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Research article

The effect of platelet-rich concentrates on orthodontic tooth movement: A review of randomized controlled trials

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ABSTRACT

Objectives: Platelet-rich concentrates, namely platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), have recently shown potential roles in accelerating orthodontic tooth movement (OTM) and reducing treatment duration. Our study aims to systematically evaluate the effect of platelet-rich concentrates on OTM.

Materials and methods: An electronic search of 11 databases, followed by a hand search of reference lists of eligible studies and related reviews, was conducted up to January 2022. Randomized controlled trials investigating OTM of patients with platelet-rich concentrates were included. Risk of bias was assessed by version 2 of Cochrane tool (RoB 2) for assessing risk of bias in randomized trials.

Results: Among 715 records initially identified, 9 studies were included, of which 3 used PRP and the other 6 applied PRF. 7 studies supported a positive relationship between platelet-rich concentrates and OTM, but the other 2 studies reported a null and a negative effect of PRF, respectively. The overall qualities of evidence were moderate to high.

Conclusions: Platelet-rich concentrates as PRP and PRF seem to be effective in accelerating OTM at early stages, while their long-term efficacy remains controversial. Repeated application of platelet concentrates may increase the accelerated stability of OTM.

1. Introduction

Duration of orthodontic treatment, one major concern for many patients, often takes more than 2 years [1]. Lengthy orthodontic treatment not only decreases patients' desire and compliance for clinical therapeutics, but also results in a high risk of adverse effects like white spot lesions, root resorption and periodontal diseases [2]. Therefore, attempts to accelerate tooth movement and reduce treatment duration are of great significance to both orthodontists and patients.

Over the past few years, approaches including surgical and non-surgical techniques have been proposed as promising ways to shorten the treatment time. However, surgery-assisted procedures like corticotomy, micro-osteoperforation and piezocision are considered to be invasive, requiring complicated procedures [3]. On the other hand, non-surgical methods show conflicting results regarding tooth movement acceleration, and some biological agents like parathyroid hormone and prostaglandin may lead to irreversible systemic complications [4, 5]. Thus, there is a need for studies investigating a less invasive remedy without compromising systemic safety.

Platelet-rich concentrates comprise four subtypes as pure platelet-rich plasma (P-PRP), leukocyte- and platelet-rich plasma (L-PRP), pure platelet-rich fibrin (P-PRF), leukocyte- and platelet-rich fibrin (L-PRF) [6]. Among them, platelet-rich plasma (PRP) is the first generation of autologous concentrations of platelets in a small volume of plasma. Platelet-rich fibrin (PRF), as the second generation, holds the advantages of easier preparations and longer effects [7, 8]. Platelet-rich concentrates are rich in variable growth factors and cytokines such as transforming growth factor β, vascular endothelial growth factor, interleukin, interferon and tumor necrosis factor α. These characteristics support their roles in multitudinous biological processes, including inflammation, angiogenesis, osteoblastogenesis and osteoclastogenesis, and as a result, motivate wound healing and bone regeneration [9, 10, 11, 12].

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Nowadays, platelet-rich concentrates are proved effective in regenerative dentistry and oral surgery such as tooth extraction, implantology, and periodontal therapy [13, 14]. Orthodontic tooth movement (OTM) refers to the tooth movement of patients under orthodontic treatment. It occurs by remodeling of alveolar bone and periodontal ligament under orthodontic force produced by orthodontic appliances like archwires and springs. Thus, platelet-rich concentrates show a prospect in orthodontic practice.

In a recently published systematic review, studies have suggested the potential function of platelet-rich concentrates in the OTM acceleration of animal models [15]. However, their roles in the OTM of humans remain unclear. As clinical studies accumulate, demands for summarized and comprehensive knowledge of OTM after the application of platelet-rich concentrates arise. Here, our study aims to systematically evaluate the effect of platelet-rich concentrates on OTM for further application.

2. Materials and methods

2.1. Protocol and registration

The review was conducted and presented according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [16] and registered in the International Prospective Register of Systematic Reviews database (CRD42021258838).

