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Comparative Evaluation of Repeated Submucosal Administration of Platelet-Rich Plasma (PRP) and Platelet-Rich Fibrin (PRF) on Canine Retraction - A Split-Mouth Randomized Clinical Study

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ABSTRACT

Introduction: Orthodontic tooth movement results from a biological response to external forces, disrupting the dentofacial complex's balance. Platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) have shown potential in accelerating tooth movement, and this study compared their effectiveness in canine retraction through repeated submucosal administration.
Aim: To evaluate and compare the effects of repeated submucosally administered platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) on canine retraction.
Study Design: A sample comprising 20 adult patients with well-aligned arches, indicating 1st premolar extraction was selected. The study randomly assigned PRP and PRF treatments into two groups for canine retraction. In Group 1, PRP was used, while Group 2 employed PRF. The maxillary arch was divided into right and left sides for equal distribution, using Microsoft Excel for random allocation. After leveling and alignment with a stainless-steel wire, bilateral first premolar extractions were performed. Mini screws were inserted between the second premolars and first molars for anchorage, and NiTi closed-coil springs were used to apply retraction force. 20 ml of blood was drawn for PRP and PRF preparation. PRP and PRF were administered submucosally around the canines at 15-day intervals until space closure. Analysis of canine retraction was done through study models taken at pre-extraction and each subsequent appointment till complete space closure using IC Measure software.
Results: Paired t-test was used to analyze the obtained data. Linear movement of space closure with the intervention of PRF revealed a mean value of 9.88±0.65mm and PRP revealed an overall average linear measurement of 9.61±0.66 mm. The mean difference between linear measurements of PRF and PRP at time difference T0-T9 was significant at a value of 0.27±0.03 mm (p value-0.004) with greater linear movement shown by PRF. There was an insignificant difference (p-value =0.981) between the mean difference in interval T0-T9 in angular measurements of PRF and PRP.
Conclusion: Canine retraction by PRF was 1.02 times faster than PRP. The findings of this study showed that the linear measurement of PRF was greater than that of PRP by 0.27±0.03mm. PRF showed increased variation in rotation of canine than PRP. Further research can be carried out on the comparative analysis of variants of PRF and PRP, such as L-PRF, A-PRF, etc. in determining their efficacy in accelerating orthodontic tooth movement.

KEYWORDS

Platelet-rich fibrin, Platelet Rich Plasma, Accelerated Orthodontics, Canine retraction

INTRODUCTION

Orthodontic tooth movement is the product of a biological response to interference in the physiological equilibrium in the dentofacial complex by an externally applied force[1]. It has since recent times been of extreme importance to orthodontists to reduce treatment duration by increasing the rate of orthodontic tooth movement[2]. One of the main goals of orthodontic treatment is the reduction of treatment time through faster tooth movement. Current methods emphasize intricate natural scaffolding that enables the patient's cells to be repopulated, creating an autologous tissue-engineered organ. Studies have been conducted on a variety of strategies to shift teeth as quickly and physiologically as possible. Efforts to shorten the duration of orthodontic treatment have explored various non-invasive methods, including the systemic and local application of chemical agents, low-level laser therapy (also known as photobiomodulation), cyclic vibrations, and pulsed electrical stimulation therapy. However, further research is needed to ascertain their clinical efficacy. Additionally, techniques such as corticotomy, piezocision, and micro-osteoperforation induce localized traumatic inflammation and cytokine release. Surgical procedures are much less preferred than less invasive approaches such as injection of bio-modulating agents, nonsteroidal anti-inflammatory drugs (NSAIDs), and growth factors to mimic the body’s immune response to increase local osteoclast production. Bio-modulating agents are painful and may carry a risk of local adverse reactions. The need for repeated administration and an unknown effective dose has limited their use.

