Review Article

Is Platelet-Rich Plasma the New Missing Link in Orthodontics?

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Abstract

Platelet-rich plasma (PRP) contains autologous concentration of platelets. PRP is rich in various cytokines and growth factors, because of which it can aid in tissue repair and regeneration. It has a variety of dental applications, including alveolar ridge preservation, alveolar bone transplantation, and improving the healing process, among others. Because of the presence of certain bioactive components, it can be used in orthodontics to help with tooth movement. This review article aims to present all the current information available on PRP and its association with accelerated orthodontic tooth movement.

Keywords: Platelet-rich plasma, Accelerated orthodontics, Growth factors, Cytokines.

Introduction

Platelet-rich plasma (PRP) is a small amount of plasma comprising autologous concentration of platelets. PRP contains a good amount of growth factors, which are indirectly involved in the process of repair and regeneration.[1]

Some of its dental applications include improving dental implant osseointegration, increasing alveolar bone height in maxillary sinus lifts, and promoting orthodontic tooth movement (OTM).[2-8]

This review article seeks to summarize all of the known information on PRP and its relationship to OTM.

Composition of PRP

PRP is composed of 5% RBC, 1% WBC, and 94% platelets. The platelet count in PRP is substantially higher than the platelet count in blood, which is around 1 lakh platelets per µliter.[9] It contains growth factors such as basic fibroblast growth factor (bFGF), interleukin (IL)-1, IL-6, IL-8, endothelial growth factor, tumor necrosis factor, granulocyte colony-stimulating factor, interferon, and cytokines.[10,11]

Repair and regeneration of any injured tissue necessitates the activation of several critical cellular processes, which are regulated by biologic mediators known as growth factors. When growth factors bind to a specific cell membrane receptor, they activate the intracellular signaling cascade. This activates certain genes, resulting in phenotypic and cellular activity changes.[12] Growth factors are important in fundamental biological processes such as mitogenesis, differentiation, chemotaxis, and metabolism. The wound healing process is eventually regulated and stimulated by these cellular activities.

Various constituents such as enzymes, binding proteins, and growth factors are responsible for a wide range of feedback processes that govern the function of a specific growth factor. With recent advancements, the significance of growth factors is more known, and this understanding will improve through time. Growth factors have been shown to increase the regulation of processes such as chemoattraction, differentiation, and proliferation, as well as the healing process, in many *in vivo* and *in vitro* investigations.[12]

When a concentrated version of PRP is administered, an anti-inflammatory reaction occurs due to the production of RANTES and inhibition of MCP-1 release from monocytes, resulting in a local inflammatory response that promotes tissue regeneration and repair.[13]

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History

Since the 1890s, several attempts have been made to improve OTM. Cunningham made one of the first attempts when he described "luxation or instantaneous procedure in the treatment of irregular teeth" at a Chicago Dental Congress.[14]

In the year 1998, PRP was initially used for mandibular defect restoration with autologous bone graft. The authors found that the bone graft alone led to a faster rate of maturation and higher bone density.[15] According to a study by Jeon *et al*., bone morphogenetic protein and PRP are equally effective in enhancing bone regeneration.[16]

PRP has been shown to boost a variety of biological functions, including osteogenesis, angiogenesis, stem cell proliferation and migration, in addition to tissue regeneration.[17]

Discussion

PRP and accelerated orthodontics

The duration of orthodontic treatment is a significant drawback which makes the patient sceptical for seeking orthodontic treatment. Bone remodeling is necessary for focused tooth displacement, which is why this procedure takes so long. Any strategy that can speed up this process is beneficial to orthodontics. A shorter treatment period also aids in differential tooth movement, increased tooth movement envelope, better stability after treatment, and minimal complications.

Since then, other treatment alternatives for accelerating orthodontic treatment have emerged. However, there is still no gold standard treatment for accelerating tooth movement. There have been several attempts in the field of study to establish a therapeutically acceptable procedure, but no method has been demonstrated to produce promising outcomes. As a result, the need of the hour is to identify a way for increasing OTM that is non-invasive, patient friendly, and simple.[18]

Earlier, thyroid hormone and prostaglandin E2 were found to be quite efficient in accelerating OTM in rats.[19] Triamcinolone acetonide also proved to be potent in decreasing orthodontic treatment time.[20] In the initial stages of orthodontic movement, nonsteroidal anti-inflammatory medications such as potassium diclofenac and dexamethasone were found to reduce bone resorption.[21] Tooth movement was accelerated by growth hormones as well. bFGFs also improved the pace of tooth movement in a concentration-dependent manner.[22]

PRP in orthodontics has gained popularity because of the availability of various growth factors that can stimulate both osteoblasts and osteoclasts, resulting in the process of bone remodeling.[10,23] Not only that, but it also contains a significant number of cytokines, which mediate processes such as differentiation, activation, and survival of osteoblast and osteoclast cells, all of which are important during OTM.[24,25] All of these considerations backed up the theory that PRP could help with orthodontic tooth mobility.

PRP can be injected locally to help with anterior crowding, tooth alignment and leveling, as well as space closure while retracting anteriors or for protracting molars.[26]

PRP preparation for orthodontics

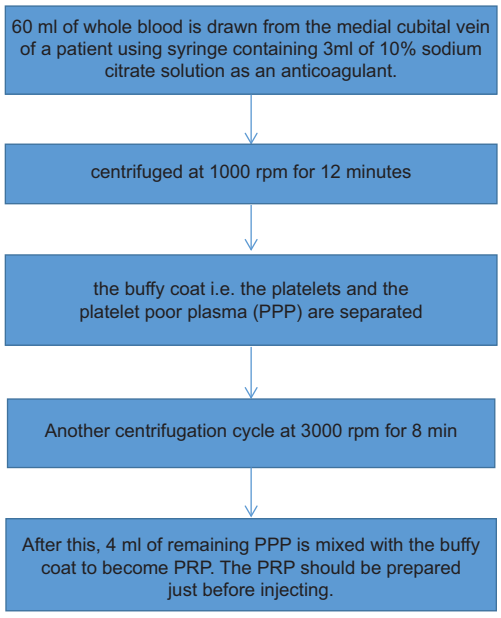
According to Liou, suitable PRP for orthodontic purposes should have a long-term effect. PRP preparation without mixing $CaCl_2$ and thrombin can have a long-lasting effect. With this, the formulation is also maintained in the liquid state so that it can be comfortably injected. Aseptic conditions should be maintained during processing of PRP[26] (Flowchart 1).

PRP and tooth movement

The previous research indicated that PRP could be useful in orthodontic therapy, although the exact means by which it causes the accelerated movement of tooth are obscure. Akbulut *et al*. measured the expressions of alkaline phosphatase (ALP), transforming growth factor-b (TGF-b), and tartrate resistant acid phosphatase (TRAP) in rats and thereby understanding the mechanism of the action of PRP. The results revealed that 100 µl of PRP had no effect on the number of osteoblast and osteoclast cells. Similarly, the expressions of TRAP, ALP, and TGF-b were not altered. In the rat model, PRP levels 4.5 times greater than baseline were ineffective in accelerating tooth movement.[18]

Another study by Güleç *et al*. compared the effects of a moderate concentration of PRP against an increased concentration of PRP on OTM. The researchers concluded that a high concentration of PRP could speed up OTM by decreasing alveolar bone density and increasing osteoclastic activity. PRP at a low concentration was not as effective as PRP at a high concentration.[27]

El-Timamy *et al*. conducted a study to assess the fastening of tooth movement after PRP was injected locally and any associated pain. They concluded that, despite initially exhibiting



Flowchart 1: Method of prp preparation

a statistically significant increase in canine retraction, PRP had no long-term effects on faster tooth movement.[28]

Rashid *et al*. investigated the clinical and histological effects of locally injected PRP on the pace of OTM in dogs. The authors pointed out that there was a statistically significant improvement in the tooth movement in the PRP with no obvious complications.[29]

Sufarnap *et al*. analyzed OTM in guinea pigs to examine bone remodeling in histology analysis in a study. With four time points of assessment, the authors could not identify a significant difference between the two groups and urged further research.[30]

L-PRP in orthodontics

PRP in leukocytes is another formulation which has gained popularity recently. This formulation is known as leukocyte-PRP (L-PRP) and has gained popularity for improved tissue regeneration ability. By upregulating cellular proliferation, viability, angiogenesis, and osteogenesis, it can enhance the process of bone regeneration.[31,32]

Furthermore, a few researches in the past have shown production of harmful metalloproteinases when the concentration of L-PRP was correlated with increased levels of catabolic cytokines.[32-34] Due to the activation of nuclear factor κB pathway because of L-PRP, bone resorptive activity is stimulated causing the bone density to decrease and leading to better bone remodeling.[17]

Nakornnoi *et al*. also studied the effects of L-PRP on tension and compression side during tooth movement. They observed an improvement in remodeling of bone on the micro-computed tomography.[35]

A previous study by Akbulut *et al*.[18] reported that PRP without leukocytes was not efficient enough in bone remodeling when administered locally. They pointed out that because leukocytes have an influence on the concentration of growth factors and cytokine levels, the role of leukocyte poor PRP in bone remodeling is barely of any significance. The presence of L-PRP makes it better than leukocyte poor PRP, due to the higher levels of growth factors.[36] The difference in the results can also be attributed to the use of different techniques.

The same authors also evaluated the role of injectable L-PRP in accelerating tooth movement in rabbits and concluded that during all time periods, L-PRP was more efficient in causing accelerated OTM.[37]

I-PRP and its effects

A second-generation platelet-rich concentrate comprising fibrin matrix completely was developed at lower centrifugation speeds and without the addition of any anticoagulants.[14,38,39] It has been reported that the upper layer of the tubes was rich in leukocytes and stimulated the growth factor release.[40,41]

Using this injectable, PRF has its own benefits like less side effects since its autogenous, minimally invasive, and less expensive procedure.[38,39,42,43] A recent study evaluated a new formulation of PRF which resulted in significant release of growth factors gradually for over a week.[44]

Dose and Composition-Related Effects of PRP

There is no gold standard for optimal concentration and dose for PRP. Various authors give different optimum concentrations and hence different results are achieved. Furthermore, the studies which have been conducted so far have all been performed under different settings and on different animals. All these factors have led to different results and we still do not know what is the actual concentration of PRP that can help us achieve better results during OTM.

Although some authors have mentioned a dose-dependent effect of PRP, for example, Güleç *et al*. discussed the effect on alveolar bone density and OTM when different concentrations of PRP are used and concluded that an increased concentration of PRP was more effective in fastening the tooth movement than the moderate concentration.[27] The authors mentioned that this could be due to the application of mechanical force. PRP has a concentration-dependent effect on bone turnover[9] and also OTM.[27] Therefore, it can be implied that various effects can occur on OTM depending on the concentration of leukocyte-platelet-rich fibrin (LPRF).[27]

There are overlapping biological effects because of the presence of cytokines, growth factors, and enzymes in LPRP and there is still more scope to understand the role of each ingredient.[12] These biological effects include both inflammatory reactions which can lead to accelerated tooth movement or anti-inflammatory effect that can lead to improved tissue healing ability.[13]

It has been shown in the previous studies that based on content of growth factor, concentration and timing of release, LPRF can either cause an inflammatory response or an anti-inflammatory responses.[45]

Conclusion

Based on all this information, it can be concluded that PRP can be a potential, non-invasive, and comparatively comfortable procedure to enhance OTM. A lot of study in this field is still required to assess the exact effect and mechanism of the action of PRP on tooth movement as well as on accelerated orthodontics. More studies should be encouraged to find the optimum concentration of PRP that can lead to best possible results in relation to orthodontic treatment.

References

1. Marx RE. Platelet-rich plasma (PRP): What is PRP and what is not PRP? Implant Dent 2001;10:225-8.
2. Schlegel KA, Kloss FR, Kessler P, Schultze-Mosgau S, Nkenke E, Wiltfang J. Bone conditioning to enhance implant osseointegration: An experimental study in pigs. Int J Oral Maxillofac Implants 2003;18:505-11.
3. Kim SG, Chung CH, Kim YK, Park JC, Lim SC. Use of particulate dentin-plaster of Paris combination with/without platelet-rich plasma in the treatment of bone defects around implants. Int J Oral Maxillofac

Implants 2002;17:86-94.
4. Kim SG, Kim WK, Park JC, Kim HJ. A comparative study of osseointegration of Avana implants in a demineralized freeze-dried bone alone or with platelet-rich plasma. J Oral Maxillofac Surg 2002;60:1018-25.
5. Rodriguez A, Anastassov GE, Lee H, Buchbinder D, Wettan H. Maxillary sinus augmentation with deproteinated bovine bone and platelet rich plasma with simultaneous insertion of endosseous implants. J Oral Maxillofac Surg 2003;61:157-63.
6. Zechner W, Tangl S, Tepper G, Furst G, Bernhart T, Haas R, *et al*. Influence of platelet-rich plasma on osseous healing of dental implants: A histologic and histomorphometric study in minipigs. Int J Oral Maxillofac Implants 2003;18:15-22.
7. Okuda K, Kawase T, Momose M, Murata M, Saito Y, Suzuki H, *et al*. Platelet-rich plasma contains high levels of platelet-derived growth factor and transforming growth factor-beta and modulates the proliferation of periodontally related cells *in vitro*. J Periodontol 2003;74:849-57.
8. Sanchez AR, Sheridan PJ, Kupp LI. Is platelet-rich plasma the perfect enhancement factor? A current review. Int J Oral Maxillofac Implants 2003;18:93-103.
9. Weibrich G, Hansen T, Kleis W, Buch R, Hitzler WE. Effect of platelet concentration in platelet rich plasma on peri-implant bone regeneration. Bone 2004;34:665-71.
10. Gerard D, Carlson ER, Gotcher JE, Jacobs M. Effect of platelet rich plasma on healing of autologous bone grafted mandibular defects in dogs. J Oral Maxillofac Surg 2006;64:443-51.
11. Suaid FF, Carvalho MD, Santamaria MP, Casati MZ, Nociti FH Jr., Sallum AW, *et al*. Platelet-rich plasma and connective tissue grafts in the treatment of gingival recessions: A histometric study in dogs. J Periodontol 2008;79:888-95.
12. Marx RE. Platelet-rich plasma: Evidence to support its use. J Oral Maxillofac Surg 2004;62:489-96.
13. 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.
14. Hassan AH, Al-Fraidi AA, Al-Saeed SH. Corticotomy assisted orthodontic treatment: Review. Open Dent J 2010;4:159-64.
15. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: Growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;85:638-46.
16. Jeon YR, Jung BK, Roh TS, Kang EH, Lee WJ, Rah DK, *et al*. Comparing the effect of nonactivated platelet-rich plasma, activated platelet-rich plasma, and bone morphogenetic protein-2 on calvarial bone regeneration. J Craniofac Surg 2016;27:317-21.
17. Yin W, Qi X, Zhang Y, Sheng J, Xu Z, Tao S, *et al*. Advantages of pure platelet-rich plasma compared with leukocyte-and platelet-rich plasma in promoting repair of bone defects. J Transl Med 2016;14:73.
18. 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.
19. Seififi M, Hamedi R, Khavandegar Z. The effect of thyroid hormone, prostaglandin E2, and calcium gluconate on orthodontic tooth movement and root resorption in rats. J Dent (Shiraz) 2015;16 Suppl 1:35-41.
20. Abtahi M, Shafaee H, Saghravania N, Peel S, Giddon D, Sohrabi K. Effect of corticosteroids on orthodontic tooth movement in a rabbit model. J Clin Pediatr Dent 2014;38:285-9.
21. Knop LA, Shintcovsk RL, Retamoso LB, Ribeiro JS, Tanaka OM. Non-steroidal and steroidal anti-inflflammatory use in the context of orthodontic movement. Eur J Orthod 2011;34:531-5.
22. Seififi M, Badiee MR, Abdolazimi Z, Amdjadi P. Effect of basic fibroblast growth factor on orthodontic tooth movement in rats. Cell J 2013;15:230-7.
23. Tan YY, Yang YQ, Chai L, Wong RW, Rabie AB. Effects of vascular en dothelial growth factor (VEGF) on MC3T3-E1. Orthod Craniofac Res 2010;13:223-8.
24. Casati MZ, de Vasconcelos Gurgel BC, Gonçalves PF, Pimentel SP, da Rocha Nogueira Filho G, Nociti FH Jr., *et al*. Platelet rich plasma does not improve bone regeneration around peri-implant bone defects. A pilot study. Int J Oral Maxillofac Surg 2007;36:132-6.
25. Andrade I, Taddei SR, Souza PE. Inflammation and tooth movement: The role of cytokines, chemokines, and growth factors. Semin Orthod 2012;18:257-69.
26. Liou E. 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.
27. Güleç A, Bakkalbasi BC, Cumbul A, Uslu U, Alec 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.
28. El-Timamy A, El Sharaby F, Eid F, El Dakroury A, Mostafa Y, Shaker O. Effect of platelet-rich plasma on the rate of orthodontic tooth movement: A split-mouth randomized trial. Angle Orthod 2020;90:354-61.
29. Rashid A, El-Sharaby 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.
30. Sufarnap E, Sofyanti E, Ilyas S. The effect of platelet-rich plasma to orthodontic tooth movement. In: International Dental Conference of Sumatera Utara 2017 (IDCSU 2017). United States: Atlantis Press; 2018.
31. Yuan T, Guo SC, Han P, Zhang CQ, Zeng BF. Applications of leukocyte- and platelet-rich plasma (L-PRP) in trauma surgery. Curr Pharm Biotechnol 2012;13:1173-84.
32. Schär MO, Diaz-Romero J, Kohl S, Zumstein MA, Nesic D. Platelet-rich concentrates differentially release growth factors and induce cell migration *in vitro*. Clin Orthop Relat Res 2015;473:1635-43.
33. Anitua E, Zalduendo M, Troya M, Padilla S, Orive G. Leukocyte inclusion within a platelet rich plasmaderived fibrin scaffold stimulates a more pro-inflammatory environment and alters fibrin properties. PLoS One 2015;10:e0121713.
34. Pifer MA, Maerz T, Baker KC, Anderson K. Matrix metalloproteinase content and activity in low-platelet, low-leukocyte and high-platelet, high-leukocyte platelet rich plasma (PRP) and the biologic response to PRP by human ligament fibroblasts. Am J Sports Med 2014;42:1211-8.
35. Nakornnoi T, Leethanakul C, Samruajbenjakun B. Effects of leukocyte-platelet-rich plasma on the alveolar bone changes during orthodontic tooth movement in rabbits: A Micro-CT study. J Indian Orthod Soc 2019;53:264-71.
36. Zimmermann R, Arnold D, Strasser E, Ringwald J, Schlegel A, Wiltfang J, *et al*. Sample preparation technique and white cell content influence the detectable levels of growth factors in platelet concentrates. Vox Sang 2003;85:283-9.
37. 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.
38. Wang X, Zhang Y, Choukroun J, Ghanaati S, Miron RJ. Effects of an injectable platelet-rich fibrin on osteoblast behavior and bone tissue formation in comparison to platelet-rich plasma. Platelets 2018;29:48-55.
39. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, *et al*. Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part IV: Clinical effects on tissue healing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:56-60.
40. Ghanaati S, Booms P, Orlowska A, Kubesch A, Lorenz J, Rutkowski J, *et al*. Advanced platelet-rich fibrin: A new concept for cell-based tissue engineering by means of inflammatory cells. J Oral Implantol 2014;40:679-89.
41. Fujioka-Kobayashi M, Miron RJ, Hernandez M, Kandalam U, Zhang Y, Choukroun J. Optimized platelet rich fibrin with the low speed concept: Growth factor release, biocompatibility and cellular response. J Periodontol 2017;88:112-21.
42. Tehranchi A, Behnia H, Pourdanesh F, Behnia P, Pinto N, Younessian F. The effect of autologous leukocyte platelet rich fibrin on the rate of orthodontic tooth movement: A prospective randomized clinical trial. Eur J Dent 2018;12:350-7.
43. Gassling VL, Acil Y, Springer IN, Hubert N, Wiltfang J. Platelet-rich plasma and platelet-rich fibrin in human cellculture. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:48-55.
44. Kobayashi E, Fluckiger L, Fujioka-Kobayashi M, Sawada K, Sculean A, Schaller B, *et al*. Comparative release of growth factors from PRP, PRF, and advanced-PRF. Clin Oral Invest 2016;20:2353-60.
45. Andia I, Maffulli N. Platelet-rich plasma for managing pain and inflammation in osteoarthritis. Nat Rev Rheumatol 2013;9:721-30.