2.2. Eligibility criteria

The eligible criteria were based on the PICOS formula: (1) participants: patients receiving fixed orthodontic treatment; (2) intervention: platelet-rich concentrates including PRP and PRF; (3) comparison: placebo or no intervention; (4) outcomes: primary outcome was the rate of OTM, secondary outcomes were the duration of treatment, pain and periodontal health; (5) study design: randomized controlled study (RCT).

The exclusion criteria were: (1) patients with periodontal diseases, craniofacial syndromes such as cleft lip or palate, systemic diseases related to bone metabolism, or a previous orthodontic treatment history; (2) non-randomized, non-prospective, or non-comparative studies as cohort studies, cross-sectional studies, case reports, review, abstracts, editorials, and opinions.

2.3. Information sources, search strategy and study selection

PubMed, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Embase, Web of Science, Scopus, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, ProQuest Dissertation & Theses Database, Systematic for Information on Grey Literature in Europe, ClinicalTrials.gov were searched up to January 2022 without language restriction. The reference lists of eligible studies and related reviews were checked for additional studies. The details of database search are presented in Supplementary Table 1. Two reviewers selected studies independently and in duplicate. Any disagreement was resolved by discussion with two senior authors.

2.4. Data collection and data items

Two authors extracted data from eligible studies using piloted forms: author and year, country of study, study design, patient characteristics, treatment protocols, outcome measurements, results, conclusions and details of intervention with platelet-rich concentrates.

2.5. Risk of bias in individual studies

The risk of bias (RoB) of RCTs was evaluated by version 2 of Cochrane tool for assessing risk of bias in randomized trials (RoB 2) [17] by two authors independently and in duplicate. Disagreements were resolved by two senior authors.

2.6. Summary measures and synthesis of results

Meta-analysis to determine the pooled estimates of platelet-rich concentrates was preplanned. However, the heterogeneity in methodology and clinical features precluded quantitative analysis. As a result, the results were qualitatively analyzed.

2.7. Risk of bias across studies and additional analysis

Analyses for small-study effects, publication bias and subgroup analysis were not conducted although originally planned owing to an insufficient number of studies identified. The quality of evidence was appraised with the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach [18].

3. Results

3.1. Study selection

A total of 715 studies were initially identified. Then, 36 articles remained after screening the titles and abstracts. 27 studies were excluded with reasons (Supplementary Table 2) and 9 were included in the systematic review (Figure 1) [19, 20, 21, 22, 23, 24, 25, 26, 27].

3.2. Study characteristics

Table 1 shows the characteristics of included studies. A total of 158 patients were examined, with mean age ranging from 16.45[22] to 33 years [21]. Among 9 RCTs included, 8 adopted split-mouth design [19, 20, 21, 22, 23, 25, 26, 27]. 3 studies tested PRP [20, 26, 27], and the other 6 investigated PRF, of which 1 applied PRF clot [19], 1 applied PRF membrane [21], and 4 applied PRF injection [22, 23, 24, 25]. The OTM rate was measured by space closure in 1 study [19], incisor retraction in 1 study [24] and canine distalization in another 7 studies [20, 21, 22, 23, 25, 26, 27], with periods lasting from 4 weeks [24] to 1.5 years [26]. Table 2 presents the details of the intervention with platelet-rich concentrates.

3.3. Risk of bias within studies

RoB 2 was used to assess the RoB of included studies. 5 studies [20, 22, 24, 25, 27] were determined to be low RoB, and 4 were of having some concerns for different reasons [19, 21, 23, 26]. Table 3 summarized the details of RoB assessment.