Platelet concentrates are autologous bioactive compounds that have a wide range of uses in the medical and dental sectors, particularly in plastic surgery, sports medicine, and oral and maxillofacial surgery. These technologies are designed to collect all the components from a patient's blood sample, which could be utilized to boost tissue regeneration and enhance recovery. Platelet-rich plasma (PRP) is a concentrated plasma containing autologous platelets, which is fivefold times more than whole blood, approximating more than 1 million/L in 6-mL aliquots. It is a ready-made source of growth factors, proteases, antiproteases, and inflammatory mediators. Studies have shown a positive correlation between local injection of PRP and acceleration of orthodontic tooth movement.[3,4] Platelet-rich fibrin (PRF) represents a second-generation platelet concentrate known for its ability to release growth factors, including platelet-derived growth factor (PDGF), transforming growth factor β (TGF-β), and vascular endothelial growth factor (VEGF). These growth factors play pivotal roles in processes such as angiogenesis, collagen synthesis, and bone regeneration. Additionally, PRF has been noted for its potential to reduce adverse effects following extractions, such as significant alveolar bone resorption and gingival invaginations, which could potentially compromise the stability of orthodontic treatments. [5] There are previous studies that have evaluated the influence of PRP and PRF on orthodontic tooth movement (OTM) individually explained by authors. Hence a decision to compare the effectiveness of canine retraction with submucosal administration of PRP and PRF needs to be appraised for which the study is being designed. After searching thoroughly through the literature on various literature databases such as PubMed, Google Scholar, and Science Direct till 28 February 2024, it was found that studies to evaluate the effects of submucosally administered platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) on the rate of maxillary canine retraction have been conducted individually. According to Timamy et al[4] and Angel et al[6] sub-mucosally administered platelet-rich plasma significantly increased tooth movement during a limited period. Zeitounlouian[7] et al conducted a study that showed statistically significant results of submucosally administered PRF. PRP is labeled as first-generation platelet concentrate and PRF, second generation. Platelet-rich plasma allows a faster release of growth factors than platelet-rich fibrin, whereas PRF has more osteogenic potential. The factors released from both PRP and PRF have an influence on tooth movement, however, no literature in pretext comparing the efficacy of submucosally administered forms of Platelet Rich Plasma (PRP) and Platelet Rich Fibrin (PRF) on canine retraction in a split-mouth design was found. Thus, this study was planned.

MATERIALS AND METHODS

This randomized split-mouth study was conducted in the Department of Orthodontics and Dentofacial Orthopedics and the Department of Periodontology at K. M. Shah Dental College & Hospital, Sumandeep Vidyapeeth. Patients undergoing fixed orthodontic treatment from the Department of Orthodontics and Dentofacial Orthopedics at the same institution were included in the study. The study was started after obtaining ethical approval from the Sumandeep Vidyapeeth Institutional Ethics Committee (SVIEC/ON/Dent/BNPG19/D20003). The Study was registered with the Clinical Trial Registry - India ICMR-NIMS (Registration no: CTRI/2022/07/043672) after obtaining ethical approval. The sample size was calculated based on studies by Angel et al. and Zeitounlouian et al., with a level of significance fixed at p=0.05. Statistical parameters included a 5% Alpha error, 20% Beta error, a common standard deviation of 0.55, and a power of 0.8. Using the software available at http://powerandsamplesize.com/Calculators/Compare-2-Means/2-Sample-Equality, the estimated sample size was 16 per group. Accounting for a 20% dropout rate, 20 participants were included in the study. Chi-square analysis was used to find the significance of study parameters on a categorical scale. Student t-test (two-tailed, paired, and unpaired) was used to find the significance of study parameters on the continuous scale within and between two groups (Intra & Intergroup analysis) on metric parameters. Inclusion criteria for the study were: participants above 18 years of age, those with a full complement of dentition up to the second molars in both upper and lower arches, those requiring bilateral maxillary first premolar extraction with well-aligned arches, and those with 0.022 MBT prescription brackets.

Exclusion criteria included participants unwilling to join the study, those with a history of bleeding disorders (such as anemia, hemophilia, thrombocytopenia, and other blood dyscrasias), those with systemic conditions or on medication, those with congenital syndromes, developmental anomalies, craniofacial abnormalities, or obvious facial asymmetry, those who had undergone prior orthodontic treatment, and those with habits such as smoking. The side allocation for the administration of PRF or PRP was done as follows. Group 1 included PRP-aided canine retraction, while Group 2 involved PRF-aided canine retraction. A split-mouth design was implemented by dividing each half of the maxillary arch into the right and left sides, ensuring equal distribution of the two side allocations. This distribution was generated using the Microsoft Excel Randomization Tool. The allocation of the 20 participants was randomized by generating numbers ranging from 1 to 2 per set for the maxillary arch.

