRP side, the rate showed a decrease in the 2nd month, increased again in the 3rd followed by the 4th month. El-Timamy et al.,<sup>[18]</sup> reported 15% faster

tooth movement in PRP side in the first month, and 5% in the second month followed by deceleration in the third month following cessation of PRP injection. They attributed this deceleration to a negative feedback mechanism in growth factor release by the platelets which might lead to decrease in the normal production of growth factors during OTM following PRP injection. Deceleration also observed in our study by 3% in the second month following cessation of PRP injection. The acceleration achieved in our study was higher than El-Timamy et al.,<sup>[18]</sup> which may be due to difference in the injection technique used.

Loss of anchorage in experimental sides was  $(0.36 \pm 0.41\text{mm})$  while mean value in control sides was  $(0.46 \pm 0.52\text{mm})$ . There was no statistically significant difference between both sides. Our study anchorage losses were considered not clinically significant based on Cochrane review that demonstrates anchorage loss values ranged between -0.06 to 0.78 mm of miniscrew-supported anchorage studied in the review<sup>[29]</sup>.

### Conclusions:

Submucosal PRP injection can be effective and safe method for acceleration of orthodontic tooth movement on short term.

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