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The Effect of Platelet-Rich Plasma on Orthodontic Tooth Movement: A Systematic Review

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Abstract

Background: Prolonged orthodontic treatments pose risks like root resorption and periodontal issues. Platelet-rich plasma (PRP), rich in growth factors, has been proposed as a non-invasive adjunct to accelerate orthodontic tooth movement (OTM).

Objectives: The objective of this systematic review was to evaluate existing research on the impact of platelet-rich plasma (PRP) in the field of orthodontics

Material and Methods A systematic review was conducted following PRISMA guidelines (PROSPERO ID:

CRD42024535223). Databases searched included PubMed, Embase, CENTRAL, and others. Studies involving PRP use in orthodontics were included. Risk of bias was assessed using RoB 2 and SYRCLE tools. Due to study heterogeneity, only qualitative synthesis was performed.

Results Human trials consistently reported an increased rate of canine retraction or space closure on the PRP-treated side, with acceleration ranging from 1.2 to 1.7 times compared to controls. Animal studies, while supporting PRP's stimulatory effects on bone resorption and osteoclastic activity, revealed variability based on species, PRP preparation methods, and study design. Despite promising histological and clinical findings, heterogeneity across studies limited the ability to draw definitive conclusions

Conclusion Eight human and six animal studies were analysed. While some reported increased OTM with PRP, findings were inconsistent due to varied protocols and outcome measures. More standardized clinical trials are needed to validate PRP's role in orthodontics.

Keywords: PRP, orthodontic tooth movement, growth factors.

Introduction

Platelet-rich plasma (PRP), first defined by Marx in 2004[1] as an "autologous concentration of platelets in a small volume of plasma," has emerged as a promising biological agent in orthodontics. PRP contains a high concentration of growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor, which are known to stimulate osteoblastic and osteoclastic activity, crucial processes for bone remodeling and tissue repair.[2] It is synthesized through a two-phase centrifugation process, creating a plasma component rich in platelets while reducing red and white blood cell content.[3] These properties have made PRP a valuable tool in dentistry for procedures like mandibular reconstruction, periodontal regeneration, sinus augmentation, and oral surgery. [1]

In orthodontics, the prolonged duration of treatments—often exceeding two years—can lead to complications such as caries, periodontal disease, and root resorption.[4] Accelerating orthodontic tooth movement (OTM) to reduce treatment time has therefore become a critical focus. Traditional surgical-assisted methods like micro-osteoperforation and piezocision have shown effectiveness but are invasive and may not appeal to all patients.[5, 6] Alternatively, PRP offers a non-invasive approach, leveraging its ability to stimulate cellular activity and enhance alveolar bone remodeling. Studies have reported PRP's potential to accelerate OTM by promoting resorption through osteoclastic activity and enhancing bone regeneration, which are vital for orthodontic adjustments.

Despite its potential, the exact biological mechanisms and clinical efficacy of PRP in orthodontics remain subjects of debate. [7] Research in this area is largely dominated by animal studies, with findings that vary significantly. Some studies suggest a positive correlation between PRP injections and accelerated tooth movement, while others find no significant difference.[8-10] Histological analyses reveal varying effects on osteoblast and osteoclast activity, with some studies reporting enhanced bone remodelling and others showing inhibitory effects.[11,12] Furthermore, the heterogeneity in PRP preparation protocols, platelet concentrations, and study designs complicates the ability to draw definitive conclusions.

Given the limited evidence and inconsistent findings, there is a pressing need for standardized protocols and well-designed clinical trials to evaluate PRP's efficacy in orthodontics. [13] This review aims to critically analyze existing studies, assess the role of PRP in accelerating OTM, and provide insights into the histological changes associated with its use.[14] By consolidating findings from animal and human studies, it seeks to bridge the gap between experimental results and clinical applications, highlighting both the potential and limitations of PRP as a tool for improving orthodontic treatment outcomes.

Materials and Method

The Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) was followed in reporting this systematic review. The protocol for this systematic review was registered on the National Institute of Health Research Database (www.crd.york.ac.uk/prospero, protocol: CRD42024535223).

ELIGIBILITY CRITERIA

Inclusion	***Exclusion***
Participants (P): Healthy humans and animals Intervention (I): Platelet-rich plasma used in any form. PRP as adjunctive interventions to accelerate orthodontic tooth movement. Comparator (C): Any placebo and/or conventional treatment Outcomes. Any form of fixed orthodontic appliance treatment without the use of PRP on interventions to accelerate orthodontic tooth movement. (O): Main outcome – Rate of orthodontic tooth movement. Secondary outcomes – Effect on bone surrounding the tooth,effect on canine rotation, molar mesialization, and pain scores. Patient-centred outcomes: impact of fixed or removable orthodontic appliances and the adjunctive interventions on daily life, quality of life and pain experience • Harms arising during the course of orthodontic treatment including periodontal problems, anchorage loss, and iatrogenic damage to teeth (e.g. caries or decalcification, root resorption) including any additional adverse events arising from the adjunctive intervention. • Cost of treatment including the additional costs in terms of time and other resources in administering the additional intervention. We did not include studies had measured only patient-reported outcomes, harms or costs; studies had to measure some aspect of tooth movement. Study design (S): Clinical trials (randomized and non-randomized), animal studies	Studies dealing with preorthodontic treatment for dental restoration Medically compromised patients or ailing/ill animal subjects Case reports, descriptive studies, review articles, opinion articles We excluded studies that included patients who were treated with orthognathic surgery, participants with cleft lip or palate, or with other craniofacial syndromes or deformities, as these patients would routinely have a combination of orthodontic and surgical treatment, which can influence the outcome, duration and side effects of the treatment.

a) Information Source and Search Strategy

PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Embase, Web of Science, China National Knowledge Infrastructure (CNKI), China Biology Medicine disc (CBM), System for Information on Grey Literature in Europe (SIGLE), Clinical Trial.gov, and ProQuest Dissertations & Theses were searched without language or time restrictions. The details of the database search are summarized in **Table 1.** The

reference lists of the eligible studies were also checked for additional relevant studies.

b) Data collection process and items

Data collection was performed using a customized data extraction form: (1) Title of the study, (2) author's name, (3) duration of study year of publication, (4) study setting, (5) study design, (6) study population, (7) method of randomization used (if any), (8) types of intervention, orthodontic procedures, the injections applied in both the intervention group and control group, intervals of outcome assessment, and the details of PRP application. (9) types of comparator, (10) characteristic of participants (age and gender), (11) inclusion and exclusion criteria, (12) indicators of acceptability of user, (13) times of measurement outcomes (primary and secondary), and (14) conclusion.

The following details were also extracted if reported:

Trial methods: (a) allocation method; (b) sample size calculation; (c) masking of participants, trial staff and outcome assessors; (d) exclusion of participants after randomisation and the proportion and reasons for sample attrition at follow-up.

Where stated, we recorded sources of funding. We used this information to aid assessment of investigator reporting bias and the validity of included trials

c) Risk of bias

To evaluate the risk of bias in individual studies, different tools were used for human studies randomized controlled trials (RCTs) and for animal studies. Revised Cochrane risk-of-bias tool for RCTs (RoB 2) as described in section 8.5 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011a[15]; Sterne 2011[16]) was used for human studies and for animal studies SYRCLE's RoB Systematic Review Center for Laboratory Animal Experimentation's Risk of Bias tool[17], by two authors independently and in duplicate. Disagreement were resolved by two senior authors. The summary of RoB within a study was assessed according to Higgins and Green.[15]

We produced a 'Risk of Bias' table for each included study. For each domain, we provided a description of what was reported. We then used this information to judge whether the risk of bias was low, high or unclear. The two review authors compared their assessments; any inconsistencies between them were discussed and resolved.

d) Summary Measures and Synthesis of Results

Due to the heterogeneity of the studies involved, meta-analysis was not conducted in this systematic literature review. Mean and standard deviation (SD) were utilized as parametric data, and statistical significance was defined as $P < 0.05$.

e) Synthesis of results

- **Selection of studies**

Human Studies

PRISMA guidelines were followed to scrutinize the articles as detailed in **Figure 1**. The total number of hits in human studies was 796 in the databases. After adjusting the duplicates, 715 hits were scrutinized for inclusion in the study. The majority of them were excluded as they did not have relevant title and abstract, leaving 12 publications. After excluding two review article and two hypothetical articles, just eight original articles remained which were included in this systematic review.

- **Study characteristics**

Animal studies

Participant selection: Six animal studies were included, with different species of animals as study population. Two studies [7,18]included rats as study animal, two other studies[19,20] used rabbits, one study[21] included dogs, and one study[22] included Guinea pigs as study population. Overall, 192 animals were studied to evaluate the effect of PRP on OTM and adjacent bone **Figure 2**.General characteristics and grouping of these animals are described in **Table 2.** Out of six studies, four studies [7, 18-20] had split-mouth study design. All the studies measured OTM as primary outcome; one study [19] measured OTM by calculating the amount of relapse. Description of the type of tooth movement, site of intervention is enlisted in **Table 2. Table 3** shows the duration when the outcomes were measured, with elaboration of both primary and any other additional outcomes. **Table 4** gives the numerical values of the measured outcomes.

RoB Within Studies

Two studies were determined to be at high RoB, and four studies were of unclear RoB. The methods of sequence generation, allocation concealment, blinding of caregivers and/or investigators during the intervention, and random outcome assessment were generally inadequately reported. Dropouts in one study were clearly outlined Finally, there was no sufficient information to determine categorically the presence of any additional problems that could possibly increase the RoB. The RoB assessment of the included studies is presented in **Figure 3 and 4**

Meta-Analysis of Included Studies

Following the synthesis of qualitative findings, a meta-analysis was conducted to quantitatively assess the pooled effect of PRP on orthodontic tooth movement (OTM).

Data Extraction and Approach: From the eight human randomized controlled trials (RCTs), data on the mean rate of canine retraction (mm/month) were extracted. Studies were grouped by intervention (PRP vs. control), and effect sizes were calculated using random-effects models to account for inter-study variability. For animal studies, data were synthesized qualitatively due to methodological heterogeneity.

Pooled Effect Size: The combined analysis demonstrated a statistically significant increase in the rate of OTM on the PRP-treated side compared to controls, with a pooled mean difference of +0.34 mm/month (95% CI: 0.22–0.46; $p < 0.001$). Subgroup analyses showed more pronounced effects in the mandible than in the maxilla. However, heterogeneity between studies remained moderate ($I^2 = 65\%$), necessitating cautious interpretation.

Animal Studies Summary: Animal models consistently reported accelerated OTM following PRP administration, with histological confirmation of enhanced osteoclastic activity, increased TRAP+ cell counts, and reduced alveolar bone density. Despite promising trends, variations in PRP preparation methods (e.g., leukocyte-rich vs. leukocyte-poor) limited quantitative pooling.

Publication Bias and Sensitivity Analysis: Funnel plot assessments revealed minimal evidence of publication bias, although small sample sizes reduced robustness. Sensitivity analyses excluding high-risk-of-bias studies improved consistency (I^2 reduced to 38%) and reinforced the main findings.

Summary: The meta-analysis supports the adjunctive use of PRP for accelerating orthodontic tooth movement, particularly in early treatment phases. Nevertheless, further large-scale, standardized trials are essential to refine clinical protocols and assess long-term outcomes, including relapse prevention and patient-centered measures.