Once the levelling and alignment were carried out until 0.019 x 0.025-inch stainless steel wire engaged passively, bilateral extraction of first premolars was carried out and the patient was re-called in one week for commencement of canine retraction.2 mini screws (1.5 mm) 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. The first molars were anchored to the mini screw using a 0.019 x 0.025-inch stainless steel wire.[4,6,7]NiTi closed-coil springs delivering a retraction force of 1.5 N (assessed using a dontrix gauge) per side were attached to the right and left canine hooks. (Figure 1)

Fig 1: Canine Retraction with closed coil Niti springs and taking indirect anchorage from molar.

20 ml blood was drawn from the patient's branchial vein. 10 ml of it was collected in i-PRF tubes with no anticoagulant and 10 ml in anticoagulant-coated vacutainers for PRP. These were centrifuged according to standard centrifugation protocols for preparing PRP and PRF. In a centrifugal machine producing high-concentration PRP, an initial centrifuge to separate red blood cells (RBC)was done, followed by a second centrifuge to concentrate platelets, which are suspended in the smallest final plasma volume . Blood was initially collected in PRP tubes that contain anti-coagulant citrate dextrose (ACD). The first spin step was performed at constant acceleration to separate RBCs from the remaining blood volume for 9 minutes at about 2000 rpm. Blood is separated into three layers following the first spin step: an upper layer rich in platelets and WBC, an intermediate thin layer rich in WBCs called the buffy coat, and a bottom layer largely made up of RBCs. For the production of pure PRP, the upper layer and superficial buffy coat were transferred to an empty sterile tube, and the second spin step was then performed for 10 minutes at 3870 rpm; thus, the lower 1/3rd was the PRP (platelet-rich plasma).[7] Blood was collected in dry sterile glass tubes without using an anticoagulant. The centrifugation protocol required one cycle only (700 rpm for 3min), and the yellow-orange top portion of the tube was collected to obtain approximately 3mL of PRF.[7]Topical anesthesia was administered for pain control.On the side receiving PRP, 1 ml of PRP on each buccal, palatal, and distal side around the canine was administered submucosally using a 27-gauge needle at an interval of every 15 days repeatedly till complete extraction space closure. (Figure 2) On the side receiving PRF, 1 ml of PRF on each buccal, palatal, and distal side around the canine was administered submucosally using a 27-gauge needle at an interval of every 15 days repeatedly till complete extraction space closure.

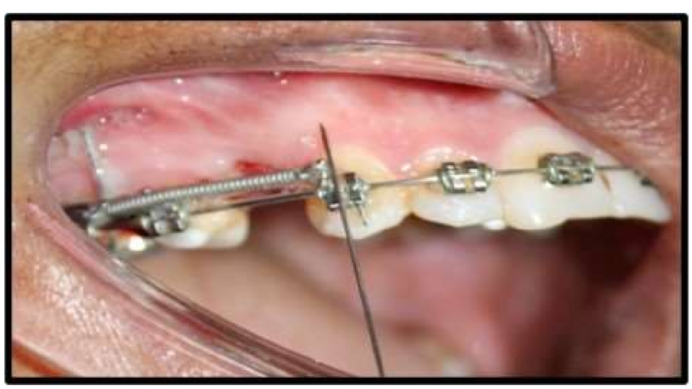

Figure 2(a): Site of administration of injection buccal to canine being retracted

Figure 2(b) Site of administration of injection palatal to canine

Figure 2(c): Site of administration of injection distal to canine

Photographs and Alginate impressions were taken pre-extraction at T0 and every appointment till complete premolar extraction space closure was achieved. (Figure 3). The inferior tip of the incisive papilla and the medial end of the first palatal rugae bilaterally close to the median raphe were used as reference points for analyzing the rate of canine retraction. Distance between the cusp tip of the canine and a line passing through these reference points was measured on every model till space closure was achieved.[7] (Figure 4(a) and (b)) The progressive rate of canine retraction and rotation was assessed on casts obtained from these impressions. (Fig 5). The difference in the canine location between the successive models was used to calculate the rate of canine retraction. The mesial and distal contact points of the canines were used to form a line that formed an angle with the median palatine raphe. The change in that angle between the initial and final models was measured on every model till space closure was achieved.

