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APPLICATIONS OF PLATELET RICH FIBRIN IN ORAL AND MAXILLOFACIAL SURGERY

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Abstract:

Maxillofacial reconstructions, oral implants, esthetic facial procedures, regenerative procedures, etc. are highly dependent on successful regeneration of tissues. Healing of both hard and soft tissues has become one of the greatest challenges faced in clinical research in the development of bioactive surgical additives responsible for regulating inflammation and increasing healing. Understanding the process og healing at microcellular level is still not complete, but it is a proven fact that platelets do play an important role in wound healing. The potential benefit of biologic therapy has evolved with the addition of growth factors and reparative cells being the trailblazers which not only augment the normal body healing process but also restore normal form and function. Platelet-rich fibrin (PRF) represents a new step in the platelet gel therapeutic concept with simplified processing minus artificial biochemical modification. The purpose of this paper is to shed light on its clinical application in various oral surgical procedures.

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INTRODUCTION:

It was first described by Choukroun [1] in 2000, and since then PRF has become an important surgical adjuvant in oral surgical procedures. PRF is a second-generation platelet concentrate [2] produced without biochemical blood manipulation, and is constituted of three key parameters: first, the presence of platelets and their activated growth factors that are substantially embedded into the fibrin matrix during the natural polymerization process [3]; second, the presence of leucocytes and their cytokines that contribute to anti-infectious action and immune regulation in the healing process [4] ; third, the density and complex organization of the fibrin matrix architecture produced by a natural polymerization, without the addition of any anticoagulant or gelling agent. [5] The strong fibrin architecture distinguishes it from other kinds of platelets concentrates, like platelet-rich plasma (PRP). This fibrin matrix seems responsible for the slow release of growth factors during the proliferation stage of wound healing, over a period of 7–14 days, and it is composed of thin fibres with micropores that can serve as a scaffold for cell migration and differentiation. PRF is an important reservoir of numerous growth factors to promote angiogenesis, such as transforming growth factor β (TGF-β) and vascular endothelial growth factor (VEGF). There are still large amounts of platelet-derived growth factors (PDGFs) in platelet α-granules, which act as an essential regulator for collagen production and mesenchymal cell migration and proliferation. [3,5]

Tissue adhesives (fibrin glues) were the precursors of platelet concentrates. Afterward, different types of platelet concentrates were developed. Based on the leukocyte content and fibrin structure, platelet concentrates can be classified into four main categories. [6]

1. Pure platelet-rich plasma (P-PRP) without leukocytes and with a low-density fibrin network after activation.
2. Leukocyte- and platelet-rich plasma (L-PRP) with leukocytes and with a low-density fibrin network after activation
3. Pure platelet-rich fibrin (P-PRF) without leukocytes and with a high-density fibrin network
4. Leukocyte- and platelet-rich fibrin (L-PRF) with leukocytes and a high-density fibrin network

The Second Generation of Platelet Concentrates: Platelet-Rich Fibrin

PRF can be seen as an autologous biomaterial made of a fibrin matrix that contains the following

- The highest concentration of platelets
- The highest concentration of growth factors, including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor (TGF)
- A representative concentration of fibrin, fibronectin, vitronectin, and thrombospondin
- An approximately 65% concentration of leukocytes

Nowadays, PRF can be regarded as the least expensive and most streamlined way to produce platelet concentrate. PRF is classified according to its leukocyte content as either L-PRF or P-PRF. L-PRF contains up to 90% of the platelets and at least 75% of the leukocytes present in the patient's blood.

PRF PROTOCOL:

After veinpuncture, 20-60 ml of blood are taken and put in several 9 ml test tubes without anticoagulants, and it immediately goes through the centrifugation process at 2700 rotations per minute, for 14 minutes.

Preparation of L-PRF

Blood samples (9–10 mL) are collected in sterile glass or plastic-coated tubes. The tubes are placed in pairs and centrifuged at 400 *g* relative centrifugal force (RCF) for 14 min; 400 *g* RCF is equivalent to 2700 rpm. It is very important that the collection of blood and placement of the tubes in the centrifuge happen as rapidly as possible, before the spontaneous coagulation process occurs. Ideally, the tubes should be centrifuging within 60 seconds after the start of the venipuncture. This often requires loading the centrifuge with tubes two by two or one by one. In the latter case, a tube filled with the same amount of glycerine or saline should be considered to balance the centrifugation.

There is no manipulation of the blood; no anticoagulants are used in the tubes, and hence there is no need for animal thrombin and calcium chloride for fibrin polymerization. Plastic tubes are coated with silica and silicon to activate the coagulation. The absence of anticoagulants allows the activation of platelets in contact with the inner walls of the tube. After a few minutes, a coagulation cascade is initiated. Initially, the fibrinogen is positioned in the upper part of the tube. However, after centrifugation, due to the activation of autologous thrombin, it is converted to fibrin and a fibrin clot is created. After

centrifugation, three distinct layers can be seen in the tube: red blood cells (RBCs) at the bottom of the tube, platelet-poor plasma (PPP) at the top of the tube, and the fibrin clot (containing most leukocytes and platelets) in the middle of the tube.

