

## Review Article

# Role of platelet-rich plasma in maxillofacial surgery

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## ABSTRACT

Platelet-rich plasma (PRP) has been reported as an efficacious modality that can enhance the process of wound healing and tissue regeneration and has been validated in different medical settings, including cardiovascular surgery, otolaryngology, head and neck surgery, and maxillofacial surgery. In dental and oral surgery settings, PRP has been reported as an efficacious approach with favorable outcomes in different settings. Some of these procedures include surgical repair of the alveolar cleft, mandibular reconstruction, ablative surgical procedures, placement of osseointegrated implants, periodontal plastic surgery, and management of infrabony periodontal defects. In the present study, we aim to discuss the role and mechanisms that PRP plays in the settings of maxillofacial surgery based on evidence from the relevant studies in the literature. Evidence indicates the wide acceptance of the modality, which has been proven to increase the rate of wound healing and reduce the frequency of pain and swelling. The administration of PRP has been reported to dispense with the need for invasive approaches that might be furtherly associated with complications and different morbidities. However, in most of the favorable events where the PRP administration of was associated with enhanced outcomes, the modality was used in combination with another therapeutic approach. Therefore, further research is needed to validate the efficacy of the modality in the different settings.

**Keywords:** Maxillofacial, Dental surgery, Management, Platelet-rich plasma, PRP

## INTRODUCTION

Platelet-rich plasma (PRP) has been reported as an efficacious modality that can enhance the process of

wound healing and tissue regeneration and has been validated in different medical settings, including cardiovascular surgery, otolaryngology, head and neck surgery, and maxillofacial surgery.<sup>1</sup> Generally, PRP is administered in the form of a gel preparation, which is

mixed with calcium chloride and thrombin. In addition to having a high concentration of platelets, it has been demonstrated that the modality also has some concentration of fibrinogen.<sup>2,3</sup>

In dental and oral surgery settings, PRP has been reported as an efficacious approach with favorable outcomes in different settings. Some of these procedures include surgical repair of the alveolar cleft, mandibular reconstruction, ablative surgical procedures, placement of osseointegrated implants, periodontal plastic surgery, and management of infrabony periodontal defects.<sup>4,5</sup> In the present study, we aim to discuss the role and mechanisms that PRP plays in the settings of maxillofacial surgery based on evidence from the relevant studies in the literature.

## METHODS

This literature review is based on an extensive literature search in Medline, Cochrane, and EMBASE databases which was performed on 2nd October 2021 using the medical subject headings (MeSH) or a combination of all possible related terms, according to the database. To avoid missing potential studies, a further manual search for papers was done through Google Scholar, while the reference lists of the initially included papers. Studies discussing the role of PRP in maxillofacial surgery were screened for useful information, with no limitations posed on date, language, age of participants, or publication type.

## DISCUSSION

PRP has been widely used in the settings of oral and maxillofacial surgeries as an efficacious modality for enhancing the associated outcomes with these modalities. Evidence shows that they are being used in the different related settings to this field, and studies indicate the favorable outcomes following the administration of the modality. In the following paragraphs, we will discuss the role of PRP in the different procedures together with the reported outcomes as reported by previous investigations in the literature.

### *Potential advantages and adverse events*

PRP has been developed as an autologous that utilizes the patient's blood in an amount that has been previously reported to be remarkably small. Accordingly, evidence shows that the administration of the modality in these settings is safe, together with being efficacious. In this context, there has been no evidence among the different studies in the literature about any risk of immunogenic reactions, disease transmission (like Creutzfeldt-Jacob disease, hepatitis, or HIV), infections, or any other side effects or complications that might be related to the administration of the modality.<sup>6</sup> Past evidence shows that bovine thrombin (which has been reported to be a modality that activates and polymerizes fibrin into a soluble gel) was significantly associated with the development of serious

coagulopathies, which was also reported to be life-threatening when used in preparing PRP.<sup>7</sup> However, it should also be noted that the reported adverse events were related to the quantity and source of the used thrombin in the formation of PRP. In this context, evidence indicates that the topical low-dose administration of clotted bovine thrombin, with no reach to the systemic circulation, does not have a serious effect on the development of administration-related adverse events.<sup>8</sup> Additionally, it has been reported that calcium chloride can effectively inhibit the adverse events related to the administration of thrombin, and therefore, alleviating the efficacy of PRP. Accordingly, no further serious adverse events were reported with the administration of the modality.<sup>9,10</sup>

In another context, the administration of PRP in some cases might be impacted by the cost-outcome benefit from using the modality in the maxillofacial surgeries. Processing PRP has been reported to be associated with high costs, in addition to the estimated potential economic burden over the corresponding patients. Blood drawing and venipuncture procedures, which are routinely done when PRP therapy is intended, were also reported to potentially represent another restriction to the administration of PRP.<sup>2,8</sup> On the other hand, two main advantages were reported for the administration of PRP, including the associated time and clinical efficacy, and being easy-obtainable, representing a favorable modality to the patient and clinician.

Researchers and clinicians show that the administration of PRP procedure can take up to 30 minutes and requires an additional surgical step, however, the modality can simultaneously be done during the surgical setting and would not be still time-consuming if it has been done by the experienced surgeon during the surgical setting.<sup>8,11</sup>

### *Mechanism of action*

PRP has been introduced as an increased concentration of platelets within a small amount of plasma.<sup>12,13</sup> In the human blood, the normal physiological platelets counts range around 150,000-350,000/1 L, while in PRP,  $\geq 1,000,000/1$  per L of autologous platelets are concentrated within a 5 mL volume of plasma. After triggering the coagulation process within the wound site, it has been reported that alpha granules are released from the autologous. This process aims to activate and enhance the release of the different growth factors that play important roles in cellular differentiation, chemotaxis, and proliferation, which can significantly enhance the process of osteogenesis. Initiation and persistence of the process of wound healing were also associated with the release of the different growth factors, which remarkably increase tissue vascularity, promote the proliferation of growth factors, and accelerate bone repair, in addition to the procoagulant impact of these modalities. Calcium chloride and thrombin and mixed with PRP to formulate a PRP gel. This is usually done to automatically activate the alpha granules, which are responsible for the significant release of the different

growth factors in this process.<sup>14</sup> Some of the released growth factors include epithelial cell growth factor, epidermal growth factor (EGF), insulin-like growth factor-I, vascular endothelial growth factor (VEGF), transforming growth factor-beta (TGF- $\beta$ ), and platelet-derived growth factor (PDGF).<sup>8</sup> The latter has been reported to be responsible for many of the potential effects of PRP administration, playing a key role in the process of soft-and hard-tissue healing. Replication, mitogenesis, and chemotaxis of the different stem cells were also reported to be stimulated in the presence of PDGF within the site of the injured tissue. Accordingly, this has been reported with remarkable outcomes regarding angiogenesis and bone matrix formation, and promoting the further release and formation of VEGF. The latter can initiate a state of neovascularization which can significantly enhance the process of wound healing. The release of fibronectin has also been associated with PDGF, which enhances the process of wound healing, and promotes wound remodeling, and contraction.<sup>15</sup> Connective tissue repair and bone regeneration were also reported secondary to the administration of PRP gel due to the increased amounts of TGF- $\beta$ 1, and TGF- $\beta$ 2. Inducing the production of cellular fibronectin and collagen, in addition to stimulating fibroblasts' chemotaxis and stimulating the activities of protease inhibitors, and reducing the actions of proteases, which can remarkably inhibit collagen degradation, were reported secondary to the increased amounts of these growth factors. Other effects regarding bone regeneration were also reported by previous investigations in the literature indicating the favorable effects of the PRP administration.<sup>16,17</sup>

### ***Efficacy of PRP in the different maxillofacial surgeries***

PRP has been reported to enhance the quality of bone regeneration and deposition rate, and therefore, it has been effectively used for augmenting edentulous sites for potential implant placement. In the settings of amending peri-implant defect, a previous investigation by Sanchez et al reported that PRP can be effectively used in this setting together with barrier membranes and bone grafts.<sup>18</sup> Infusion of a resorbable barrier membrane material with PRP was also previously reported in another investigation by Panda et al.<sup>19</sup> This membrane can be used as a short-term modality to reduce the process of platelet degranulation and prolong its potentially expiring growth activities, which usually occur within 3-7 days and ten years, respectively. Using bone grafts in combination with PRP was also previously validated in the study by Marx et al. that reported that the maturity index of bone graft reconstructions of mandibular continuity defects that are  $\geq 5$  cm was twice and slightly  $<$ twice the actual maturity rates at 2 and 4 months, respectively.<sup>20,21</sup> Therefore, it has been concluded that the administration of these modalities significantly enhances the associated efficacy and reduces the time of healing. Different investigations also reported similar outcomes in the different maxillofacial and oral surgeries, indicating the favorable events on bony density and tissue healing following the administration of PRP.<sup>22,23</sup>

Regenerative treatment in the settings of periodontics was also validated by previous researchers that introduced the favorable events of using PDGF. In this context, a previous investigation evaluated the efficacies of different growth factors in these settings based on the cell type and source. The authors of this investigation reported that stimulated migration of the periodontal ligament fibroblasts was only noticed following the PDGF administration only among other administered growth factors.<sup>24-26</sup> The administration of PRP modalities was also furtherly introduced in the settings of temporomandibular disorders and has been reported to effectively improve mouth opening and reduce the associated pain that is usually reported in this setting.<sup>27</sup> In this context, a previous review concluded that compared to saline or hyaluronic acid injections, the administration of PRP was more frequently associated with relieving clinical manifestations related to temporomandibular joint disorders among 4 out of 6 included investigations.<sup>28</sup>

The PRP administration was also reported in the settings of cleft lip and palate, which are owing to congenital defects in the nasal and maxillary processes. These defects are primarily managed by surgical approaches, and it has been validated that the administration of PRP can significantly reduce the incidence of oronasal fistula by promoting the process of wound healing, leading to a complete closure of the corresponding cleft palate, which has been reported to be more efficacious than performing the surgical procedure alone.<sup>29</sup> Accordingly, it has been estimated that such combinations effectively reduce the need to perform further additional surgeries. In cases of recurrent palate fistulas, evidence shows that bone grafts and PRGF were associated with complete closure in 90.9% of patients.<sup>18</sup> However, evidence in this context is not strengthened by many investigations and further studies are needed. PRP administration was also validated in the settings of alveolar graft reconstruction in combination with iliac bone grafting.<sup>30,31</sup> Nevertheless, studies show that no favorable outcomes were noticed with this approach, and further studies are needed for further validation.<sup>32,33</sup> In cases with bisphosphonate-related osteonecrosis of the jaw, studies show that PRP can be effectively used to enhance the outcomes when used together with surgery.<sup>34</sup> A previous study also reported that enhanced healing was noticed when PRP was combined with bone morphogenetic protein 2.<sup>35</sup> However, a meta-analysis reported that combining PRP in these cases has not been evidenced by adequate investigations.<sup>36</sup> In the settings of oroantral communication, a previous study reported that the administration of PRP was significantly associated with pain relief and reduced swelling, in addition to accelerated wound healing when compared to the outcomes of buccal advancement flap.<sup>37</sup> Demetoglu et al furtherly reported that in cases of oroantral communication ( $\leq 5$  mm), a platelet-rich fibrin membrane can be used to manage these cases.<sup>38</sup> Osteoradionecrosis of the jaw was also previously reported to be effectively managed by the administration of PRP.<sup>39</sup> An investigation by Bilimoria et al reported that at one year of follow-up, complete healing was noticed among 67% of the cases

after surgical debridement with piezosurgery in combination with platelet-rich fibrin to manage patients with osteoradionecrosis.<sup>40</sup> This technique seems promising and will reduce the need to perform bone resection. Nevertheless, there is limited evidence about the efficacy and safety of this approach, and therefore, further research is needed. PRP was also effectively introduced to manage alveolar sinus and ridge augmentation, socket preservation, implant surgery, and jaw cysts, indicating the wide acceptance and promising future of this modality in the field of maxillofacial surgery.<sup>4,5</sup>

## CONCLUSION

Evidence indicates the wide acceptance of the modality, which has been proven to increase the rate of wound healing and reduce the frequency of pain and swelling. The PRP administration has been reported to dispense with the need for invasive approaches that might be furtherly associated with complications and different morbidities. However, in most of the favorable events where the administration of PRP was associated with enhanced outcomes, the modality was used in combination with another therapeutic approach. Therefore, further research is needed to validate the efficacy of the modality in the different settings.