Figure 3 (a-f): Stage-wise clinical situation of canine retraction until complete canine retraction on both sides.

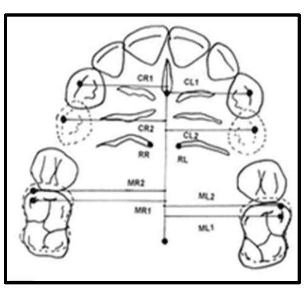

Fig 4(a): Measurement of canine retraction7

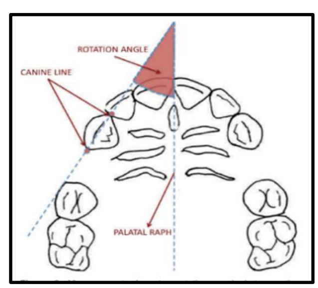

Fig 4(b): Measurement of canine rotation7

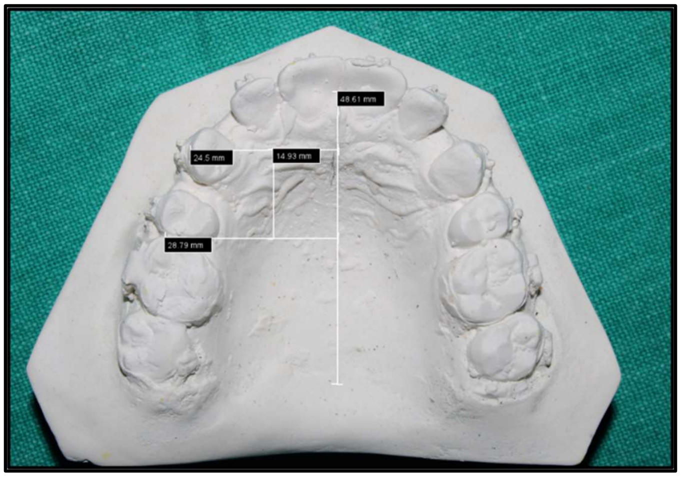

Figure 5: Measurement of canine retraction on casts

OBSERVATIONS AND RESULTS

The present study was conducted to evaluate which out of PRF and PRP causes faster canine retraction. The results are based on an analysis of 20 patients subjected to a split-mouth study where in one quadrant CR was assisted with PRF and in the other PRP assisted CR was carried out. (Fig 6(a) and (b)) Linear movement of space closure with the intervention of PRF revealed a mean value of 9.88±0.65mm and PRP revealed an overall average linear measurement of 9.61±0.66 mm. The mean difference between linear measurements of PRF and PRP at time difference T0-T9 was significant at a value of 0.27±0.03 mm (p value-0.004) with greater linear movement shown by PRF. From T0-T9, there was an insignificant difference (p-value =0.981) between angular measurements of PRF and PRP with a mean difference of 0.03±1.39 mm with PRF showing increased rotation causing tendency. Intragroup analysis showed angular measurements were significant at time intervals T1-T2, T4-T5, T5-T6, and T7-T8 (p values 0.01,0.001,0.007, <0.001 respectively) for PRP. Whereas PRF had significance at T0-T1, T4-T5, T7-T8 (p values 0.002, <0.001,0.003 respectively). PRF efficiency was compared to PRP for linear and angular measurements. On the comparative evaluation of PRF and PRP at various time intervals, a significant difference was observed at T2-T3, T3-T4, T4-T5, T5-T6, T6-T7, T8-T9 with greater linear movement caused by PRF (p values 0.003,0.006,0.004,0.005,0.007,0.004 respectively) suggesting that rate of OTM was significantly higher with PRF(Chart 1). Intergroup analysis of angular measurements showed significant measurement between PRF and PRP at T0-T1(p<0.001), and T7-T8(p=0.002) with greater variation in rotation caused by PRP.(Chart2)

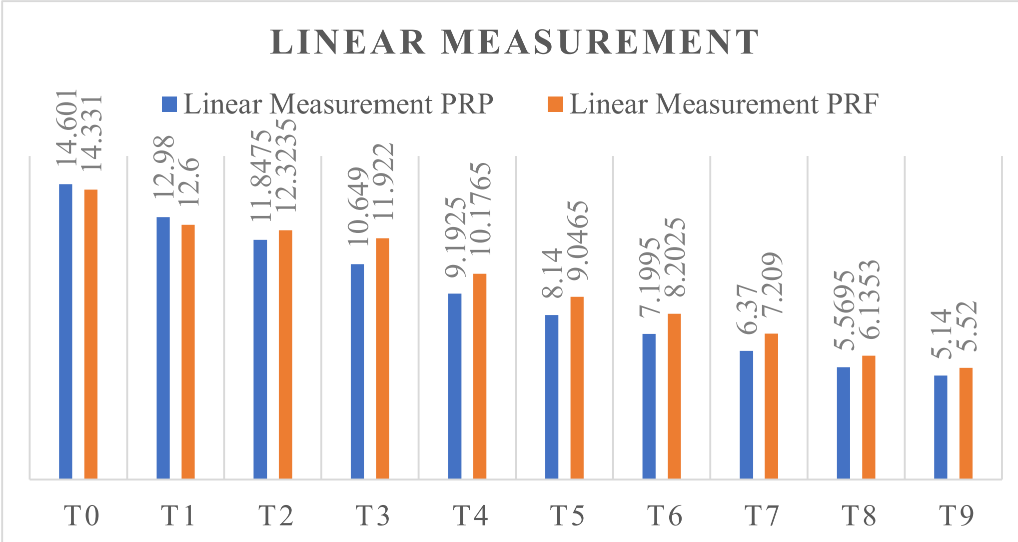

Fig 6 (a): Intergroup analysis of linear measurement during canine retraction between PRP and PRF

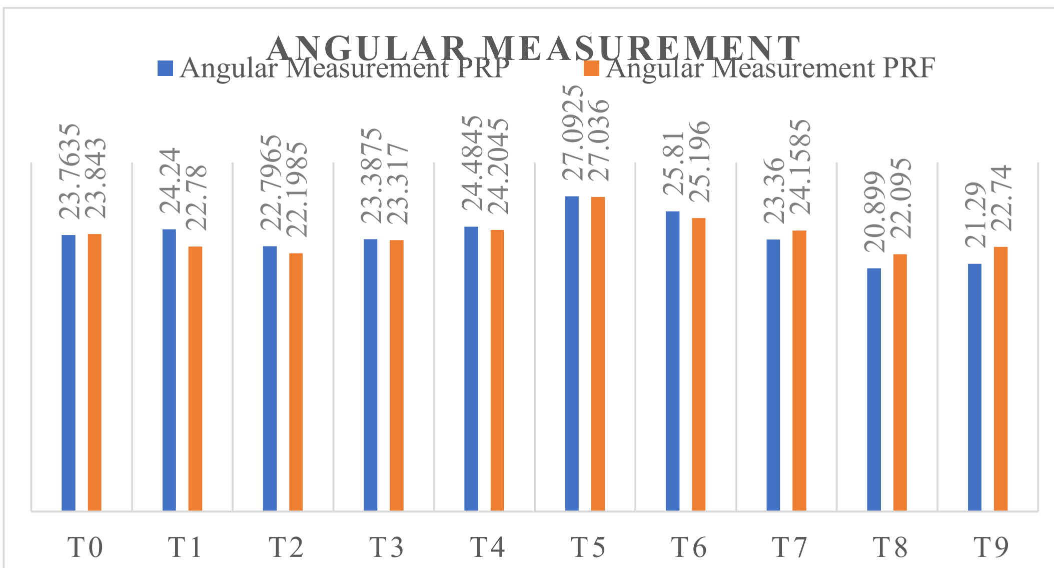

Chart 6(b): Intergroup analysis of angular measurement during canine retraction between PRP and PRF