3.4. Effect of PRP on OTM

Angel et al. [27] examined the OTM after PRP injection, finding that OTM rate increased by 35% in the first month (2.06 $\pm$ 0.36 mm vs. 1.34 $\pm$ 0.28 mm, $P = 0.001$) and by 14% in the second month (1.12 $\pm$ 0.32 mm vs. 0.96 $\pm$ 0.2 mm, $P = 0.015$). Joy et al. [26] also found that the OTM rate in PRP group was 1.24 times faster than that of control group (0.87 $\pm$ 0.12 mm/month vs. 0.7 $\pm$ 0.13 mm/month, $P < 0.001$). Interestingly, El-Timamy et al. [20] showed that the rate of canine retraction was faster in the first 2 months (1.55 $\pm$ 0.63 mm vs. 1.35 $\pm$ 0.62 mm, $P = 0.049$; 1.33 $\pm$ 0.87 mm vs. 1.27 $\pm$ 0.40 mm, $P = 0.772$), but slower at the 3rd month (0.59 $\pm$ 0.96 mm vs. 1.01 $\pm$ 0.63 mm, $P = 0.020$) on the intervention side. As a result, the total distance during 4 months of study period was similar in both groups (4.57 $\pm$ 1.32 mm vs. 4.53 $\pm$ 1.12 mm, $P = 0.895$). In addition, canine rotation was comparable, with a mean difference of 1.036° ($P = 0.710$) [20].

3.5. Effect of PRF on OTM

6 studies focused on the effect of PRF on OTM, of which 4 supported the acceleration of OTM by PRF application. Tehranchi et al. [19] reported that linear distance between mid-marginal ridges of adjacent teeth decreased more on the experimental side during 4 months of study, revealing teeth with L-PRF placed in extraction sockets moved faster than the control side ($P = 0.006$). Çağlı Karcı et al. [22] found that the experimental side with PRF injection exhibited greater canine distal movement ($P = 0.011$) and amount of extraction space closure ($P = 0.049$) after 12 weeks, while Erdur et al. [23] concluded that PRF injection facilitated canine tooth movement at all time points within 12 weeks and mean movement increased in weeks after PRF injection ($P < 0.001$). Karakasli et al. [24] noted that the study group with PRF injection had faster incisor movement than the control group and the values were higher within the first week after PRF application.

However, the other 2 studies with a period of 5 months had different perspectives. Zeitounlouian et al. [25] found that the rate of canine retraction on experimental side with PRF injection was only statistically greater in the 2 nd month than the control side ($P = 0.018$) and the overall movements were comparable between two groups ($P = 0.918$). Pacheco et al. [21], using L-PRF membrane, reported that PRF decreased canine distalization rate, based on the results that mean distalization rates were 0.67 mm and 0.90 mm per month on experimental and control sides, respectively ($P = 0.004$).

As for other types of tooth movements, Pacheco et al. [21] reported that canine inclination was greater on the control side ($P = 0.001$) and was weakly correlated with distalization rate. Çağlı Karcı et al. [22] reported that PRF had no effect on molar mesialization, canine rotation or transversal measurements. Zeitounlouian et al. [25] reported that there was no difference between the two sides in molar mesialization and canine rotation.

3.6. Additional outcomes as treatment duration, pain and periodontal health

Joy et al. [26] demonstrated that the mean time to complete canine retraction in the PRP group and control group were 5.96 ± 0.94 and 7.42 ± 1.12 months, while Zeitounlouian et al. [25] showed that overall duration on the experimental side with PRF injection (3.28 ± 1.00 month) was similar to that in control side (3.57 ± 1.16 month). According to El-Timamy et al. [20], pain increased following each PRP injection, with no difference between two sides. Çağlı Karcı et al. [22] found that there was no difference in periodontal parameters as probing depth, plaque index or gingival index between PRF and control sides.

3.7. Risk of bias across studies and additional analysis

Small-study effects, publication bias, or subgroup analysis were not analyzed. The quality of evidence, graded with GRADE system, ranged from moderate to high (Table 4, Supplementary Table 3).

4. Discussion

Platelet-rich concentrates, namely platelet-rich plasma and platelet-rich fibrin, have shown great potential in regenerative medicine, owing to their superior characteristics as reservoirs and scaffolds for platelets, leucocytes, growth factors and cytokines. Recently, numerous studies have been performed to explore their merits in various aspects of orthodontic treatment, including post-orthodontic stability [28], rapid

