REVIEW ARTICLE

Influence of Platelet Concentrates on Postextraction Socket Healing: A Literature Review

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Abstract

Socket healing after extraction of teeth leads to a significant decrease in residual bone in both vertical and horizontal dimensions. This dimensional loss of bone volume poses a challenge when replacing these teeth. Implant placement and grafting procedures include the use of platelet concentrates. Platelets play a role in socket healing. Autologous blood derivatives have a high concentration of platelets. Hence, they have been used to preserve and correct defects due to loss of bone volume after extraction. The use of bioactive materials started with fibrin glue and now includes two generation of platelet products comprising various subtypes. Bioactive materials such as platelet concentrates were first used to prevent and control hemorrhage in surgical procedures. The platelet concentrates are categorized based on their preparation protocols and concentration of leukocytes and platelets. This review article aims to summarize the classification, applications, efficacy, indications, and benefits of platelet concentrates.

Keywords: Extraction, Platelet concentrates, Platelet-rich fibrin, Platelet-rich plasma, Socket preservation.

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Introduction

Tooth extraction is a routine dental procedure for managing fractures, extensive decay, periodontal disease, orthodontic treatment, and so on. Studies have demonstrated a significant dimensional change following tooth extraction. This loss of bone volume occurs in both vertical and horizontal planes and may have substantial clinical implications when attempts are made for restoring the missing teeth.[1] Several procedures have been suggested to prevent this postextraction bone loss, such as early or immediate implant placement and the use of biomaterials for socket preservation. With a plethora of grafts to choose from, the choice of material is critical as each graft varies significantly in its bone forming capacity.[2]

Physiologic healing of a socket wound involves a complex cascade of events. The entire mechanism is unclear. However, studies have demonstrated the vital function that platelets have in maintaining homeostasis and healing of wounds. Growth factors present in platelets are acknowledged in the literature for the presence of healing cytokines. This led to the development of several platelet concentrates and their derivatives for oral and maxillofacial surgery.[3] The present article aims to explore and summarize the historical and current perspective on the use and effects of platelet concentrates in healing of postextraction sockets.

Platelet Concentrates

Platelets are rich in growth factors such as transforming growth factor beta 1 (TGFβ-1), platelet derived growth factor-AA (PDGF-AB), capable of stimulating cell proliferation, angiogenesis, and remodeling. Originally, platelet concentrates were used to prevent and treat hemorrhage in patients undergoing prolonged surgical procedures. Numerous protocols and kits are currently available for the preparation of platelet concentrates. Despite their similarities, these techniques differ in terms of their preparation protocols.[4,5] The platelet concentrates are divided into two generations:

- First-generation: platelet-rich plasma (PRP)
- Second-generation: platelet-rich fibrin (PRF)

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They can be further categorized depending upon their endogenous fibrin content as:

- Pure PRP (P-PRP)
- Pure PRF (P-PRF)
- Leukocyte PRP (L-PRP)

Fibrin Glue

Use of biomaterials derived from blood and its products started with the advent of fibrin glue 40 years ago.[4] The mechanism of action of fibrin glue is similar to the last phase of the coagulation cascade, where the presence of thrombin and factor XIII leads to the conversion of fibrinogen to fibrin. Despite their advantages, the application of fibrin glue remains limited due to the high cost, extensive processing, risk of viral disease transmission, and complexity.[6] Autologous products with high platelet concentrations were developed to overcome the shortcomings of fibrin glues by combining their properties with that of platelets to make a delivery system for growth factors at the site of injury.[3]

Platelet-rich Plasma

In 1997, Whitman et al. Introduced platelet gel in oral surgery as an alternative to fibrin glue.[7] Platelet-rich plasma or PRP is the first generation of platelet concentrates. Platelets are a cell type that initiates wound healing and enhances cell adhesion, migration, and proliferation by active secretion of growth factors and also form a bulk of the constituents of PRP. Platelet-rich plasma found many applications in the field of dentistry.[8,9] In the preparation of PRP, the first step involves separating blood into three layers. Platelet poor plasma (PPP) forms the supernatant, red blood cells (RBCs) sediment at the base, and the platelet concentrates form a middle buffy coat. Pure platelet-rich plasma and L-PRP are both liquid suspensions of platelets that differ in their concentration of leukocytes. In the field of sports medicine, platelet concentrates have been routinely used in the form of injections. L-PRP is defined as a platelet concentrate comprising leukocytes in a fibrin network. To minimize the processing of blood samples and to increase standardization of the products, specific kits and protocols have been devised. These products can be used in a solution, gel, or liquid.[10] However, the use of PRP is limited since it involves the use of bovine thrombin in the preparation procedure, which could potentially trigger an immune response in patients.[11]

