Iran J Orthod. 2022 June; 17(1):e1038. doi:10.22034/IJO.2022.548710.1038.
Published online 2022 June 1 Original Article

Comparison of Tooth Movement Using Platelet Rich Plasma and Conventional Method in Patients with Moderate Crowding: A Split-Mouth Study

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Received: 2022 February 12; **Revised:** 2022 April 19; **Accepted:** 2022 April 20

Abstract

Aim: The objective of this study was to compare tooth movement using platelet-rich plasma (PRP) and the conventional method in patients with moderate crowding during the leveling and aligning phase.
Methods: Fifty patients with moderate crowding in the maxillary arch were chosen. Split-mouth design was planned with one quadrant allotted as the experimental group (PRP side) and the other as the control group. Five injection sites were pre-defined: distal surface of the root of the central incisor, mesial and distal root surfaces of the lateral incisor and canine. After the extraction of the permanent maxillary first premolars, PRP was injected at various sites on the experimental side while the other side served as the control group. In each group, four times were studied: 0(T0), 21(T1), 42(T2), and 63(T3) days after injection. Tooth movement was measured using a digital vernier caliper and statistical analysis was done using paired t-test.
Results: Significant amount of tooth movement was seen at 21 days ($p<0.001$). No significant difference in tooth movement was found at 42 days ($p=0.265$) and 63 days ($p=0.104$) after injection.
Conclusion: Platelet-Rich Plasma is responsible for accelerating orthodontic tooth movement in patients with moderate crowding when injected during the leveling and aligning phase for the first 21 days after injection although it was non-effective after 42 and 63 days.

Keywords: Accelerated Tooth Movement, Measurement, Platelet Rich Plasma

1. Background

The inconvenience of lengthy orthodontic treatments is a major discouraging factor for patients, causing them to refuse such treatments. One such time-consuming and typical treatment is the leveling and aligning of dental crowding, which may take up to eight months (1). Now that adult patients are increasingly seeking orthodontic treatments. Thus, acceleration of orthodontic tooth movement to resolve prolonged treatment duration is also increasing (2).

Presently, many invasive and non-invasive strategies to accelerate orthodontic tooth movement have been developed. Invasive procedures include corticotomy (3,4), piezocision (5), and micro-osteoperforations(6). Several other non-invasive procedures are biomechanical procedures (e.g., self-ligating brackets), physiological approaches (e.g., direct electric current stimulation) (7,8), low-level laser therapy (LLLT) (9), cyclic forces (vibratory forces) (10), and photobiomodulation (11). Studies have shown that invasive approaches cause injury to the alveolar bone. The mechanical simulation as a result of invasive methods generates greater osteoclastic activity that provokes the resorption of the alveolar bone, minimizing the bone's density and resulting in loss of the bone of the targeted teeth (2). However, such damage to the alveolar bone does not occur in non-invasive procedures. Hence, biological supplements including cytokines such as

prostaglandin (12), hormones like relaxin (13), and metabolites like vitamin D (14) are used to achieve correspondingly effective biological responses from the minimally invasive methods. Nonetheless, using supplementary hormones or other allogenic products can produce undesirable systemic side effects and the need for routine injections of the supplements.

Platelets, which comprise growth factors such as PDGF, TGF-β, EGF, etc., aid the soft and hard tissue wound healing process. These growth factors have a vital role in regulating and stimulating wound healing process and are necessary for regulating cellular processes such as mitogenesis, chemotaxis, differentiation, and metabolism. Osteoblastic and osteoclastic activities could be stimulated by the array of platelet-rich plasma (PRP) growth factors and its substantial composition of cytokines, which are vital during orthodontic tooth movement during mediating differentiation, activation, and for the survival of all bone cells. Hence, PRP could potentially influence orthodontic tooth movement and autologous PRP injections could be a superior option for invasive surgeries.

To achieve satisfactory results for orthodontic purposes, PRP should be injectable and offer long-term effects. Producing an injectable form of PRP requires combining PRP with an anti-coagulant to preserve it in a liquid form. The present study was conducted to compare orthodontic tooth movement using PRP and the conventional method in patients with moderate crowding.

2. Methods

The study was conducted in the Department of Orthodontics and Dentofacial Orthopaedics and the Department of Oral and Maxillofacial Surgery, Saraswati Dental College, Lucknow, and the Department of Pathology, Saraswati Hospital and Research Centre, Lucknow. This study was approved by the Institutional Human Ethics Committee (IHEC) and Institutional Research Development Committee (IRDC) of the Institution. The study was registered in the Clinical Trials Registry of India (CTRI: www.ctri.nic.in) (CTRI No.: CTRI2020/01/022730; registered on: 13/01/2020).