The L-PRF clot can be removed from the tube with surgical tweezers. With an instrument similar to a spatula, the RBC fraction can be gently separated from the fibrin clot. The clot by itself contains a great amount of exudate, which is rich in growth factors. This exudate can be expressed by gentle compression of the clot (about 5 min) in order to obtain stronger L-PRF membranes. For this compression, one can utilize a specially engineered box. The box contains a weighted press plate that is designed to express serum from the L-PRF clot in a controlled manner. It forms standard 1-mm-thick L-PRF membranes. The membranes remain stable at room temperature for several hours. [7,8]

General Characteristics of L-PRF Membranes

Platelets in L-PRF

After centrifugation, at least 90% of the platelets derived from the blood sample are present in the fibrin clot. The platelets are mainly present in the lower portion of the clot, at the border between the RBCs and the clot itself and is most biologically active. The platelet cytoplasm contains many cytokines and many active substances such as serotonin, von Willebrand factor, factor V, osteonectin, and antimicrobial proteins. The principal role of the platelets is the maintenance of homeostasis; however, they are capable of binding, aggregating, and internalizing microorganisms, which enhances the clearance of pathogens from the bloodstream.

Leukocytes in L-PRF

More than 75% of the leukocytes remain within the L-PRF membrane whereas the concentration in the L-PRF exudate is very low. The latter, however, contains a high concentration of growth factors.

Growth Factors in L-PRF

Platelets have an important function in the release of growth factors. The alpha-granules in platelets contain PDGF, insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), VEGF, and TGF-β, which initiate wound healing by attracting and activating macrophages, fibroblasts, and endothelial cells. Their release occurs specifically in the first hours, and they are completely dissolved in the medium after 3 days due to the chemical activation of the platelet content.

Fibrin in L-PRF

Fibrin is an insoluble clotting protein that plays a major role in platelet aggregation during hemostasis and wound healing. Fibrinogen, the precursor of fibrin, is converted by thrombin into fibrin, which forms long, nonsoluble strands that bind to platelets. Present in physiologic concentrations, thrombin allows the formation of a fibrin matrix in a slow and physiologic manner. The fibrin wires tend to polymerize and form a biochemical structure with trimolecular or equilateral junctions, providing a fine and flexible fibrin network that favors the entrapment of cytokines and cell migration.[8]

APPLICATIONS:

1. In osseous regeneration after cystic enucleation:
Four critical factors that influence bone regeneration after the periapical surgery are primary wound closure, angiogenesis as a blood supply and source of undifferentiated mesenchymal cells, space maintenance, and stability of the wound (PASS principle). Osteoinductive growth factors that are involved in bone formation are transforming growth factor-β (TGF-β), BMPs, insulin like growth factors and fibroblasts growth factors. The vasculature is formed by two mechanisms: Vasculogenesis and angiogenesis. During wound healing and repair of ischemic tissues, the endothelial cells and their precursors actively participate in the healing process. The major angiogenic factors includes fibroblasts growth factors, platelet-derived growth factors (PDGFs), and vascular endothelial growth factors (VEGF). [9]

Surgeons have long sought of a product that could act both as a tissue regenerator as well as a hemostatic agent and PRF satisfactory fulfills this purpose. The scientific reason behind use of PRF lies in the fact that its abundance in growth factors plays a crucial role in hard and soft tissue repair mechanisms. Use of autologous PRF as an adjunct to promote healing and osseous regeneration in mandibular 3 rd molar extraction site have shown promising results.The improvement in wound healing, decrease in pain, and increase in bone density signifies and highlights the use of PRF as a valid method in promoting and accelerating soft and hard tissue regeneration. PRF is efficacious clinically and radiologically in treatment of intrabony defects after enucleation of various periapical lesions, where complete bone regeneration is seen within 6 th months postoperatively. The use of PRF in intraoral bony defects after cystic

enucleation promotes faster regeneration because of gradual release of growth factors lodged in the fibrin matrix. [10]

2. Alveolar ridge preservation following tooth extraction:

The healing of an extraction socket is characterised by both internal and external changes that ultimately affect the shape of the alveolar ridge. Alveolar ridge preservation is a relatively new surgical procedure aimed at retaining maximum bone and soft tissue after a tooth has been removed. By maintaining the original ridge morphology, there will be a minimal need for augmentation procedures thereby allowing the resultant restoration to be placed in an aesthetically and functionally ideal position for further dental implant placement. [11] The biomaterial acts by releasing high-concentration growth factors to the wound site, thereby stimulating healing, increase the rate of bone deposition and improve the quality of regenerated bone. Use of L-PRF is a simple method that requires minimal cost and reduces the need for specialised grafting material. Because it is a completely autologous product, the risk of disease transmission and graft rejection is negated.