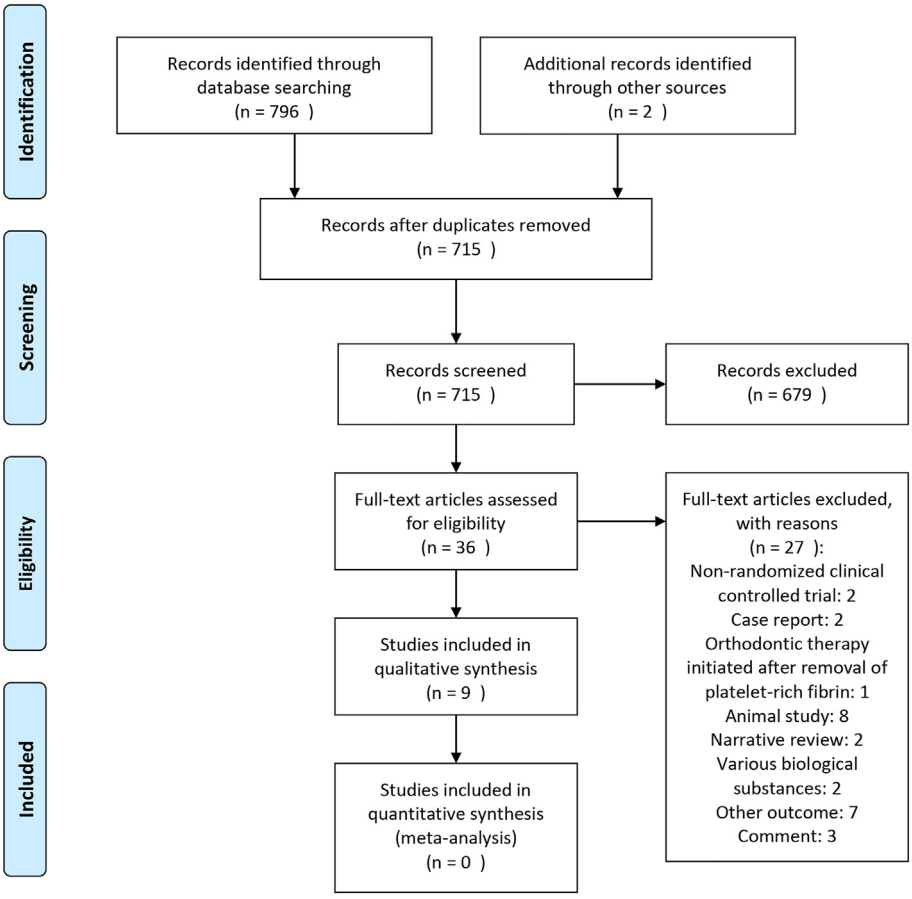

Figure 1. PRISMA flow-chart diagram of literature selection.

Table 1. Characteristics of included studies.[a]