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## REFERENCES

- Alves R, Grimalt R. A Review of Platelet-Rich Plasma: History, Biology, Mechanism of Action, and Classification. *Skin Appendage Disorders*. 2018;4(1):18-24.
- Carlson NE, Roach RB, Jr. Platelet-rich plasma: clinical applications in dentistry. *Journal of the American Dental Association* (1939). 2002;133(10):1383-6.
- Kao RT, Murakami S, Beirne OR. The use of biologic mediators and tissue engineering in dentistry. *Periodontology* 2000. 2009;50:127-53.
- Albanese A, Licata ME, Polizzi B, Campisi G. Platelet-rich plasma (PRP) in dental and oral surgery: from the wound healing to bone regeneration. *Immunity & ageing : I & A*. 2013;10(1):23.
- Al-Hamed FS, Mahri M, Al-Waeli H, Torres J, Badran Z, Tamimi F. Regenerative Effect of Platelet Concentrates in Oral and Craniofacial Regeneration. *Frontiers in cardiovascular medicine*. 2019;6:126.
- Sánchez AR, Sheridan PJ, Kupp LI. Is platelet-rich plasma the perfect enhancement factor? A current review. *The International journal of oral & maxillofacial implants*. 2003;18(1):93-103.
- Martínez-Zapata MJ, Martí-Carvajal A, Solà I. Efficacy and safety of the use of autologous plasma rich in platelets for tissue regeneration: a systematic review. *Transfusion*. 2009;49(1):44-56.
- Nikolidakis D, Jansen JA. The biology of platelet-rich plasma and its application in oral surgery: literature review. *Tissue engineering Part B, Reviews*. 2008;14(3):249-58.
- Dugrillon A, Eichler H, Kern S, Klüter H. Autologous concentrated platelet-rich plasma (cPRP) for local application in bone regeneration. *Int J Oral Maxillofac Surg*. 2002;31(6):615-9.
- Landesberg R, Roy M, Glickman RS. Quantification of growth factor levels using a simplified method of platelet-rich plasma gel preparation. *J Oral Maxillofac Surg*. 2000;58(3):297-300.
- Kaushick BT, Jayakumar ND, Padmalatha O, Varghese S. Treatment of human periodontal infrabony defects with hydroxyapatite +  $\beta$  tricalcium phosphate bone graft alone and in combination with platelet rich plasma: a randomized clinical trial. *Indian journal of dental research : official publication of Indian Society for Dental Research*. 2011;22(4):505-10.
- Marx RE. Platelet-rich plasma (PRP): what is PRP and what is not PRP? *Implant dentistry*. 2001;10(4):225-8.
- Marx RE. Platelet-rich plasma: evidence to support its use. *J Oral Maxillofac Surg*. 2004;62(4):489-96.
- Marx R, Genco R, Lynch S. *Tissue engineering: applications in maxillofacial surgery and periodontics*. Edited by Lynch SE, Genco RJ, Marx RE Chicago: Quintessence. 1999:71-82.
- Yang D, Chen J, Jing Z, Jin D. Platelet-derived growth factor (PDGF)-AA: a self-imposed cytokine in the proliferation of human fetal osteoblasts. *Cytokine*. 2000;12(8):1271-4.
- Rose LF, Rosenberg E. Bone grafts and growth and differentiation factors for regenerative therapy: a review. *Practical procedures & aesthetic dentistry : PPAD*. 2001;13(9):725-34.
- Cochran DL, Wozney JM. Biological mediators for periodontal regeneration. *Periodontology* 2000. 1999;19:40-58.
- González-Sánchez JG, Jiménez-Barragán K. Closure of recurrent cleft palate fistulas with plasma rich in growth factors. *Acta otorrinolaringologica española*. 2011;62(6):448-53.
- Panda S, Doraiswamy J, Malaiappan S, Varghese SS, Del Fabbro M. Additive effect of autologous platelet concentrates in treatment of intrabony defects: a systematic review and meta-analysis. *Journal of investigative and clinical dentistry*. 2016;7(1):13-26.
- Moraschini V, Barboza Edos S. Use of Platelet-Rich Fibrin Membrane in the Treatment of Gingival Recession: A Systematic Review and Meta-Analysis. *Journal of periodontology*. 2016;87(3):281-90.
- Prataap N, Sunil PM, Sudeep CB, Ninan VS, Tom A, Arjun MR. Platelet-rich Plasma and Incidence of Alveolar Osteitis in High-risk Patients Undergoing Extractions of Mandibular Molars: A Case-control Study. *Journal of pharmacy & bioallied sciences*. 2017;9(1):S173-9.

22. Meschi N, Castro AB, Vandamme K, Quiryne M, Lambrechts P. The impact of autologous platelet concentrates on endodontic healing: a systematic review. *Platelets*. 2016;27(7):613-33.
23. Metlerska J, Fagogeni I, Nowicka A. Efficacy of Autologous Platelet Concentrates in Regenerative Endodontic Treatment: A Systematic Review of Human Studies. *Journal of endodontics*. 2019;45(1):20-30.e21.
24. Moussa M, El-Dahab OA, El Nahass H. Anterior Maxilla Augmentation Using Palatal Bone Block with Platelet-Rich Fibrin: A Controlled Trial. *The International journal of oral & maxillofacial implants*. 2016;31(3):708-15.
25. Torres J, Tamimi F, Alkhraisat MH. Platelet-rich plasma may prevent titanium-mesh exposure in alveolar ridge augmentation with anorganic bovine bone. *Journal of clinical periodontology*. 2010;37(10):943-51.
26. Ali S, Bakry SA, Abd-Elhakam H. Platelet-Rich Fibrin in Maxillary Sinus Augmentation: A Systematic Review. *The Journal of oral implantology*. 2015;41(6):746-53.
27. Ahmad M, Schiffman EL. Temporomandibular Joint Disorders and Orofacial Pain. *Dental clinics of North America*. 2016;60(1):105-24.
28. Bousnaki M, Bakopoulou A, Koidis P. Platelet-rich plasma for the therapeutic management of temporomandibular joint disorders: a systematic review. *Int J Oral Maxillofac Surg*. 2018;47(2):188-98.
29. El-Anwar MW, Nofal AA, Khalifa M, Quriba AS. Use of autologous platelet-rich plasma in complete cleft palate repair. *The Laryngoscope*. 2016;126(7):1524-8.
30. Gupta C, Mehrotra D, Mohammad S. Alveolar bone graft with Platelet Rich Plasma in cleft alveolus. *Journal of oral biology and craniofacial research*. 2013;3(1):3-8.
31. Marukawa E, Oshina H, Iino G, Morita K, Omura K. Reduction of bone resorption by the application of platelet-rich plasma (PRP) in bone grafting of the alveolar cleft. *J Craniomaxillofac Surg*. 2011;39(4):278-83.
32. Saruhan N, Ertas U. Evaluating of Platelet-Rich Fibrin in the Treatment of Alveolar Cleft With Iliac Bone Graft By Means of Volumetric Analysis. *J Craniofac Surg*. 2018;29(2):322-26.
33. Omidkhoda M, Jahnabin A, Khoshandam F. Efficacy of Platelet-Rich Fibrin Combined with Autogenous Bone Graft in the Quality and Quantity of Maxillary Alveolar Cleft Reconstruction. *Iranian journal of otorhinolaryngology*. 2018;30(101):329-34.
34. Mauceri R, Panzarella V, Maniscalco L. Conservative Surgical Treatment of Bisphosphonate-Related Osteonecrosis of the Jaw with Er,Cr:YSGG Laser and Platelet-Rich Plasma: A Longitudinal Study. *BioMed research international*. 2018;2018:3982540.
35. Park JH, Kim JW, Kim SJ. Does the Addition of Bone Morphogenetic Protein 2 to Platelet-Rich Fibrin Improve Healing After Treatment for Medication-Related Osteonecrosis of the Jaw? *J Oral Maxillofac Surg*. 2017;75(6):1176-84.
36. Lopez-Jornet P, Sanchez Perez A, Amaral Mendes R, Tobias A. Medication-related osteonecrosis of the jaw: Is autologous platelet concentrate application effective for prevention and treatment? A systematic review. *J Craniomaxillofac Surg*. 2016;44(8):1067-72.
37. Bilginaylar K. Comparison of the Clinical Outcomes of Buccal Advancement Flap Versus Platelet-Rich Fibrin Application for the Immediate Closure of Acute Oroantral Communications. *J Craniofac Surg*. 2019;30(1):e45-9.
38. Demetoglu U, Ocak H, Bilge S. Closure of Oroantral Communication With Plasma-Rich Fibrin Membrane. *J Craniofac Surg*. 2018;29(4):e367-70.
39. Scala M, Gipponi M, Mereu P. Regeneration of mandibular osteoradionecrosis defect with platelet rich plasma gel. In vivo (Athens, Greece). 2010;24(6):889-93.
40. Bilimoria R, Young H, Patel D, Kwok J. The role of piezoelectric surgery and platelet-rich fibrin in treatment of ORN and MRONJ: a clinical case series. *Oral Surgery*. 2018;11(2):136-43.

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