A total of 50 patients with a mean age of 20.64±2.71 years opted for being a part of the study, out of which 29 were males and 21 were females. Inclusion criteria were: subjects aged between 15 and 25 years, with moderate crowding in the anterior maxilla, and no history of orthodontic treatment and systemic diseases (specifically blood-related disorders). Patients who had blood-related disorders, constricted maxillary arch, severe tooth displacement like ectopic canine, and who reported the use of systemic medications were excluded from the study.

Proper diagnostic records including pre-treatment impressions, pre-treatment photographs, and pre-treatment radiographs (OPG and lateral cephalogram) were taken. The pre-treatment casts were made using dental stone and were named T0. Little's Irregularity Index (15) was used to score all the casts and the mean value was 5.11±0.48 mm, which indicates moderate crowding according to the index. Extraction of the first maxillary premolars was planned accordingly. The parent and patient first received an explanation of the complete procedure including all the risks and complications involved for the patient and then informed consent was taken from the parent/patient.

After the extraction of the two maxillary first premolars and a healing period of seven days, the patients were recalled and the fixed orthodontic treatment was initiated. Pre-formed molar bands were cemented with welded lingual sheath for placement of the trans-palatal arch for reinforcing anchorage. Canine lacebacks were placed with 0.009" ligature wire to resist mesial canine tipping. Initial leveling and aligning began using ligating 0.014" NiTi wire. The archwire was bent back immediately distal to the molar buccal tube of the most distally banded molar to minimize forward tipping of the anterior teeth.

To prepare the PRP, 10 ml of the subjects' blood was drawn from their median cubital vein. Blood was transferred into vacutainer blood collecting tubes (BD vacutainer; 4 ml) containing sodium citrate to be centrifuged. A centrifugation machine (Remi Laboratory Instruments, Mumbai, India) was used to prepare the PRP.

The whole blood was first centrifuged at 1000 rpm (112 g) for 12 min at room temperature. The blood was separated into its three elementary constituents with the RBCs at the bottom, the buffy coat (platelets) in the middle, and the Platelet Poor Plasma at the top (PPP) (Fig. 1A). The RBCs were disposed of and the remaining buffy coat and PPP were collected by a 2 ml syringe and transferred to another vacutainer blood collecting tube and centrifuged for a second time at 3000 rpm for 8 min. Then the PPP was discarded so that only 0.5 ml remained, and the remaining PPP was combined with the buffy coat to produce PRP (Fig. 1B). The PRP was collected into insulin syringes (Dispovan; 40 U/1 mL) (Fig. 1C). The total PRP collected for a single patient was 4 ml. Next, topical local anesthesia (lidocaine) was sprayed on the intended sites to relieve pain associated with the multiple

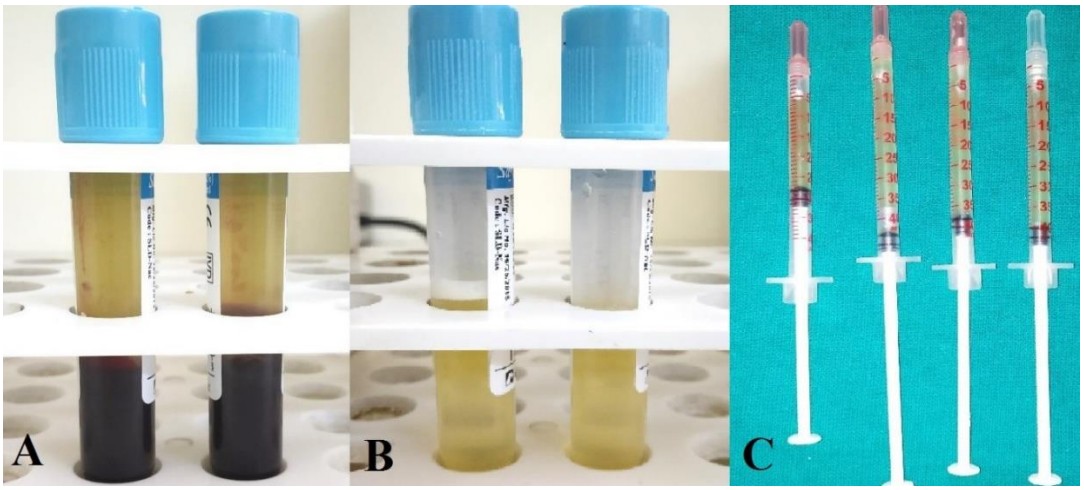

Figure 1. A) Blood centrifuged after first spin divided it into three components; RBC at the bottom, WBC and platelets in the middle, platelet poor plasma (PPP) at the top; B) Platelet Rich Plasma (PRP) formed after the second spin; C) Platelet Rich Plasma (PRP) collected into the insulin syringes

needle pricks the patient had to receive. PRP (0.6 ml) was injected using an insulin syringe via attached gingiva in the oral mucosa to prevent leakage.

The present study was designed as a split-mouth study with one quadrant allotted as the experimental side and the other as the control side. Five injection sites were pre-defined: distal surface of the root of the central incisor and mesial and distal root surfaces of the lateral incisor and canine. PRP was injected submucosally rather than sub-periosteally. (Fig. 2), which was similar to the injection of local anesthesia with no particular injection pattern. Patients were instructed not to take any nonsteroidal anti-inflammatory drugs during the treatment period for intraoral pain due to the neutralizing effects of NSAIDs on PRP.

The patients were recalled after 21, 42, and 63 days. Their impressions were taken again and casts were made (T1, T2, and T3 respectively). No specific space closure mechanics (loops, springs, elastics, or tiebacks) were used to distalize the canine. The space closure, if achieved, would be due to relieving of the crowding by alignment and not by the mesial movement of the posterior teeth because the transpalatal arch, bendbacks, and lacebacks had already been placed at the start of the treatment.

On all the casts (T0, T1, T2, and T3), the space between the canine and the second premolar was measured by a digital vernier caliper. The two beaks of the vernier caliper were placed on the distal contact surface of the canine and the mesial contact surface of the second premolar (Fig. 3). All the measurements, which were done by the same person to avoid any inter-operator error, were done thrice and the average values were noted. All the data was compiled on a Microsoft Excel datasheet and statistical analysis was done.