	Study ID	Origin	Study design	Participants	Malocclusion	Study groups	Intervention	Outcomes
1	Tehranchi 2018 [19]	Iran	Split-mouth design	8 patients, 3 females, 5 males (30 extraction sockets). Age: 17.37 ± 12.48 years, range 12–25 years.	Not recorded	Experimental side: extraction socket with L-PRF. Control side: no intervention, secondary healing.	L-PRF clot	Space closure: horizontal linear distance between mid-marginal ridges of adjacent teeth, measured on study casts using a digital caliper.
2	El-Timamy 2020 [20]	Egypt	Split-mouth design	15 female patients. Age: range 18 ± 3 years.	Severe crowding or protrusion requiring first premolars extractions.	Experimental side: PRP injection with 10% $CaCl_2$ activating solution. Control side: 10% $CaCl_2$ injection only.	PRP injection	Canine distalization: rate of canine retraction detected by change in canine position in superimposed models
3	Pacheco 2020 [21]	Brazil	Split-mouth design	17 patients, 12 females, 5 males. Age: mean of 33 years, range 20–45 years.	Angle Class I (14) or Class II Division 1 (3) malocclusion needing extraction of maxillary first premolars.	Experimental side: alveolus with L-PRF membranes. Control side: no intervention.	L-PRF membrane	Canine distalization rate: monthly distalization rate of maxillary canines measured using a flexible ruler placed at dental midline from maxillary central incisors to mesial surface of canines.
4	Çağlı Karcı 2021 [22]	Turkey	Split-mouth design	12 patients, 7 females, 5 males. Age: 16.45 ± 0.27 years.	Angle Class II malocclusion with dentoalveolar protrusion or moderate crowding.	Experimental side: PRF injection. Control side: no intervention.	PRF injection	Canine distalization and space closure: amount of canine distal movement and closure extraction space in superimposed dental model scans.
5	Erdur 2021 [23]	Turkey	Split-mouth design	20 patients, 12 females, 8 males. Age: 21.4 ± 2.9 years.	Angle Class II Division 1 malocclusion requiring maxillary first premolar extraction.	Experimental side: PRF injection. Control side: sham injection.	PRF injection	Canine distalization: distance between midpoints of vertical lines drawn from incisal edge to cervical line over marginal ridge of lateral and canine teeth on dental cast measured by digital caliper.
6	Karakasli 2021 [24]	Turkey	Parallel	40 patients, 23 females, 17 males. Age: 20.7 ± 1.45 years.	Angle Class II Division 1 malocclusion requiring maxillary first premolar extraction and incisor retraction.	Experimental group: PRF injection. Control group: no intervention.	PRF injection	Incisor retraction: linear distance between distal contact point of lateral incisor and mesial contact point of canine on plaster models recorded with a digital caliper.
7	Zeitounlouian 2021 [25]	Syria	Split-mouth design	21 patients, 15 females, 6 males. Age: 20.85 ± 3.85 years, range 16–28 years.	Angle Class II Division 1 requiring extraction of maxillary first premolars.	Experimental side: PRF injection. Control side: no intervention.	PRF injection	Canine distalization: distance between medial end of third palatal rugae and cusp tip of upper canine.
8	Joy 2021 [26]	India	Split-mouth design	15 patients, 9 females, 6 males. Age: 21.7 ± 2.52 years.	Any malocclusion requiring lower first premolar extraction and canine retraction.	Experimental side: PRP injection. Control side: no intervention.	PRP injection	Canine distalization: distance between mandibular canine cusp tip and first molar central fossa evaluated using digital Vernier caliper.
9	Angel 2022 [27]	India	Split-mouth design	10 patients, 6 females, 4 males. Age: 19.05 ± 3.3 years, range 16–24 years.	Bimaxillary protrusion or Angle Class II division 1 malocclusion requiring maxillary first premolar extraction.	Experimental side: PRP injection. Control side: no intervention.	PRP injection	Canine distalization: rate of canine movement assessed using digital model superimposition.

	Study ID	Measurement time	Primary results	Additional outcomes	Conclusions	Level of evidence
1	Tehranchi 2018 [19]	T0: before placement of L-PRF. T1-T8: every 2 weeks during 2–16 weeks after study commencement.	The linear distance decreased more in experimental side, experimental group showed higher rate of OTM (P = 0.006).	Not recorded	Application of L-PRF may accelerate OTM, particularly in extraction case.	Moderate
2	El-Timamy 2020 [20]	T0: before canine retraction. T1-T4: monthly until 4th month.	Rate of canine retraction was faster on intervention side in first 2 months (T0-T1: P = 0.049, T1-T2: P = 0.772), but slower in 3rd month (P = 0.02). Total distances of both groups in 4 months were similar (P = 0.895)	1. Canine rotation was comparable, with a mean difference of 1.036° (P = 0.71). 2. Pain increased following each injection without difference between two groups.	PRP injection increased OTM during early stages (first 2 months), but did not exhibit long-term acceleration effects. Repeated PRP injection to maintain a steady accelerated OTM warrant further investigation.	High
3	Pacheco 2020 [21]	T1: beginning of retraction phase. T2: end of fifth month.	Mean distalization rate was 0.909 mm/mo (95% CI, 0.8–1 mm) in control side, while 0.668 mm/mo (95% CI, 0.6–0.7 mm) in experimental side (P = 0.004). Difference was 0.23 mm/mo (95% CI, 0.07–0.39 mm).	1. Canine inclination was greater on control side (8.57 ± 3.07°) than experimental side (5.81 ± 3.09°) treated with L-PRF (P = 0.001).	L-PRF decreased the distalization rate of maxillary canines in young adult patients.	Moderate

(*continued on next page*)

Table 1 (*continued*)