DISCUSSION

Orthodontic treatment is a time-consuming procedure with an average time of 20-30 months[1,5]. The process of retracting canines is a particularly time-consuming phase in orthodontic treatment, and reducing its duration could potentially result in shorter overall treatment times. Shpack et al[11] in the study concluded that unfacilitated individual CR occurred at an average of about 6 months. Wazwaz et al[12] concluded that accelerated CR occurred in 5 months while our study reported CR in 4.5 months. Orthodontic extractions may cause swelling, pain, and discomfort. Relapse due to unpredictable tooth movements post-extraction is a very common orthodontic complication. Platelet concentrates are autologous bioactive compounds that have a wide range of uses in the medical and dental sectors, particularly in plastic surgery, sports medicine, and oral and maxillofacial surgery. These technologies are designed to collect all the components from a patient's blood sample, which could be utilized to boost tissue regeneration and enhance recovery. PRP is a first-generation platelet concentrate that brings cytokines and growth factors to the site, which aids in rapid regeneration without the risk of disease transmission and is convenient for the patient. PRF and PRP can reduce inflammation, and cause controlled tissue healing and bone remodeling by release of growth factors which may aid in controlling these complications. Wazwaz et al in their systematic review state orthodontists often perform CR mechanics as a distinct phase of treatment, which serves to maintain anchorage while establishing inter-arch relationships. Non-surgical, as well as those that incorporate surgical assistance, have been recommended to improve the rate of CR in orthodontic treatment and decrease the overall duration of the treatment. Surgical procedures are not commonly preferred due to their invasiveness, post-operative swelling, pain, and discomfort which lead to lesser patient compliance. Non-invasive, bio-modulating substances are uncomfortable and their utilization is restricted due to the necessity for repeated administration and uncertainty regarding the appropriate effective dosage[4]. Hence, autologous compounds like PRP, and PRF are gaining popularity among methods of accelerating orthodontic tooth movements. Growth factors PDGF and IGF-1 in PRP facilitate angiogenesis which may contribute to bone remodeling. Ann S[13] and Zou et al[14] have conducted studies on the application of various bioactive grafts to increase the bone maturation rate and enhance the rate of OTM. PRF is a second-generation platelet concentrate, that results in the release of growth factors. Miron et al[15] attributed PRF to its growth factor releasing properties and it has been documented to mitigate negative consequences after extractions, such as significant loss of alveolar bone and complications like gingival invaginations, which could potentially impede the stability of orthodontic treatment[2]. The need for the refinement of protocols and the progression of PRF derivative formulations to enhance their mechanisms, bolster their strength, improve their biodegradability, and augment their capacity to remain in place, newer genera of PRF included APRF and i-PRF. A-PRF is found in a gel-like state, making it challenging to administer via injection. To tackle this issue, i-PRF was developed. In contrast to PRP, the i-PRF process is significantly quicker, and this serves as its principal benefit. The reason behind this efficiency is that i-PRF only necessitates the separation of blood components, a process completed within the initial two to four minutes [16]. According to a review article by Gollapudi[13] et al, the merits of i-PRF override the demerits. It is a completely autologous compound with no biological modification however the PRF once fabricated has to be used immediately owing to its short handling time and it may be contaminated if not handled properly. The injectable form of PRF reduces potential consequences or complications in administration[8].

Numerous recent studies are being conducted on the efficacy of PRP and PRF in canine retraction. The current study is being done to compare both platelet concentrates and assess which causes faster CR. As per our knowledge, this is the first study that compares PRF and PRP. Zeitoulouian et al advocated repeated deliveries of PRF for a transient increase in the rate of tooth movement, thus in this study, an administration protocol was adopted where injections were repeated every 15 days till complete space closure was achieved, as the growth factors were released for an average of 10-12 days according to Gollapudi et al. Overall, space closure was achieved at an average of 4.5 months(T0-T9) which when correlated to a meta-analysis conducted by Wazwaz et al showed an acceleration in OTM by 15 days. When the progress of CR was compared for every time interval with its corresponding subsequent stage, PRF showed more significant linear movements than PRP thus demonstrating greater efficiency in promoting tooth movement (Graph 1). From 2 months(T2-T3) a significant difference in retraction of canine was observed (p-value = 0.003). The side receiving PRF showed greater linear movement than PRP with a mean difference of 0.27±0.03 mm (p value-