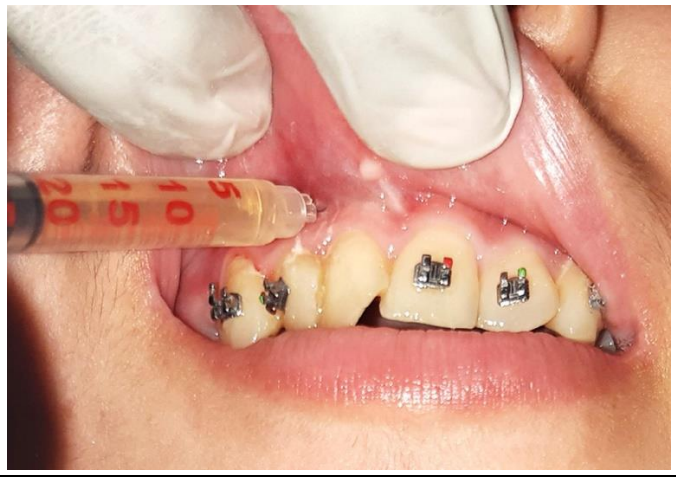

Figure 2. PRP being injected submucosally

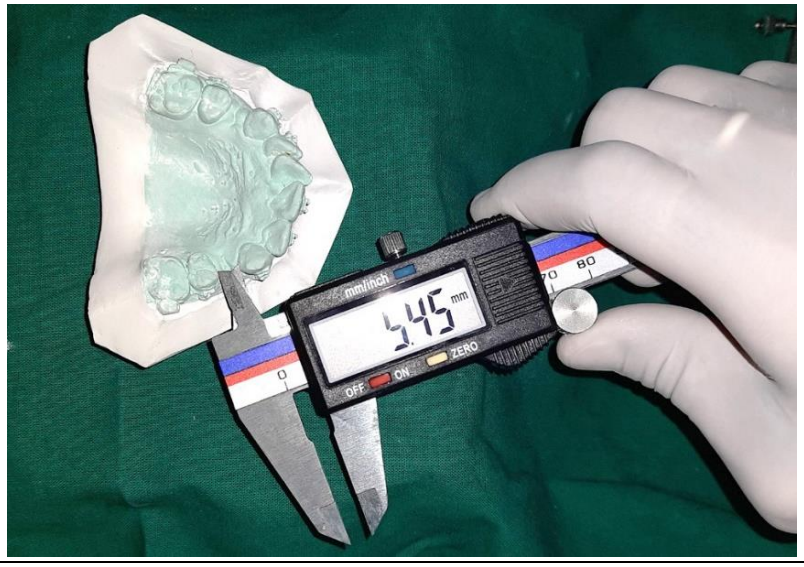

Figure 3. Measurement of tooth movement with digital vernier calliper

Statistical Analysis

The results were presented in frequencies, percentages, and mean±SD. The SPSS version 23 (Chicago, Inc., USA) was used for all the analyses. All data showed normal distribution. Data were explored for normality using Kolmogorov-Smirnov test. Paired t-test was used to compare tooth movement at different time periods. P-value <0.05 was considered significant.

3. Results

Tooth movement was measured. The intra-class reliability coefficient for repeated measurements was 0.92, confirming the reliability of the measurements. The space present between the maxillary canine and second premolar at the start of the study (T0) was 6.78±0.47 mm on the experimental side and 6.85±0.52 mm on the control side (Table 1). These were mean spaces present after the extraction (extraction spaces). The values for T1, T2, and T3 on the experimental side (5.75±0.53 mm, 5.28±0.52 mm, and 4.97±0.52 mm respectively) were less than on the control side (6.13±0.54 mm, 5.68±0.53, and 5.38±0.53 mm respectively), showing more tooth movement on the experimental side. This indicates that PRP may have an accelerating effect on tooth movement after the first 21 days of injection.

Table 2 shows the comparison of tooth movements that were measured at different times. At 21 days (T0-T1), the amount of tooth movement showed a statistically significant difference (p<0.001) between the two sides with a mean value of 1.04±0.16 mm for the experimental side compared to 0.72±0.18 mm for the control side, showing an acceleration of tooth movement due to the injection of PRP. In the subsequent measurements at 42 (T1-T2) and 63 (T2-T3) days, there was no significant difference in the mean amount of tooth movement between the control and the experimental side.

Table 1. Comparison of spaces during the study

Time period	Groups	Mean (mm)	SD	t-value	p-value
T0 (at the start of the study)	Experimental Group	6.78	0.47	-2.11	0.040
	Control Group	6.85	0.52		
T1 (at 21 days)	Experimental Group	5.75	0.53	-12.74	<0.001
	Control Group	6.13	0.54		
T2 (at 42 days)	Experimental Group	5.8	0.52	-12.93	<0.001
	Control Group	5.68	0.53		
T3 (at 63 days)	Experimental Group	4.97	0.52	-12.83	<0.001
	Control Group	5.38	0.53		

Table 2. Comparison of tooth movement during the study

Time period	Groups	Mean(mm)	SD	t-value	p-value
T0-T1 (at 21 days)	Experimental Group	1.04	0.16	18.96	<0.001
	Control Group	0.72	0.18		
T1-T2 (at 42 days)	Experimental Group	0.47	0.11	3.94	0.265
	Control Group	0.46	0.11		
T2-T3 (at 63 days)	Experimental Group	0.30	0.06	1.66	0.104
	Control Group	0.30	0.06		

During the entire duration of the study, the total tooth movement was more on the experimental side with a mean value of 1.81±0.24 mm than on the control side with a mean value of 1.47±0.24 mm. Thus, the amount of tooth movement that was achieved was found to be more on the side where PRP was injected where its effects were noticeable. However, its effects were shown during the first 21 days only, and the amount of tooth movement was comparable after 42 and 63 days of injection.

4. Discussion

Platelet Rich Plasma was introduced into dentistry by Marx et al (16) in 1998 to supplement mandibular reconstructive procedures and improve radiographic maturation rate of the graft. PRP is rich in many growth factors like IL-1β, TGF, EGF, VEGF, TGF-β, PDGF, etc. (17) and is produced from an autologous concentration of human platelets in a minuscule volume of plasma, making the term PRP preferable to autologous platelet gel, plasma-rich growth factors (PRGFs), or autologous platelet concentrate. PRP is a readily available source of growth factors that aid bone and soft tissue healing by accelerating cellular proliferation, matrix formation, osteoid production, connective tissue healing, angiogenesis and collagen synthesis (18).