	Study ID	Measurement time	Primary results	Additional outcomes	Conclusions	Level of evidence
4	Çağlı Karcı 2021 [22]	T0: first premolar extraction and onset of canine distalization. T1-T6: every 2 weeks of 12 weeks after onset of canine distalization.	Experimental side exhibited greater canine distal movement than control side ($P = 0.011$), as the same tendency as the amount of closure extraction space at T0-T1 ($P = 0.018$) and T0-T6 ($P = 0.049$)	1. There were no difference in molar mesialization, canine rotation, transversal measurements ($P > 0.05$). 2. Periodontal parameters (plaque index, gingival index, probing depth) showed no difference ($P > 0.05$).	PRF accelerated OTM.	Moderate
5	Erdur 2021 [23]	T0: before tooth extraction. T1-T4: 1, 4, 8, 12 weeks from beginning of distalization.	Study group has higher rates of canine movement at all time points, and a higher total movement (6.06 ± 0.29 mm) than control group (3.89 ± 0.34 mm) ($P < 0.001$). Mean movement increased in weeks that PRF was injected ($P < 0.001$).	Not recorded	PRF injection facilitated OTM and shortened treatment duration by stimulating expression of inflammatory cytokines.	Moderate
6	Karakasli 2021 [24]	T0: before incisor retraction. T1–T4: 1–4 weeks after incisor retraction initiation.	Study group showed higher weekly and total incisor movement than control group ($P < 0.001$). Incisors moved faster in T1-T0 and T3-T2 intervals ($P < 0.05$)	Not recorded	PRF injection increased rate of maxillary incisor retraction and shortened treatment duration.	Moderate
7	Zeitounlouian 2021 [25]	T0: before canine retraction. T1-T5: monthly up to 5 months.	Monthly rate of canine retraction on experimental side were greater at T2, T3 and T4, but only significant at T2 ($P = 0.018$). Total movements were comparable ($P = 0.918$).	1. Molar mesialization and canine rotation showed no difference at all time points ($P > 0.05$). 2. Overall duration of canine retraction between experimental (3.28 ± 1.00 months) and control (3.57 ± 1.16 months) sides was not significant.	Rate of canine retraction was not significantly greater on experimental side than control side except at 2 nd month. Repeated PRF injection might be needed but merit more researches.	High
8	Joy 2021 [26]	T0: before canine retraction. T1: at completion of retraction.	Rate of canine retraction for PRP group and control group was 0.87 ± 0.12 and 0.7 ± 0.13 mm/mo, respectively ($P < 0.001$).	1.Overral duration canine retraction for PRP group and control group was 5.96 ± 0.94 and 7.42 ± 1.12 months, respectively.	PRP injection accelerated OTM rate by 1.24 times.	Moderate
9	Angel 2022 [27]	T0: before canine retraction. T2-T3: 30 or 60 days.	OTM rate on PRP side increased by 35% in first month ($P = 0.001$) and by 14% at the end of second month ($P = 0.015$).	Not recorded	Local administration of PRP increased OTM rate during 60-day period.	High

[a] L-PRF, leukocyte platelet-rich fibrin; OTM, orthodontic tooth movement; PRF, platelet-rich fibrin; PRP, platelet-rich plasma.

maxillary expansion [29], root resorption [30], temporomandibular joint disorders [31] and cleft lip or palate [32]. However, their actual effects on OTM need to be clarified. Here, we conducted an evidence-based review on this topic.

According to the studies included, debatable conclusions were presented. 7 studies [19, 20, 22, 23, 24, 26, 27] supported a positive acceleration of OTM by PRP or PRF, while the other 2 studies [21, 25] showed different ideas. Zeitounlouian et al. [25] reported no benefit of PRF to tooth movement. Pacheco et al. [21] even claimed that PRF decreased the rate of canine distalization. These controversial results may attribute to the different intervention procedures they adopted in dosage, delivery methods (plug, membrane or injection), concentrate presentation (PRP, PRF or L-PRF) and observation periods.

El-Timamy [20] and Angel [27] showed that PRP injection exerted a promising role in accelerating OTM at the early stages (first 2 months) of tooth movement (Supplementary Table 4). The short-term positive results were proved by animal studies. For example, Güleç et al. [33] reported that tooth movement on the high-concentration PRP side was 1.4 times faster than that in the moderate-concentration group, and 1.7 times faster than that in the control group detected on day 21. Rashid et al. [34] found that, after 63 days of retraction, first premolars with repeated PRP injection showed greater tooth movement than those on the control side by 2.13 times. In a long-term observation, Joy [26] reported a 0.17067 mm/month accelerated OTM rate in the PRP group, while El-Timamy [20] found no difference after 4 months. Although, Liou [35] stated that PRP could last for 5–6 months after a single injection in clinical applications, with a fastest rate of acceleration during 2–4 months. The difference may be partially explained by different preparation procedures and doses they choose, as different techniques can result in different concentrations of leukocytes, platelets and growth factors [36, 37], and PRP functions in a dose-dependent manner [38, 39].

It is inadvisable to draw a conclusion by simply synthesizing the ultimate conclusion of each included study due to their varied periods of trials, but we can gain a deeper insight into the effect of PRF by time-dependent analysis of the data shown in every study (Supplementary Table 4). Firstly, within a short term as first 3 months, PRF seemed to be effective in accelerating OTM, with the highest rate of acceleration at around the 2nd monthly interval. All of the four studies [19, 22, 23, 25] that reported data during the first 3 months supported an accelerating effect of PRF on OTM. Meanwhile, three of them [19, 23, 25] showed a maximal difference in OTM rate between the experimental side and control side in the 2 nd month after PRF application, implying that PRF exerted the greatest effect on OTM acceleration after the first month.

However, no consensus was reached from a long-term view over 4 months. Two studies [19, 25] reported comparable amounts of tooth movement between intervention and control groups in the end, while Pacheco et al. [21] indicated a decreased OTM rate after 5 months. It seems that after the accelerative period at the early stage, OTM decreases as time goes on. In another prospective cohort study, Nemtoi et al. [40] demonstrated that PRF placed in extraction socket still showed a positive efficiency in accelerating OTM after 6 months. Taken together, we tend to believe that single-dosage PRF exerts no, or even a negative effect on OTM in the long term, as several studies [19, 22, 25] reported comparable values or decreasing tendencies in the PRF group compared with

Table 2. Details of platelet-rich concentrates.[a]

	Study ID	Intervention	Preparation protocol	Application method	Sites	Dose	Application interval
1	Tehranchi 2018 [19]	L-PRF clot	2700 rpm, 12 min	L-PRF plugs were placed gently into sockets, and sutured using 4-0 Vicryl sutures	Extraction socket of premolars	Not recorded	only once immediately after premolar extraction (day 0)
2	El-Timamy 2020 [20]	PRP injection	Not recorded	Intraligamental injection	Middle, distobuccal and distopalatal areas of distal surface of canines, together with submucosal injections buccally and palatally	25 units	0, 21, 42 days
3	Pacheco 2020 [21]	L-PRF membrane	2700 rpm, 14 min	The experimental alveolus was preserved with L-PRF membranes and sutured with a 4–0 nylon suture	Alveoli after first premolars extractions	Not recorded	only once 15 days before retraction initiation
4	Çağlı Karcı 2021 [22]	PRF injection	800 rpm, 3 min	Submucosal injection	Buccal, palatal and distal surfaces of maxillary canine	0.7 mL	0, 4, 8 weeks
5	Erdur 2021 [23]	PRF injection	700 rpm, 3 min	Intraligamental injection	Distobuccal and distopalatal sides of canine tooth	4 mL	0, 2 weeks
6	Karakasli 2021 [24]	PRF injection	700 rpm, 3 min	Intraligamental injection	Periodontal ligament space of incisors	2–3 mL	0, 2 weeks
7	Zeitounlouian 2021 [25]	PRF injection	700 rpm, 3 min	Submucosal injection	Buccal and palatal sides through attached gingiva	3 mL	0, 1 month
8	Joy 2021 [26]	PRP injection	1000 rpm, 12 min	Submucosal injection	Attached buccal gingiva and lingual mucosa of canine and first premolar extraction site.	1 mL	Only once at same appointment as canine retraction initiation (day 0).
9	Angel 2022 [27]	PRP injection	Not recorded	Submucosal injection	Buccal, palatal and distal sites around canine.	1.8 mL	Only once at same appointment as canine retraction initiation (day 0).

[a] L-PRF, leukocyte platelet-rich fibrin; PRF, platelet-rich fibrin; PRP, platelet-rich plasma.

Table 3. Risk of bias assessment by the version 2 of Cochrane tool for assessing risk of bias in randomized trials (RoB 2).

	Study ID	Bias arising from the randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bia in measurement of the outcome	Bias in selection of the reported result	Overall assessment
1	Tehranchi 2018 [19]	Low risk	Some concerns	Low risk	Low risk	Some concerns	Some concerns
2	El-Timamy 2020 [20]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
3	Pacheco 2020 [21]	Low risk	Low risk	Low risk	Some concerns	Some concerns	Some concerns
4	Çağlı Karcı 2021 [22]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
5	Erdur 2021 [23]	Low risk	Low risk	Low risk	Some concerns	Low risk	Some concerns
6	Karakasli 2021 [24]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
7	Zeitounlouian 2021 [25]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
8	Joy 2021 [26]	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
9	Angel 2022 [27]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

the control group regarding the OTM rate at the late stages. As a result, repeated intervention with PRF might help maintain the accelerated OTM, but more studies are needed to clarify its effectiveness and repetition procedures like time interval between applications and dosage in each usage [20, 25]. Though the underlying mechanism remains unclear, we can assume that 1) immediately after PRF application, increased cells and cytokines enhance bone remodeling and then accelerate OTM [23], 2) after a specific period, as PRF degrades and exogenous growth factors and cytokines lower, autogenous growth factors and cytokines may decrease OTM through a negative feedback mechanism [20]. But the actual effects and mechanism of PRF, as well as PRP, need to be elucidated by further well-designed studies with standard protocols and PRP/PRF parameters.

This review systematically analyzes the time-dependent effect of platelet-rich concentrates on OTM in clinical trials, and the results may provide a reference for clinical applications and future research. Overall, dentists could use PRP or PRF, by a repetition method, to accelerate OTM and reduce the duration of orthodontic treatment. For those patients seeking orthodontic treatment who need multidisciplinary therapy like tooth extraction and periodontal surgery, platelet-rich concentrates can be applied in operation, as it not only supports periodontal tissue regeneration, but also accelerates OTM. However, limitations should not be neglected. Although nine RCTs were included, the heterogeneity in study design and platelet-rich concentrate preparation makes it hard to quantitatively analyze the results. Hence, more studies with standardized designs are needed to illustrate their effects.

Table 4. GRADE Summary of Findings Table of the effects of PRP and PRF on OTM.[b]

Outcome (No. of studies)	Impact	Certainty
PRP (first 2 months) (3)	PRP injection increases OTM during early stage (first 2 months).	⊕⊕⊕⊕ HIGH
PRF (first 3 months) (5)	PRF accelerates OTM in early stages.	⊕⊕⊕◯ MODERATE[a]

[a] 2 studies are evaluated as having some concerns.
[b] GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; OTM, orthodontic tooth movement; PRF, platelet-rich fibrin; PRP, platelet-rich plasma.

5. Conclusions

Our study provides a valued insight into the time-dependent effects of these autologous derivatives. The findings indicate a prospect for clinical use of platelet-rich concentrates, and direct future research to investigate their long-term efficacy and treatment protocols. Platelet-rich concentrates as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), exhibit a short-term acceleration on orthodontic tooth movement (OTM) at early stages, while their long-term effects have yet to be concluded. Repeated application may help maintain a steady accelerated OTM. Standard protocols for the preparation and application of PRP and PRF, as well as more well-designed and standardized studies, are needed to facilitate understanding of their effects and development of clinical applications.

Declarations

Author contribution statement

Ke Yao, Yongzhi Wu and Jingyi Cai: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Yigan Wang: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Yu Shen: Conceived and designed the experiments; Analyzed and interpreted the data.

Dian Jing and Zhihe Zhao: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

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Data availability statement

Data included in article/supp. material/referenced in article.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

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