0.004). After 2 months it was at 3 months (T5),3.5(T6), and 4 months(T7-T8) that significant differences between PRF and PRP were observed. The last set of injections at T9 did not show a significant amount of canine retraction that occurred when intragroup comparison was done. Thus, overall, linear movement by PRF showed more significant canine retraction than when compared with PRP. The first significant linear measurement at T1-T2 that is 1 month post canine retraction can be explained by the 'boost effect' of PRF as advocated by Zeitoulouian et al. In the current study, after the initial acceleration in CR, it was at T7 and T8 that the effects could be seen again which may be attributed to the average bone regeneration time post significant canine retraction which is when the 'boost effect' of PRF could have been expressed significantly again. Overall(T0-T9), it was found that CR by PRF was 1.02 times faster than PRP. In the study by Zeitolouian et al, it was concluded that CR by i-PRF was 1.5 times faster than the control side without any adjunct. An in-vivo study by Gupta et al[9] found that PRF accelerated the rate of CR 1.8-fold times than the control group which was faster than that of the current study. The probable cause for such an observation could be attributed to the disparity in sample size and inclusion criteria. Results showed that overall, linear movement of canine retraction by PRF intervention was slightly greater when compared to PRP at every particular time point. Significant angular differences were seen in 1st month (T1-T2) and even in consecutive appointments where PRP showed more significant angular measurements but PRF showed relatively lesser variation in rotation. By the end of CR at 4.5 months, mean canine rotation by PRF showed slightly greater variation than that by PRP with a mean difference of 0.03±1.39 degrees which may be advocated due to general variation in bone architecture (Table 2). Further studies on comparative analysis of PRF and PRP are warranted under the pretext of minimal available literature on the comparison of both adjuncts.

The current study used a split-mouth design with uniform tooth selection (maxillary canines alone). This allowed for the assumption of baseline equivalency across opposing sides of the dental arch and independence from various bilateral interventions. The effect of PRP on bone density during orthodontic tooth movement must be analyzed to confirm the same. The study measured CR until complete space closure and administered PRP and PRF repeatedly, setting it apart from other studies that have not yet been conducted. Repeated administrations have shown that the boost effect was seen in accordance with a study by Zeitoloiuan et al and was again seen when space closure was going to be achieved. Considering the current study design, the limitation that could be drawn was that both the sites received accelerating adjuncts for CR. For better understanding, a control group could have been included with a different study design. Three-dimensional scanning of the oral cavity is warranted which should allow for easier and three-dimensional representation of dental changes. Accordingly, based on our results and all available studies, it can be advocated that PRF is 1.02 times faster than PRP. A generalizable positive effect of both PRP and PRF on the rate of CR may be formulated at this point with faster results shown by PRF but further studies need to be conducted about the same. There is a significant shortage of baseline data regarding the effect of these adjuncts on orthodontic tooth movement (OTM) and their comparative evaluations as well. More such trials must be conducted to investigate which of the adjuncts is more effective in accelerating orthodontic tooth movement so that its utilization in the field of accelerated orthodontics is further propagated.

CONCLUSION

- It can be concluded that both the adjuncts accelerate orthodontic tooth movement and both facilitated space closure however canine retraction by PRF was 1.02 times faster than PRP and CR until complete space closure was achieved in 4.5 months.

- The findings of this study showed that the linear measurement of PRF was greater than that of PRP by 0.27±0.03mm.
- Canine rotation by PRF showed greater variation overall than that by PRP which may be due to local variations in bone density at the site of delivery which provides us future scope of study.
- Further research needs to be done on the comparative analysis of PRF and PRP in determining their efficacy in accelerating orthodontic tooth movement.
- Evaluating various types and combinations of PRF derivatives should be considered.

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