Orthodontic tooth movement needs some amount of mechanical stress to direct osteoblastic and osteoclastic activities and modify bone metabolism. Moreover, bone metabolism may be regulated by other factors that regulate osteoblastic and osteoclastic activity (e.g., hormones, growth factors, and inflammatory or pro-inflammatory cytokines) (19). Due to the many growth factors in PRP, it could possibly be used in orthodontic tooth movement as the literature indicates. The efficacy of PRP on orthodontic tooth movement has been tested on experimental animals prior to its use on humans including dogs by Rashid et al. (17), guinea pigs by Sufanap et al. (18), rats by Gulec et al. (20) and Akbulut et al. (19), and rabbits by Nakarnoi et al. (21). In humans, the studies on PRP were done by Alomari et al. (22), Mahmood et al. (23), and El-Timamy et al. (24).

In our study, PRP was prepared by the double centrifugation technique as described by Liou et al. (25) and Mangal (2). Various PRP preparation techniques were mentioned by Alves et al. (26), but Chahla et al. (27) concluded that PRP preparation protocols in clinical studies are very inconsistent, and sufficient information was not provided by the majority of studies so that a protocol could be reproduced.

We injected PRP similar to the injection of local anesthesia. This technique was developed by Liou (25) and followed by Alomari et al. (22) and Mahmood et al. (23), but El-Timamy et al. (24) used intra-ligament injections to deliver PRP. In present study, 0.6 ml PRP was injected at five different targeted sites (distal surface of the root of the central incisor, mesial and distal root surfaces of the lateral incisor and canine on the buccal sides) through attached gingiva to avoid any leakage of PRP following the protocols used by Liou et al. (25). Mahmood et al. (23) gave six injections of 0.8 ml each on the buccal and palatal mucosa of the tooth and El-Timamy et al. (24) reported intra-ligament injection of 0.25 ml PRP on three sides of a tooth (middle, distobuccal, distopalatal) and submucosa injection on the buccal and palatal sides.

Previous studies investigating the impact of injection of local pharmacologic agents to accelerate tooth movement, applied one or two submucosal or gingival injection sites (12, 13, 14). In accordance with the studies by Liou et al. (25) and Mahmood et al., we also injected PRP only once before the start of the initial phase (23). Conversely, three injections (one every month) were used by El-Timamy et al. (24).

The results of our study showed increased tooth movement on the side where PRP was injected in the first 21 days with a mean movement of 1.04±0.16 mm on the experimental side and 0.72±0.18 mm on the control side. Although the increase in tooth movement was statistically significant in the first 21 days and non-significant) in 42 days and 63 days, the results reflected a positive correlation between PRP injection and

acceleration of orthodontic tooth movement. Since PRP was injected once, the results also showed accelerated tooth movement during the first 21 days only. Thereafter, the amount of tooth movement was nearly the same on both the control and the experimental side on days 42 and 63. The outcomes could be due to a negative feedback mechanism in the release of growth factors, like the hormonal negative feedback that ensues together with elevated blood and/or tissue concentration. Therefore, increasing the tissue concentration of growth factors coincidental with the local injection of PRP might have influenced the normal production of growth factors during orthodontic tooth movement (28,29). El-Timamy et al.'s study reported similar outcomes (24) in which they injected PRP three times to cause accelerated tooth movement. After the effects of PRP diminished, the tooth movement on the control side was similar to the intervention side.

In the studies by Gulec et al. (20) and Rashid et al. (17), acceleration of tooth movement by 1.4 -1.7 and 2.13 times was reported, respectively. These higher values of acceleration could be due to the differences in the studies, which were animal based with different compositions of PRP.

In our study, it can be concluded that PRP was effective only for the first 21 days after it was injected, which resulted in some amount of accelerated tooth movement. However, subsequently, its effect faded out, which resulted in comparable tooth movement on the experimental and control sides on days 42 and 63 after the injection of PRP. Hence, the PRP injections during each appointment could possibly result in increased tooth movement and thus, decreased treatment duration.

This study had some limitations such as using more invasive procedures like multiple needle punctures required during every appointment. In patients with trypan phobia (phobia of needles), this procedure would not be tolerated and they would most likely reject the procedure.

Conclusion

The following conclusions can be made from the proposed study:

Platelet Rich Plasma may be responsible for accelerating the orthodontic tooth movement in patients with moderate crowding when injected during the leveling and aligning phase as was evident from our results for the first month after injection.

The tooth movement was faster on the experimental side during the first 21 days while it came out to be the same as the control side as the effects of PRP diminished thereafter.

The results of this study are non-conclusive as more descriptive studies with larger sample sizes and more frequent PRP injections throughout the treatment need to be done to reach a more conclusive result.

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