Platelet-rich Plasma in Socket Healing

Ogundipe et al. investigated the effects of PRP on healing and bone regeneration and patient-centered outcomes such as pain, swelling, and trismus in mandibular third molars. One group was treated with the application of PRP gel, whereas in the other, PRP was not used. Socket healing was assessed radiographically, and patient-centered outcomes were expressed on a 10-point Visual Analog Scale (VAS).[12] Compared with the control group, PRP logged a significant reduction in postoperative pain, swelling, and trismus and enhanced bone healing.[12] Ahmad et al. investigated the outcomes of the application of medical-grade calcium sulfate hemihydrates (MGCSH) and PRP for the preservation of extraction sockets.[13] When MGCSH was used in adjunct with PRP, it enhanced bone healing and increased vital bone volume at 3 months compared to the use of PRP-free resorbable collagen graft. The effect of PRP on the healing of tissues in patients treated with and without the application of PRP was assessed by Alissa et al.[14] The authors concluded that PRP aids in soft tissue healing and reduces postoperative complications such as alveolar osteitis.

Marx et al., in 1998, treated 88 patients with reconstruction using PRP in addition to autogenous bone.[15] Reports suggested two times faster bone maturation on combing PRP and autogenous bone graft when assessed radiographically and a denser bone on a histomorphometric analysis. A similar study was conducted by Fennis et al. in an animal model, where they reported that the PRP group showed superior healing at 6–12 weeks post-treatment.[16] In contrast, Aghaloo et al., in 2002, reported no significant difference in radiographic bone gain following treatment with autogenous bone graft alone or a combination thereof.[17]

The efficacy of PRP, along with autogenous bone grafting for augmentation of maxillary sinus was reported in literature. Jakse et al.[18] used iliac crest graft and PRP for sinus floor elevation in sheep. Platelet-rich plasma group showed a 3–4% higher percentage of bone gain than the group treated with autogenous bone alone.

Even though the difference was not clinically significant, the authors declared PRP as having low potency in terms of regenerative capacity. Butterfield et al. and reported identical outcomes in PRP's efficacy in sinus augmentation in the rabbit model.[19]

Numerous studies have assessed the efficacy of PRP as an adjunct to anorganic bone such as Bio–Oss. Kim et al. grafted cranial defects in 20 rabbits with Bio-Oss and PRP.[20] Appreciably greater bone density was seen on digitized plain films and computed tomography (CT) scans with the use of PRP at both time intervals. Freymiller et al. compared bone formation in three groups–autogenous bone, Bio-Oss, and Bio-Oss with PRP. A significantly higher percentage of bone formation was seen when PRP was added to Bio-Oss rather than Bio-Oss alone.[11,17] Two immediate implants were placed through the facial sinus wall following bilateral sinus lift on 12 minipigs, using Bio-Oss alone on one side and Bio-Oss mixed with PRP on the other.[21] Osseointegration of the implants was measured at three time intervals, and this was used instead of new bone formation as an outcome measure. There was an increase in the percentage of implant-to-graft contact and the number of contacts between the grafted bone and implant in both the groups. Gruber and Zechner. assessed the amount of vital bone following bilateral sinus lift procedures performed for three patients. Each patient was treated with Bio-Oss in one sinus and Bio-Oss, along with PRP in the other.[21] No difference was observed in the group treated with PRP as an adjunct compared with Bio-Oss alone.

PRP combined with organic bone matrix has shown mixed outcomes. Freymiller et al. used freeze-dried bone allograft (FDBA) for performing alveolar ridge augmentation on three patients. A barrier membrane was placed in order to protect the graft, which was placed by mixing PRP at the time of surgery. The authors observed no significant improvement in the quality of new bone formation following the use of PRP as an adjunct as compared to GBR alone.[11] The varying concentration of platelets in the animal models used in the study compared to human subjects and the differences in techniques used to obtain the platelets could be associated with such inconsistent data in the literature. The concentration of platelets in humans compared to animals, and variation in techniques used to sequester the platelets and prepare the PRP. Differences in isolation and preparation could influence platelet degranulation. Additionally, using bovine thrombin for the PRP preparation poses a significant threat of disease transmission and can potentially elicit an immune response. The application of PRP has been further limited by the technique sensitive production protocols and the risks associated with crossinfection.[22]

Platelet-rich Fibrin

Choukroun et al. pioneered the development of PRF, that is, the second-generation platelet derivatives, for its application in oral and maxillofacial surgery.[4,23,24] Platelet-rich fibrin is prepared with centrifuged blood without any addition of anticoagulants or bovine origin thrombin. 10-mL tubes without anticoagulants are used to collect the blood samples. The tubes are then placed in a centrifuge for 10 minutes at 3,000 rpm instantaneously. Coagulation of blood samples occurs as soon as it touches the glass tube in the absence of an anticoagulant. After a few minutes of centrifugation, fibrinogen is concentrated in the middle and top layers of the tube. Hence, the speed at which the blood is collected and centrifuged determines the success of this technique. A delay in centrifuging after blood collection may lead to failure, implying that the PRF obtained is clinically unusable. During centrifugation, PRF polymerizes slowly and naturally. Since bovine thrombin is not added, the concentrations acting on the autologous fibrinogen collected are within the physiologic range.[22]

The difference between P-PRF and L-PRF is that the latter shows the presence of leukocytes, whereas the former does not. During centrifugation, platelets are activated, which results in a robust meshwork of fibrin, which could be either natural (L-PRF) or artificial (P-PRF). Pure-PRF shows a low density of leukocytes, whereas L-PRF is densely packed with leukocytes.[23,25-27] Tunali et al. modified Choukrans PRF and introduced a novel method using titanium tubes in place of the traditional glass tubes and termed it T-PRF.[28]

After PRF processing, two distinct parts were obtained: the supernatant consisting of platelet-poor plasma and an exudate that results from the entrapment of solutions in a meshwork of fibrin. Neither the supernatant nor the bottom layer rich in RBCs showed the presence of platelets. The platelets are present mainly at the junction of the RBCs and the fibrin clot on the bottom segment.[4,29]

On biochemical analysis, PRF consisted of structural glycoproteins and cytokines inside a network of fibrin. The synergetic effects of these components on the process of healing are well documented[7,23] Ehrenfest et al. demonstrated that significant amounts of growth factor (TGFβ1, platelet derived growth factor-AT [PDGF-AT], vascular endothelial growth factor [VEGF]) and thrombospondin-1 (TSP-1) are released slowly from an L-PRF membrane for a minimum of seven days.[30]

Platelet-rich Fibrin in Socket Healing

Several studies have demonstrated that PRF effectively enhances both hard and soft tissue healing in extraction sites.[31-34] Temmerman et al. investigated the efficacy of L-PRF in ridge preservation by using it as a socket filling material in the test site.[35] They reported significant differences for socket fill between both the groups. A systematic review conducted by Del Fabbro et al. investigated autologous platelet concentrates (APCs) and their efficacy in preserving fresh extraction sockets. APCs showed a reduced amount of pain, swelling, and trismus.[36] Probing pocket depth, acute infections, percentage of new bone formation, and alveolar osteitis incidence showed no disparity among the groups at the end of 1 month. The authors concluded that APCs could improve radiographic as well as clinical outcomes such as postoperative complications, soft tissue healing, and bone density. Marenzi et al. assessed the effect of L-PRF on the soft tissue healing and pain following tooth extractions.[37] Results showed faster socket closure and enhanced healing on the side treated with L-PRF. Similar outcomes were reported by various authors.[31,38-44] Mozzati et al. evaluated the effect of concentrated growth factors (CGFs) compared to L-PRF to enhance postextraction socket healing.[26] No significant difference in outcomes was found, except for pain at day 1 and socket closure at day 7 postextraction.

Medikeri et al. investigated the effect of DFDBA combined with PRF in immediate implant placement and survival.[45] Authors reported that the adjunctive use of DFDBA with PRF at periapically infected sites revealed accelerated bone healing and reduced bone resorption postextraction. A case report by Zhao et al. demonstrated that PRF application on fresh extraction sockets does not clinically impact the healing[46], although, at 3 months, PRF positively influenced socket healing and decreased alveolar ridge resorption. Choukroun et al., in their fourth part of a four-article series, evaluated the biology of PRF for its application suggesting that PRF could be considered a biomaterial that can positively influence.[4,23,24,29] PRF is a tetra-molecular structure that incorporates leukocytes, platelets, and cytokines in a polymerized fibrin network. These features are all necessary parameters for optimal healing. Baslarli et al. evaluated osteoblastic activity in PRF-treated extraction sites.[47] They reported no significant difference between bone healing in areas treated with PRF and without PRF at 30 and 90 days postoperatively. Results suggested no enhancement of bone healing with PRF might result in extraction sockets of impacted mandibular third molars.

Advantages of PRF over PRP

The ease of preparation and application of PRF distinguishes it from its precursors. Preparation of PRF does not require any extrinsic anticoagulants or bovine thrombin for direct activation, significantly reducing the time and cost of preparation. Platelet-rich fibrin retains many growth factors and cytokines in a supportive three-dimensional fibrin scaffold for cell migration owing to its fibrous structure. In tissues, PRF forms a fibrin matrix that is remodeled into a natural blood clot.[22,25] Platelet-rich fibrin is limited in its systematic usage for general surgery because it is produced in low quantities.[3]

Conclusion

Bone loss following tooth extraction is a common occurrence. Platelet concentrates are routinely used for socket preservation. There is inconclusive proof to corroborate their positive influence over grafting alone. Hence, rationalization of their extensive application is crucial. Additionally, randomized controlled clinical trials should be conducted to estimate clinical outcomes and long-term benefits linked to the use of these platelet concentrates.

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