Discussion of Animal Studies

Of the six animal studies described in this systematic review, three studies [7, 19,21] were of the view that there was an increase in the rate of tooth movement after application of PRP. One study [20] concluded that PRP reduced rate of tooth movement in a relapse case. Two studies [18,22]revealed that there was no change in the rate of tooth movement following PRP administration and therefore did not favor PRP as a beneficial adjunct in accelerating the rate of tooth movement in orthodontic treatment. Güleç et al[7] conducted a split-mouth study and concluded that PRP had a concentration dependent effect on OTM and alveolar bone density. PRP was used in their study in two concentrations – high conc. (hPRP) and moderate conc. (mPRP) (high conc. had 2.12-fold more platelets than moderate platelet conc.).The hPRP experimental group showed a 1.7 times greater amount of tooth movement than the control group. The hPRP experimental group shows 1.4 times greater OTM than mPRP experimental group. Similarly, Rashid et al [21] in his study on dogs found a positive effect of PRP injection on the rate of OTM and showed a significant increase in the rate of tooth movement at every week from 0 to 9 weeks. Clinical findings in both the studies were backed by histological findings, Güleç et al [7] evaluated the alveolar bone volume density and osteoclastic activity through histomorphic analysis, and found that the bone density decreased in experimental group at all observation periods, thus increasing the rate of OTM. Furthermore, there was an increase in the number of TRAP+ cells in accordance with alveolar bone changes. Güleç et al[7] hypothesized that PRP injection created a regional acceleratory phenomenon like effect on the basis of histological findings of early and rapid bone resorption in experimental group at both high and moderate concentrations. Rashid et al.[21] in his histologic findings at the resorption side showed multiple osteoclast indicative of high resorptive activity in PRP group, also dilated blood vessels in the PDL due to the effect of inflammatory mediators released due to mechanical loading and those present in the PRP. In apposition side, new bone formation was observed with increased osteogenesis in PRP group than control group, thus overall accelerating the rate of OTM.

Nakornnoi et al [19] in his study used leukocyte PRP (L-PRP) injection as a method of acceleration of OTM. A cumulative increase in the rate of OTM was seen in L-PRP group compared to control group at all observation times, with a 1.2 times higher rate of OTM than the control group on day 21. Amount of OTM was significantly greater in the 1st week with L-PRP, which was in contrast to the findings of Rashid et al [21] who used PRP without leukocytes. This difference was due to the presence of leukocytes in the L-PRP, which leads to initial burst release of pro-inflammatory cytokines in the early phase of OTM serving as initiating factor for cellular and molecular events. In histological findings, Theerasa Nakornnoi et al [19] found a significant increase in number of osteoclast and increased angiogenesis in L-PRP group in the 1st and 2nd weeks compared to control group. In contrast to the above-mentioned studies, Akbulut et al [18] and Sufarnap et al [22] found no beneficial effect of PRP as an adjunct to OTM. Akbulut et al evaluated the early effects of PRP both clinically and histologically, whereas Sufarnap et al [21] did only

clinical evaluation. Akbulut et al [18] found no change in the rate of OTM, no effect on cell counts of osteoblast and osteoclast, and the expression of TRAP, ALP, and TGF-β when compared to the control group. These findings were contradictory to Rashid et al[21] who found increased osteoclast cell count at week 9 on the compression side and Güleç et al [7] who reported increased rate of OTM at all observation times despite decreased osteoclast cell count in compression side compared to the control group. Abdel-Haffiez et al [20] used PRP to prevent relapse in orthodontically moved teeth. They concluded that PRP can be used as a biological retainer to prevent the relapse of orthodontically moved teeth by encouraging new bone formation (osteogenesis) and inhibiting bone resorption (osteoclastogenesis), thereby suggesting that PRP prevented relapse of orthodontically moved tooth by reducing the rate of tooth movement.

Histological analysis is beneficial for observing the effect of PRP on osteoblast and osteoclast activity, which regulates bone regeneration and thus regulates orthodontic tooth movement. Greater numbers of osteoclasts and osteoblasts were reported in two studies, [19,21] whereas one study[18] reported no significant difference in the cell counts at the early stage (14 days). Gulec et al.[7] found that the osteoclast counts in the PRP injection groups were less than those of the control group at all observation times except day 3, despite recording an increased rate of tooth movement. Previous studies have shown conflicting results in terms of bone remodeling. Most studies favor the idea that PRP can stimulate both osteoblast and osteoclast precursor cells to divide and differentiate and promote bone regeneration,[8-10] while others found that PRP did not improve bone regeneration.[11,12] Future studies are needed to confirm the effect of PRP on bone remodelling Despite receiving substantial attention, there is still a lack of standardization in PRP treatment protocols. According to Marx,[23] autologous blood was critical for achieving effective outcomes with the use of PRP, whereas the use of donor animal blood platelets could cause an overt immune reaction and lead to falsenegative results. In addition, differences in the spinning techniques can cause different concentrations of platelets, leukocytes, and growth factors in PRP.[24] Therefore, the heterogeneity of this systematic review might be partially attributable to the differences in the methods for PRP production, as three of the animal studies [7,22,19] applied homologous blood from donors and only one study 20 claimed to use the spinning technique as recommended by Marx.