PRF increases the concentration of PDGF and expresses a strong chemotactic effect on osteoblasts and other connective tissue cells. In addition, it has a capacity for mobilizing mesenchymal cells during bone formation and remodelling. PDGF can directly and indirectly affect bone resorption by up-regulating collagen transcription and increasing interleukin 6 expression in osteoblasts. [12]

3. Sinus Augmentation after maxillary sinus floor lift:

Maxillary sinus augmentation is used to gain adequate bone volume for the placement of dental implants in edentulous posterior maxilla. Schneiderian membrane perforation is one of the most common complications associated with maxillary sinus augmentation procedures.

Choukroun's PRF preparation creates a fibrin network very similar to the natural one with incorporation of the platelets in the fibrin meshes.This nature of PRF makes it easy to place into tight maxillary sinuses, and the self-adherent property eliminates the need for suturing. In addition, PRF can stimulate proliferation of osteoblasts, gingival fibroblasts, and periodontal ligament cells but suppress oral epithelial cell growth. [10] The cell type-specific actions of PRF may be beneficial for tissue regeneration. PRF may be a viable consideration for the repair of perforated Schneiderian membrane.

Sinus augmentation with simultaneous implant placement without bone graft material is a highly debated technique. In this technique, implants are used as tent pegs to define the required bone volume from the blood clot. The use of PRF may improve this technique. From radiologic and histologic results at 6 months after surgery, the use of PRF as sole filling material applied in simultaneous sinus lift and implantation demonstrated a new bone formation in the augmented areas. PRF seems an adequate adjuvant to secure this technique for new bone regeneration. [13]

4. As a filler injection:

Need for tissue harvesting, access incisions, postoperative recovery, and often unpredictable graft survival and longevity have encouraged physicians to consider other available minimally invasive techniques and materials. Autologous tissue would be the ideal material choice for soft-tissue augmentation in the face if it could be provided in a simple process with good predictability. Early attempts to use the patient's own collagen to promote soft-tissue augmentation showed limited persistence. Injection of cultured autologous fibroblasts was expensive and time consuming and provided equivocal results. Dermal stimulation with exogenous microparticles (eg, poly-L-lactic acid) has been shown to effectively thicken the dermis. However, the results require multiple treatments, and care must be taken to avoid nodularity and granulomas. [10]

PRF activates the body's natural mechanisms for wound repair and collagen production for use in soft-tissue augmentation. It produces sustained tissue effects as it closely mimics the body's natural wound-healing response. As opposed to PRP, it does not rely on extremely high concentrations of platelets and a massive, 1-time release of growth factors but rather on providing a more natural, sustained wound response. According to the preliminary results from an ongoing histologic study of skin treated with PRF, new collagen has been identified as early as 7 days after treatment, and maturing collagen fibers are still evident at 10 weeks. Platelet-rich fibrin matrix can be used to correct fine rhytids and deeper folds as well as for facial volumization. It can also be combined with subcision to improve the appearance of rolling acne scars. [14]

5. Miscellaneous:

a. For the treatment of non-healing ulcers.
b. For the treatment of MRONJ (Medication-

related osteoradionecrosis of the jaw)

c. Periodontal regeneration in deep intrabony periodontal defect. [10]

CONCLUSION:

In summary, PRF is found to perform better wound healing when it is used in oral surgical procedures. PRF has certainly gained tremendous attention in recent years due to its capacity to successfully regenerate either soft or hard tissues, enhancing new blood vessels (angiogenesis), and tissue formation during healing. Some advantages of PRF over PRP are the lack of blood anti-coagulants, which results in a strong fibrin matrix, and considerable growth factor that may be released over a 10- to 14-day period. The theory is that the combination of host cells, strong fibrin matrix, and growth factors, acts to result in faster wound healing. PRF has many advantages over PRP. It eliminates the redundant process of adding anticoagulant as well as the need to neutralize it. The addition of bovine-derived thrombin to promote conversion of fibrinogen to fibrin in PRP is also eliminated. The elimination of these steps considerably reduces biochemical handling of blood as well as risks associated with the use of bovine-derived thrombin. The conversion of fibrinogen into fibrin takes place slowly with small quantities of physiologically available thrombin present in the blood sample itself. Thus, a physiologic architecture that is very favorable to the healing process is obtained due to this slow polymerization process. The popularity of this material should increase considering its many advantages.

REFERENCES:

1. Choukroun J, Adda F, