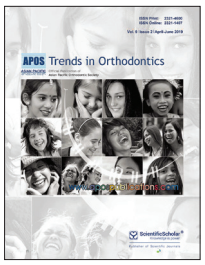
ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.apospublications.com

APOS Trends in Orthodontics



Review Article

Platelet-rich plasma: Its applications in orthodontics – A systematic review

Kanchan Prafulla Narkhede[1], Wasundhara Bhad[1], Santosh J. Chavan[1]

[1]Department of Orthodontics and Dentofacial Orthopedics, Government Dental College and Hospital, Nagpur, Maharashtra, India.

***Corresponding author:**
Kanchan Prafulla Narkhede, Department of Orthodontics and Dentofacial Orthopedics, Government Dental College and Hospital, Nagpur, Maharashtra, India.

narkhedekanchan25@gmail.com

Received : 03 April 2021
Accepted : 26 June 2021
Published : 05 October 2021

DOI:
10.25259/APOS_42_2021

Quick Response Code:

ABSTRACT

Objectives: The aim of this systematic review was to assess the available literature for the effects of platelet-rich plasma (PRP) in orthodontics.

Material and Methods: This review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines (PRISMA). The following databases were searched up to May 2020: Medline (through PubMed), Cochrane, and Google Scholar, and reference lists of the included studies were screened. Randomized controlled trials (RCTs) and controlled clinical trials using PRP an adjunct with the standard orthodontic procedures including animal and human subjects as participants were included in the study. The quality of the included human RCTs was assessed per the revised Cochrane risk-of-bias tool for randomized trials (RoB 2.0), whereas the risk of bias of the included animal studies was assessed using SYRCLES's RoB tool.

Results: Eight studies, six animal and two human studies, fulfilled the inclusion criteria. Three animal studies and one human RCT reported that PRP increased the rate of tooth movement when used as an adjunct along with orthodontic treatment.

Conclusion: According to the currently available literature, PRP is an efficient non-invasive method of tooth acceleration, but as most of the studies carried are on animals and cannot be applied to humans indistinctly.

Keywords: Platelet-rich plasma, Orthodontics, Growth factors, Tooth movement

INTRODUCTION

Platelet-rich plasma (PRP) was defined as an "autologous concentration of platelets in a small volume of plasma" by Marx in 2004.[1] Peripheral blood contains 94% of red blood cells (RBCs), 6% of platelets, and <1% of white blood cells (WBCs), while PRP contains 5% of RBCs, 1% of WBC, and 94% of platelets.[2] There are many systems available for the preparation of PRP and different protocols have been used by different authors for synthesis of PRP. It is produced through a 2-phase centrifugation process of patient's whole blood, first centrifugation separates patients whole blood components and the second centrifugation produces the final PRP,[3] which is a rich source of autologous growth factors. The high concentration of various growth factors present in PRP is responsible for its different clinical applications in the field of dentistry. The GFs reported to be present in PRP are as follows: Platelet-derived growth factor (PDGF), transforming growth factors-β (TGF-β), vascular endothelial growth factor, epithelial growth factor, insulin growth factor-1, and fibroblast growth factor.[4]

Along with GFs, PRP also contains cytokines, adhesive proteins, proteases, antiproteases, and leukocytes.

PRP made its first impression in dentistry when Marx in 1998, used it in combination with autogenous bone grafts for reconstruction of mandibular defects,[1] and concluded radiographically that PRP in addition with bone grafts revealed a higher bone density and maturation rate than bone grafts. However, controversies existed regarding these effects of PRP, some authors found that PRP favored bone formation and maturation while others were of the thought that PRP had an inhibitory effect on bone metabolism.[5]

Since then, a large number trials and reviews have been conducted and published on the use of PRP in different dental procedures such as regenerative dentistry, endodontic healing, periodontal regeneration, wound healing in oral and maxillofacial surgery, implant dentistry, sinus floor augmentation, and bone remodeling.

Recently, PRP has also been utilized in the field of orthodontics mainly to see its effects on rate of orthodontic tooth movement (OTM), response of local application of PRP on the surrounding bone, and histological changes accompanying them.

One of the paramount problems of PRP is understanding its biology and mode of action in orthodontics. PRP contents have multiple and overlapping biological effects.

For example, PDGF is a powerful chemoattractant and stimulator of cell proliferation which stimulates osteoprogenitor cells and also stimulates resorption by increasing the number of osteoclasts.[6] Another growth factor TGFβ is known to be critical for initiation or progression of tissue repair but, can actually function to increase inflammation and retard wound healing which makes it role complicated to understand in healing.[7]

A known fact about tooth movement is that it is an inflammatory process thus acceleration of tooth movement can be possible by the presence of leukocytes in PRP.

Also, cytokines such as interleukins or tissue necrosis factors have been proven to be a part of PRP and have an influence on regulation of immunologic response during tooth movement bone remodeling which plays a role in accelerated tooth movement.[8]

Thus, the efficacy of PRP not only depends on the number of platelets but also on the balance between the catabolism and anabolism and the cellular composition of PRP.[8]

Furthermore, PRP when used for orthodontic purpose should be injectable and has a long-lasting effect. This injectable form of PRP is prepared without mixing it with $CaCl_2$ and thrombin which is in contrast to that used in other fields of dentistry.[2] Literature has claimed that PRP has a stimulating effect on the rate of OTM and surrounding bone without any side effects. This has been clinically revealed by Eric Liou in the article, "The development of submucosal injection of PRP for accelerating OTM and preserving pressure side alveolar bone," where submucosal injection of PRP accelerated OTM by simulating the effects of bone insult without surgery and loss of alveolar bone.[2] Nevertheless, there is lack of evidence related to PRP increasing the rate of OTM. Thus, the aim of this systematic review is the critical and systematic appraisal of the available evidence regarding the various effects of PRP in orthodontics.

Rationale

PRP has become a valuable adjunct in various fields of dentistry. PRP has been used to treat periodontal defects, healing of extraction sockets, sinus lift augmentation, periapical osseous defects, etc., but there is a limited literature available on the diverse uses of PRP in orthodontics. Thus, the aim of this systematic review is to evaluate the different outcomes with the use of PRP in orthodontics.

Objectives

This systematic review aims at the appraisal of discrete effects of PRP when used as adjunct with the standard orthodontic procedures and to evaluate the response of PRP on acceleration of OTM and the accompanying changes on the surrounding bone.

MATERIAL AND METHODS

Protocol and registration

The Preferred Reporting Items for Systematic Reviews 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: CRD42020179187).

Eligibility criteria

Inclusion	Exclusion
Participants (P): Healthy humans and animals Intervention (I): Platelet-rich plasma used in any form Comparator (C): Any placebo and/or conventional treatment Outcomes (O): Main outcome – Rate of orthodontic tooth movement Additional outcomes – Effect on bone surrounding the tooth Study design (S): Clinical trials (randomized and non-randomized), animal studies	Studies dealing with pre-orthodontic treatment for dental restoration Medically compromised patients or ailing/ill animal subjects Case reports, descriptive studies, review articles, opinion articles

Information sources, search strategy, and study selection

A literature search was performed independently by two reviewers using the following databases:

PubMed, Central of the Cochrane library, and Google scholar.

To identify the articles reporting the effect of PRP on the rate of OTM and the changes in the bone, the database was searched from January 2000 to May 2020 with no specific filter applied during the search. All articles were found using the combination of keywords as PRP and orthodontics with Boolean characters "AND" and "OR" combination. Additional search was also carried out on review articles, bibliography, and related journals. Search strategy used in PubMed was using keywords as "Orthodontics AND platelet-rich plasma OR PRP."

The titles and abstracts of all retrieved articles were screened by three independent reviewers (a, b, and c), and irrelevant studies were excluded from the study. Full text of the eligible studies was obtained and thoroughly assessed by all the three reviewers for inclusion; disagreements were resolved by discussion between the reviewers.

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, (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.

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)[9] was used for human studies and for animal studies SYRCLE's RoB tool.[10]

SYNTHESIS OF RESULTS

Study selection

PRISMA guidelines were followed to scrutinize the articles as detailed in [Figure 1]. The total number of hits was 1375 in the databases: 57 in PubMed, 8 in Cochrane, and 1310 in Google Scholar search resources. After adjusting the duplicates, 1310 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[5,11] included rats as study animal, two other studies[12,13] used rabbits, one study[14] included dogs, and one study[15] included Guinea pigs as study population. Overall, 202 animals were studied to evaluate the effect of PRP on OTM and adjacent bone. General characteristics and grouping of these animals are described in [Table 1].

Out of six studies, four studies[5,12-14] had split-mouth study design. All the studies measured OTM as primary outcome; one study[13] measured OTM by calculating the amount of relapse.

Description of the type of tooth movement, site of intervention is enlisted in [Table 1]. [Table 2] shows the duration when the outcomes were measured, with elaboration of both primary and any other additional outcomes. [Table 3] gives the numerical values of the measured outcomes.

Human studies

Participant selection

Two human studies were assessed in this systematic review, with a total population of 34 healthy participants. One study[15] included both male and female participants, whereas other study[16] recruited only female patients. General characteristics of all the participants are mentioned in [Table 4] along with their distribution in different groups.

Out of the two studies, one study[16] measured OTM as primary outcome whereas other study[17] measured effect of PRP on the bone after RME as the primary outcome.

Details of the studies are mentioned in [Table 4]. [Table 5] gives the timing for which the studies were carried out, and the primary and secondary outcomes. Numerical findings of the measured outcomes are described in [Table 6].

Risk-of-bias/quality assessment in individual studies

Risk-of-bias assessment for animal trials done by SYRCLE'S risk-of-bias tool.[10]

[Table 7] describes the criteria from the SYRCLE'S risk-of-bias tool, which were used for the assessment using RevMan

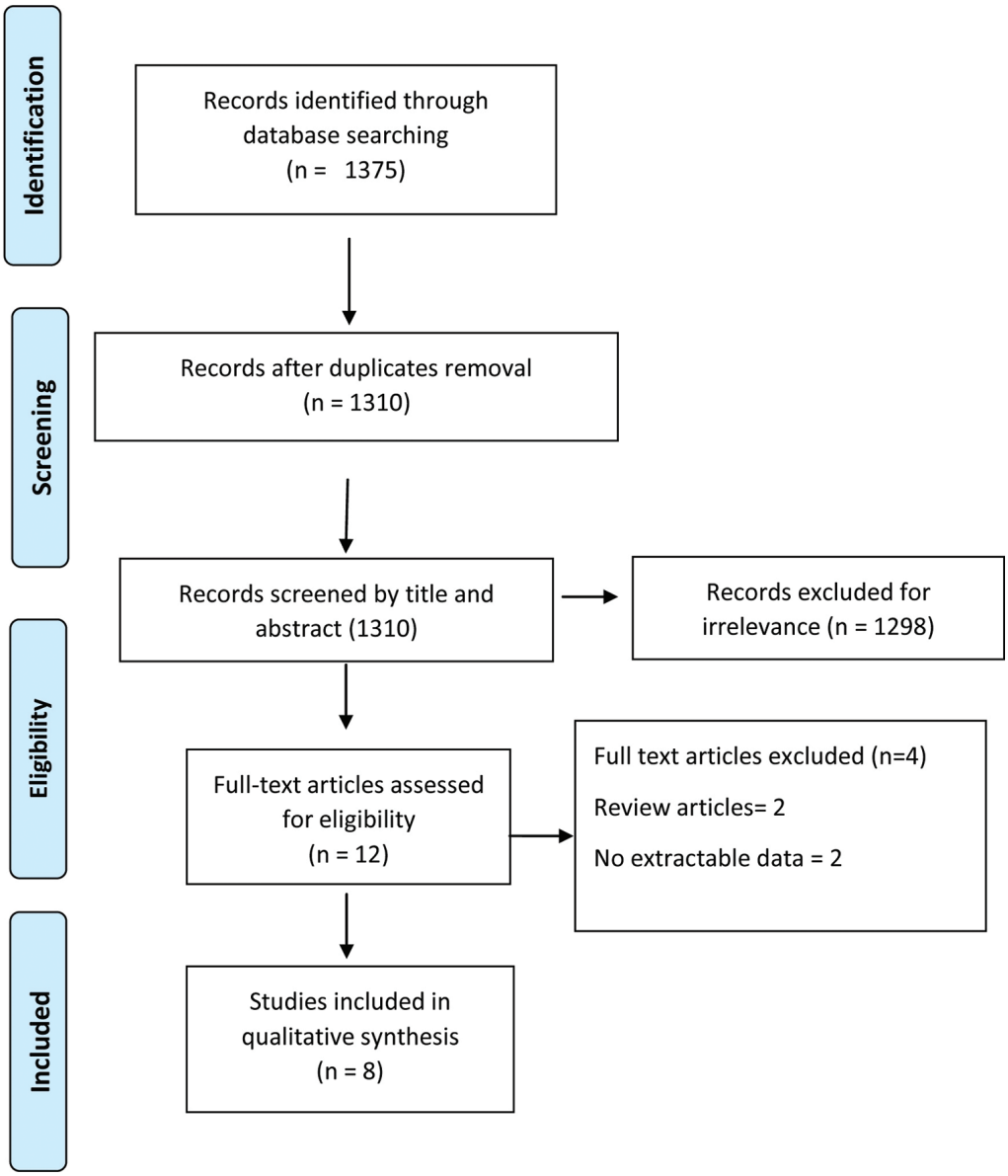


Figure 1: PRISMA Flowchart.

5.4 software and in [Figures 2 and 3] provide the risk-of-bias summary.

Risk-of-bias assessment for human RCT done by revised Cochrane risk-of-bias tool for randomized trials (RoB 2) tool[9] shown in [Table 8, Figures 4 and 5].

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

The aim of this systematic review is to ascertain the effects of PRP in orthodontic treatment. PRP is an autologous concentration of human platelets in a small volume of plasma.[1] It is also the concentration of various fundamental protein growth factors proved to be actively secreted by platelets. The effect of PRP in various fields of dentistry has been studied, but there is limited literature available on the applications and effects of PRP in orthodontics.

The results of this review show that there is a difference of opinion as to the benefits of PRP. The evaluations were based on studies using animals and humans to try to define

Table 1: Overview of animal studies.

S. No.	Author	Species	Age/sex/weight	Description of participants and grouping	Type of tooth movement	Intervention site (PRP)
1.	Güleç *et al.* (2017)[5]	Rats	9–10 weeks	*n*=76 (split mouth design) hPRP (high conc. PRP)=38 mPRP (moderate conc. PRP)=38 hPRP-E, hprp-C, mPRP-E mPRP-C (E=experimental group, C=control group)	Mesialization of maxillary right first molar	Molar buccal sulcus next to mesial root of maxillary first molar on right side
2.	Rashid *et al.* (2017)[14]	Mongrel dogs	11–15 months 13–17 kg	*n*=6 (split-mouth design)	Distalization of maxillary first premolars	Distal to first premolar distobuccal, distopalatal, buccal, and palatal sides in maxilla
3.	Erleria sufarnap *et al.* (2018)[15]	Guinea pigs	2–3 months 250–400 g	*n*=19 PRP group (*n*=9) Control group (*n*=10)	Distalization of incisors	Between maxillary central incisors
4.	Akbulut *et al.* (2019)[11]	White albino rats	6–8 weeks Male	*n*=48 PRP rich group (*n*=16) PRP poor group (*n*=16) Control group (*n*=16)	Mesialization of maxillary right first molars	Molar buccal sulcus next to distal root of maxillary first molar on right side
5.	Theerasak nakornnoi *et al.* (2019)[12]	White rabbits	3–4 months Male 2.5–3 kg	*n*=23 Leukocyte platelet-rich plasma (split-mouth design)	Mesialization of maxillary first premolars	Buccal and lingual areas of maxillary first premolar.
6.	Abdel-Haffiez *et al.* (2017)[13]	White rabbits	Not mentioned Male	*n*=30 Group A (*n*=10) Group B (*n*=10) {Groups A and B, split-mouth design} Group C (*n*=10, mock group)	Amount of relapse of mesialized mandibular first molar	Around mandibular first molar in Group A and B on one side

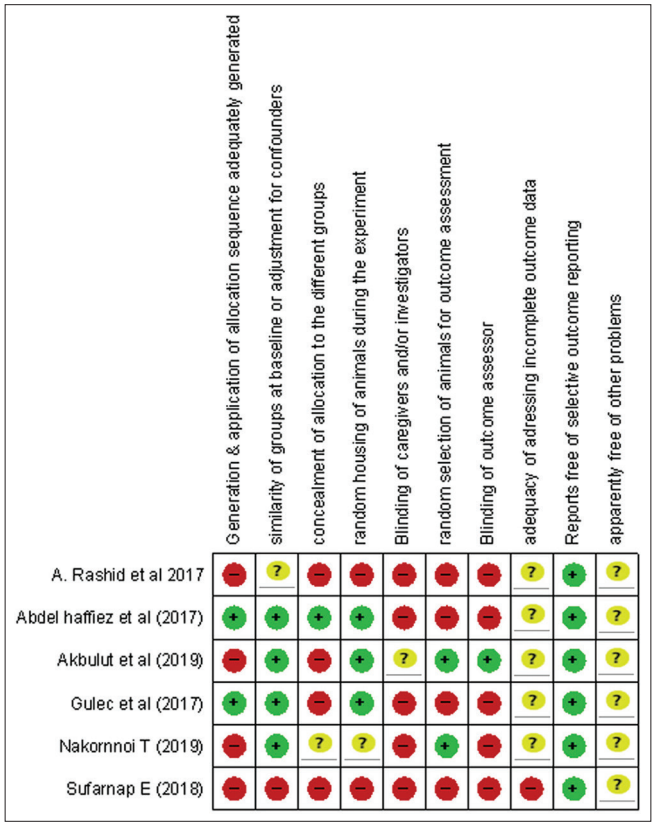


Figure 2: Risk-of-bias summary: Review authors' judgments about each risk-of-bias item (animal studies).

a course of action or protocol, as variety of study designs and parameters is reported. Researchers have based their hypotheses on the findings of cell components that occur during OTM and calculation of the tooth movement.

After thorough screening of the literature available on the effects of PRP in orthodontics, eight articles including six animal studies and two human studies were retrieved. Seven studies acknowledged that PRP had an effect on the rate of OTM and one study illustrated effect of PRP on alveolar bone resorption following rapid maxillary expansion.

Animal studies

Of the six animal studies described in this systematic review, three studies[5,12,14] were of the view that there was an increase in the rate of tooth movement after application of PRP. One study[13] concluded that PRP reduced rate of tooth movement in a relapse case. Two studies[11,15] 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.*[5] 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

Table 2: Overview of animal studies.

S. No.	Author	Platelet conc. in PRP compared to whole blood (PRP fold) and activation	Comparator	Timing of PRP injection	Timing of outcome assessment	Primary outcome	Other outcomes
1.	Güleç *et al.* (2017)[5]	hPRP=5 times the whole blood (2593.2±257 $\times 10^3$ platelets per microliter) mPRP= 2 times the whole blood (1220.4 ±154$\times 10^3$ platelets per microliter). No activation mentioned	Not mentioned	Day 0 only	3, 7, 14, 21, and 60 days	On day 21, 1.OTM in hPRP-E group 1.7 times faster than hPRP-C group 2. OTM in hPRP-E group was 1.4 times faster than mPRP-E group	Alveolar bone density decreased in experimental group at 3, 7, 14, and 21 days. On day 60 increased to original levels in all groups Increased number of TRAP cells
2.	Rashid *et al.* (2017)[14]	PRP conc. is not mentioned Activation with 10% Cacl2 solution + thrombin	Thrombin-CaCl2 solution	Day 0, 21, 42	Every week till 9 weeks	Experimental group showed Overall percentage change of 12.32% OTM, control group 5.78% with a percentage change ratio of 2.13: 1	Statistically significant increase in the no. of osteoblast, cementoblast and osteoclast in PRP group
3.	Erleria sufarnap *et al.* (2018)[15]	2.45-fold platelets. (507$\times 10^3$ platelets per microliter) No activation mentioned	Not mentioned	Day 0	6, 9, 12, and 24 days	OTM was not significantly different at 4-time points measurement. However, at day 12, OTM still increased in PRP group and the control groups were already stabilized.	No other outcome measured
4.	Akbulut *et al.* (2019)[11]	4.5-fold more platelets PRP (3617$\times 10^3$ platelets per microliter) PPP (23$\times 10^3$ platelets per microliter) No activation mentioned	Not mentioned	Day 0	0, 1, 3, 7, and 14 days	OTM was significantly less in PRP group on day 3 than control group. No other significant difference was observed among the groups on days 1, 7, or 14	No statistically significant difference was observed in no. of osteoclast and osteoblast cells, TRAP, ALP, and TGF-β in any group or at any time
5.	Theerasak nakornnoi *et al.* (2019)[12]	L-PRP=6.6-fold Platelets (2,314.44±570.82$\times 10^3$ per microliter) 1.9-fold leukocytes (6.67±2.29$\times 10^3$ per microliter) No activation mentioned	Normal saline	Day 0	0, 3, 7, 14, 21, and 28 days	Significantly higher rate of OTM on days 0-7 and 7-14 in L-PRP group.	Osteoclast no. significantly increased in L-PRP group on days 7 and 14, declined at 28 days. Peak number of osteoclasts on day 14
6.	Abdel-Haffiez *et al.* (2017)[13]	Not mentioned	Normal saline in Groups A and B on control side	At 21 day (after removal of mesializing orthodontic force)	After 1 week of relapse (Group A) After 4 weeks (Group B)	After 1 and 4 weeks of relapse period, the distance of relapse in the experimental group was reduced significantly. But no statistically significant difference in experimental group between 1 and 4 weeks	No other outcome measured

Table 3: Overview of animal studies.

S. No.	Author	Orthodontic tooth movement Statistically significant difference No statistically significant difference	Other outcomes
1.	Güleç *et al.* (2017)[5]	On day 3 NSSD between hPRP-E and hPRP-C group On day 7, 14, and 21, OTM showed SSD. Day 21 SSD between hPRP-E group (0.643±0.021), mPRP-E group (0.452±0.02), hPRP-C group (0.361±0.027)	Alveolar bone density (histomorphometric assessment) Percentage of alveolar bone volume to total bone volume was measured Percentage was less in hPRP-E than in mPRP-E and hPRP-C on days 7, 14, and 21 Osteoclastic activity SSD on day 3 in hPRP-E group and mPRP-E (less sharp), the highest osteoclastic activity levels in the hPRP-C and mPRP-C groups were observed on day 7 with steady decreases thereafter
2.	Rashid *et al.* (2017)[14]	SSD in PRP group with higher mean percentage in any 2 successive weeks with the overall percentage change in PRP group was 12.32% compared to 5.78% in the control group with a percentage change ratio of 2.13:1 At the 9th week, OTM in PRP group (15.60±1.74) was significantly higher than control group (9.46±1.23)	SSD in no. of osteoblast (16.2±1.30), osteoclasts (7.2±1.30), and cementoblast (21.8±1.30) in PRP group
3.	Erleria sufarnap *et al.* (2018)[15]	NSSD in between the groups at any 4 time points. With P-value smallest at day 12, that is, 0.054 (P>0.05)	No other outcome measured
4.	Akbulut *et al.* (2019)[11]	SSD was observed on day 3 (P=0.01), OTM in PRP group was significantly less (0.287±0.176) than PPP group (0.482±0.128) and control group (0.625±0.028)	NSSD was observed in the no. of osteoclast and osteoblast in the tension side as well as on the compression side of the PDL between the groups NSSD in ALP, TRAP, and TGF-β
5.	Theerasak nakornnoi *et al.* (2019)[12]	SSD in L-PRP group, significantly higher rate from 0 to 7 days (1.04±0.05 mm vs. 0.94±0.09 mm) and from 7 to 14 days (0.58±0.09 mm vs. 0.45±0.12 mm). NSSD at the intervals of 14–21 days and 21–28 days	SSD in the no. of osteoclast in L-PRP group on day 7 (10.6±2.07 vs. 7.4±2.30) and day 14 (16.2±3.03 vs. 11.6±3.04), but there was no significant difference on day 28 (4.2±1.78 vs. 3.8±1.48)
6.	Abdel haffiez *et al.* (2017)[13]	SSD in decrease of relapse distance after 1 week in PRP group (0.96±0.27 mm; 28.79±7.07%) than the control group (1.57±0.3 mm; 47.7±6.5%) and the mock group (1.59±0.13 mm; 48.7±2.3%) and after 4 week in PRP Group A (1.32±0.46 mm; 38.6%±10.6) than control group (3.1±0.22 mm; 93.73%±1.15%) and the mock group (3.11±0.27 mm; 93.92±1.1%) NSSD between the control and the mock groups after 1 and 4 weeks	No other outcome measured

Table 4: Overview of human studies.

S. No.	Author	Age/sex	Description of participants and grouping	Type of tooth movement	Intervention site (PRP)
1.	El-Timamy *et al.* (2020)[16]	18±3 years Female	n=16 (split-mouth study)	Canine retraction	Middle, distobuccal, and distopalatal areas on the distal surface of canine
2.	Alomari *et al.* (2019)[17]	12–16 years	n=18 (split-mouth study)	Rapid maxillary expansion	Buccal aspect of premolars and molars on the intervention side

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 showed 1.4 times greater OTM than mPRP experimental group.

Table 5: Overview of human studies.

S. No.	Author	Platelet conc. in PRP compared to whole blood (PRP fold) and activation	Comparator	Timing of PRP injection	Timing of outcome assessment	Primary outcome	Other outcomes
1.	El-Timamy *et al.* (2020) [16]	Platelet conc. in PRP not mentioned. Activation with 10% $Cacl_2$ solution	10% $CaCl_2$	0.21 and 42 days	1, 2, 3, and 4 months	OTM statistically increased in the 1st month on experimental side, but on the 3rd month, OTM was greater on control side	Canine distal – in rotation was not statistically significant between two groups Pain score increased in both the groups in the 1st, 4th, and 7th weeks
2.	Alomari *et al.* (2019)[17]	Not mentioned	Not mentioned	Day 0 (Start of expansion)	0 and 3 months	OTM not measured	No significant difference in buccal bone plate thickness (BBPT) and buccal bone crestal level of anchoring teeth between both the groups Percentage of dehiscence and fenestration increased at 3 months in both the groups, higher in PRP group

Table 6: Overview of human studies.

S. No.	Author	Orthodontic tooth movement	Other outcomes
		Statistically significant difference (SSD) **No statistically significant difference (NSSD)**	
1.	El-Timamy *et al.* (2020) [16]	SSD in OTM in the 1st month with PRP side (1.55±0.63 mm/mo) than control side (1.35±0.62 mm/mo) with *P*-value (0.049) but at the 3rd month SSD with increase OTM on control side (1.01±0.63 mm/mo) than PRP side (0.59±0.96 mm/mo, *P*-value (0.020)	Canine distal – in rotation was comparable in both the groups (1.036-degree mean value) Assessment of pain by visual analog scale, with an increase in pain score in the 1st, 4th, and 7th weeks in both the groups
2.	Alomari *et al.* (2019) [17]	Not measured	After RME, NSSD in BBPT between the groups with an average of 0.8 mm for first molars and 0.6 mm for first premolars of intervention group and 0.7 mm for control group BBCL showed NSSD in first molar region of both the groups, *P*=0.16 SSD in the first premolar region of both the groups *P* value 0.03. NSSD between both the groups. Mean increase in dehiscence in intervention group (13.2%) and control group (9.7%). The increase in percentage of fenestrations was 11.8% and 10.4% in the intervention and control groups, respectively. Thus, percentage of fenestration and dehiscence was higher in PRP group

Similarly, Rashid *et al.*[14] 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.*,[5] evaluated the alveolar bone volume density and osteoclastic activity through histomorphic analysis, and found that the bone density

Table 7: Risk-of-bias assessment animal studies.

Author (year)	Type of study	Was the allocation sequence adequately generated and applied	Were the groups similar at baseline or were they adjusted for confounders in the analysis	Was the allocation to the different groups adequately concealed	Were the animals randomly housed during the experiment	Were the caregivers and/or investigators blinded from knowledge which intervention each animal received during the experiment	Were animals selected at random for outcome assessment	Was the outcome assessor blinded	Were incomplete outcome data adequately addressed	Are reports of the study free of selective outcome reporting	Was the study apparently free of other problems that could result in high risk of bias
Rashid *et al.* (2017)[14]	Non-RCT	No	Not clear	No	No	No	No	No	Not clear	Yes	Not clear
Abdel *et al.* (2017)[13]	RCT	Yes	Yes	Yes	Yes	No	No	No	Not clear	Yes	Not clear
Akbulut *et al.* (2019)[10]	RCT	No	Yes	No	Yes	Not clear	Yes	Yes	Not clear	Yes	Not clear
Güleç *et al.* (2017)[5]	RCT	Yes	Yes	No	Yes	No	No	No	Not clear	Yes	Not clear
Nakornni *et al.* (2019)[12]	RCT	No	Yes	Not clear	Not clear	No	Yes	No	Not clear	Yes	Not clear
Sufarnap *et al.* (2018)[15]	Non-RCT	No	No	No	No	No	No	No	No	Yes	Not clear

Table 8: Risk-of-bias assessment for human studies.

Study	Randomization process	Deviations from the intended interventions (effect of assignment to intervention)	Deviations from the intended interventions (effect of adhering to intervention)	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
El-Timamy *et al.* (2020) [16]	Low	Some concerns	Some concerns	High	Low	Low	High
Alomari *et al.* (2019) [17]	Some concerns	Some concerns	Some concerns	High	High	Low	High

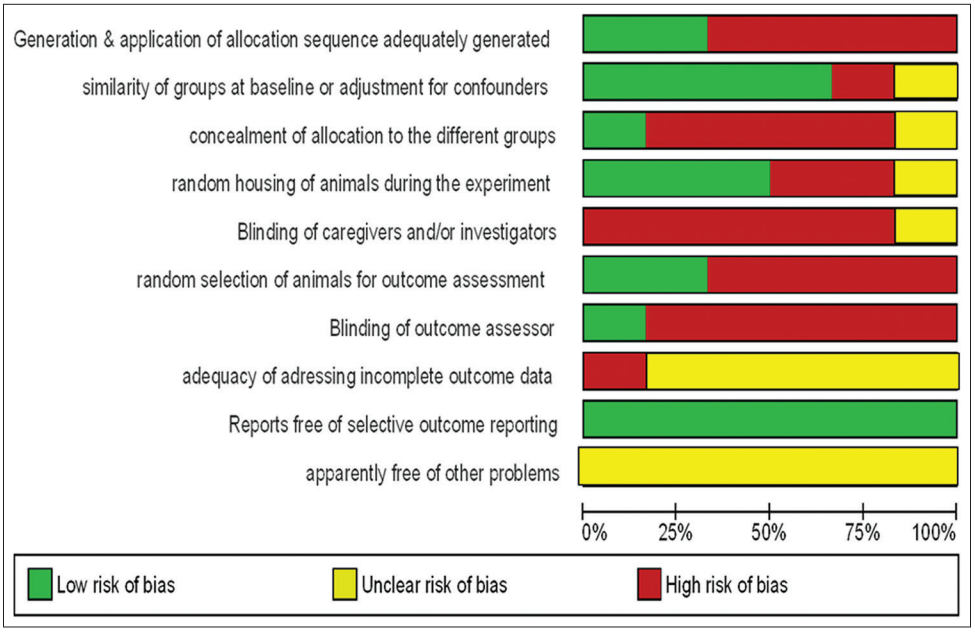


Figure 3: Risk-of-bias graph: Review authors' judgments about each risk-of-bias item presented as percentages (animal studies).

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.*[5] 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.*[14] 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.*[12] 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.*[14] 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, Theerasak Nakornnoi *et al.*[12] 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.*[11] and Sufarnap *et al.*[15] found no beneficial effect of PRP as an adjunct to OTM. Akbulut *et al.*[11] evaluated the early effects of PRP both clinically and histologically, whereas Sufarnap

et al.[15] did only clinical evaluation. Akbulut *et al.*[11] 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.*[14] who found increased osteoclast cell count at week 9 on the compression side and Güleç *et al.*[5] 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.*[13] 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.

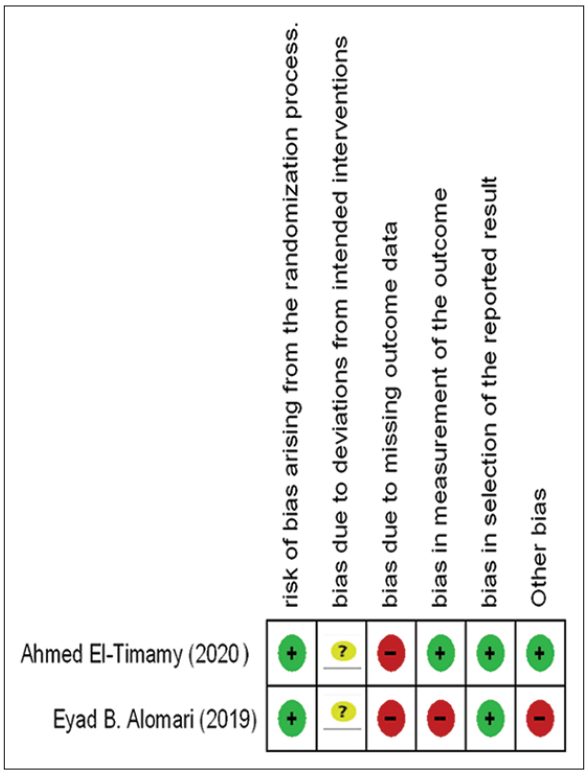


Figure 4: Risk of bias summary - Review authors judgement about each risk-of-bias item(Human studies).

Human studies

Literature search revealed only two human trials. A split-mouth RCT by El-Timamy *et al.*[16] to study the effect of PRP on rate of OTM and Alomari *et al.*[17] who studied the effect of PRP on reducing alveolar bone resorption following rapid maxillary expansion.

El-Timamy *et al.*[16] concluded that PRP group had a significant acceleration in the rate of OTM. This was the only study which evaluated the amount of pain associated with administration of PRP injection and found that pain scores increased following injections on both intervention and control side and PRP administration is not associated with pain.

Alomari *et al.*[17] in his study of rapid maxillary expansion showed no difference between the interventional and control groups of the buccal bone plate thickness and buccal bone crest level of the anchoring teeth. Furthermore, the percentage of dehiscence and fenestrations was not significantly different between the two groups.

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

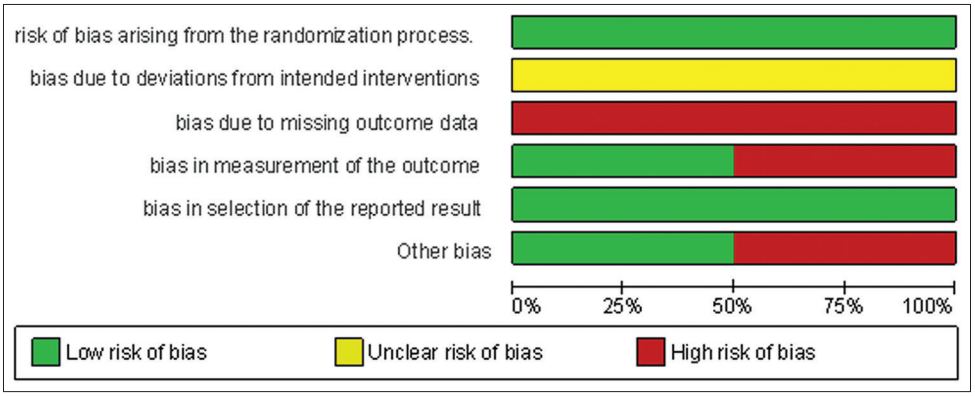


Figure 5: Risk of bias graph- Review authors judgement about each risk-of-bias item presented as percentages (Human studies).

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 well-designed human RCTs with standardized method for PRP concentration and preparation should be conducted.

Acknowledgments

We are grateful to Dr. Dheeraj Kalra for offering the statistical help in this systematic review.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Marx RE. Platelet-rich plasma (PRP): What is PRP and what is not PRP? Implant Dent 2001;10:225-8.
2. Liou EJ. The development of submucosal injection of platelet rich plasma for accelerating orthodontic tooth movement and preserving pressure side alveolar bone. APOS Trends Orthod 2016;6:5-11.
3. Franchini M, Cruciani M, Mengoli C, Masiello F, Marano G, D'Aloja E, *et al*. The use of platelet-rich plasma in oral surgery: A systematic review and meta-analysis. Blood Transfus 2019;17:357-67.
4. Han J, Meng HX, Tang JM, Li SL, Tang Y, Chen ZB. The effect of different platelet-rich plasma concentrations on proliferation and differentiation of human periodontal ligament cells *in vitro*. Cell Prolif 2007;40:241-52.
5. Güleç A, Bakkalbaşı BÇ, Cumbul A, Uslu Ü, Alev B, Yarat A. Effects of local platelet-rich plasma injection on the rate of orthodontic tooth movement in a rat model: A histomorphometric study. Am J Orthod Dentofacial Orthop 2017;151:92-104.
6. Mehta S, Watson JT. Platelet rich concentrate: Basic science and current clinical applications. J Orthop Trauma 2008;22:432-8.
7. El-Sharkawy H, Kantarci A, Deady J, Hasturk H, Liu H, Alshahat M, *et al*. Platelet-rich plasma: Growth factors and pro- and anti-inflammatory properties. J Periodontol 2007;78:661-9.
8. Andia I, Maffulli N. Platelet-rich plasma for managing pain and inflammation in osteoarthritis. Nat Rev Rheumatol 2013;9:721-30.
9. Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, *et al*. RoB 2: A revised tool for assessing risk of bias in randomised trials. BMJ 2019;366:l4898.
10. Hooijmans CR, Rovers MM, de Vries RB, Leenaars M, Ritskes-Hoitinga M, Langendam MW. SYRCLE's risk of bias tool for animal studies. BMC Med Res Methodol 2014;14:43.
11. Akbulut S, Yagci A, Yay AH, Yalcin B. Experimental investigation of effects of platelet-rich plasma on early phases of orthodontic tooth movement. Am J Orthod Dentofacial Orthop 2019;155:71-9.
12. Nakornnoi T, Leethanakul C, Samruajbenjakun B. The influence of leukocyte-platelet-rich plasma on accelerated orthodontic tooth movement in rabbits. Korean J Orthod 2019;49:372-80.
13. Abdel-Haffiez SH, Ismail HI, Elharouni NM, Ali HM. The effect of platelet rich plasma injection on relapse of orthodontically moved teeth in rabbits. Egypt Orthod J 2017;51:41-57.
14. Rashid A, ElSharaby FA, Nassef EM, Mehanni S, Mostafa YA. Effect of platelet-rich plasma on orthodontic tooth movement in dogs. Orthod Craniofac Res 2017;20:102-10.
15. Sufarnap E, Sofyanti E, Ilyas S. The effect of platelet-rich plasma to orthodontic tooth movement. In: Abbot PV, Tseng PS, Porto I, Lestari W, editors. Proceedings of the International Dental Conference of Sumatera Utara 2017. Vol. 8. Paris, France: Atlantis Press; 2017. p. 80-3.
16. El-Timamy A, El Sharaby F, Eid F, El Dakroury A, Mostafa Y, Shakr O. Effect of platelet-rich plasma on the rate of orthodontic tooth movement: A split-mouth randomized trial. Angle Orthod 2020;90:354-61.
17. Alomari EB, Sultan K. Efficacy of injectable platelet-rich plasma in reducing alveolar bone resorption following rapid maxillary expansion: A cone-beam computed tomography assessment in a randomized split-mouth controlled trial. Angle Orthod 2019;89:705-12.

How to cite this article: Narkhede KP, Bhad W, Chavan SJ. Platelet-rich plasma: Its applications in orthodontics – A systematic review. APOS Trends Orthod 2021;11:235-46.