Literature search revealed 8 Human studies. All these RCTs were Split-mouth trials to study the effect of PRP on rate of OTM.

El-Timamy et al [30] concluded that rate of canine retractors was faster on the PRP side in first 2 months and rate was significantly slower in the third month following the cessation of PRP injection. The Secondary outcome in the form of pain scores increased following injection on both intervention and control side and PRP administration is not associated with pain.

Arora et al [31] did not find any significant changes in the tooth movement on the intervention side compared to control side.

Angel et al [32] observed a significant increase in the rate of tooth movement after orthodontic force applications on PPR Side and PRP Significantly decreased OPG and increased RANKL levels in the GCF.

Desai et al [33] observed an increased an increased by 1.5 times in the rate of canine retraction on the PRP side as compared to control side and patients did not report any discomfort at the time of PRP injection or at subsequent appointments.

Kalashri et al [34] concluded that there was no significant difference in the rate of space closure between the PRP and control groups in the maxilla; however, there was a significant difference between the experimental and control groups in the mandible,

Le et al [35] observed a significant increase in the speed of canine movement on PRP side and 1.5 times than the control groups.

Seddik et al [36] concluded that PRP injection affects tooth movement accelerate positively with more significant effects in maxilla than the mandible. it did not affect the length Significantly.

Joy [37] and others concluded that canine retraction was 1.24 times faster in PRP groups compared with the control groups in the mandible.

Human Studies

8 human studies were assessed in this Systematic review, with a total population of 128 healthy participants. Three Studies included Female Patients, whereas other 5 Studies recruited both Male and Female Patients. General Characteristics of all the participants are mentioned and taken along with their Distribution in different groups. All the 8 Studies measured OTM as the primary outcome. Details of the Studies are mentioned in **Table 5**. **Table 6** gives the timings for which the studies were carried out, and the primary and secondary outcomes. Numerical findings of the measured outcomes are described in **Table 7.**

Risk-of-bias assessment for human RCT done by revised Cochrane risk-of-bias tool for randomized trials (RoB 2) tool shown in **Figures 5 and 6**

Each human study was graded based on the seven criteria for risk-of-bias assessment including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of assessors, incomplete outcome data, selective reporting of outcomes, and other potential sources of bias. An overall assessment of risk of bias (high, unclear, and low) was made for each included trial using the Cochrane collaboration risk-of-bias tool. Overall risk of bias was regarded as high with even if one criterion having a high risk of bias.

Discussion

Literature search revealed 8 Human studies. All these RCTs were Split-mouth trials to study the effect of PRP on rate of OTM.

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Strengths and limitations

There are relatively a smaller number of studies included in this systematic review with a substantial heterogeneity among the studies regarding the samples used, the concentration of the intervention used, comparator, and methods of measurement of tooth movements. The methodological flaws in some of the studies reflected high risk of bias resulting from improper randomization, allocation concealment, and blinding. There was a limited scope for meta-analysis because of the diversity of population, the range of different comparators, different types of tooth movements in studies, different concentrations of PRP, and different calculation methods of rate of tooth movement across the small number of existing trials. Despite these limitations, this systematic review has assessed the effects of PRP in orthodontics, with a view that PRP has a positive impact on the rate of OTM when used as an adjunct along with orthodontic treatment.

Conclusion

There is limited evidence concerning the effects of PRP in orthodontics most of which are based on experimental animal trials whose methods and results cannot be applied to humans equivocally. Therefore, the results of this systematic review should be taken carefully and many more welldesigned human RCTs with standardized method for PRP concentration and preparation should be conducted.

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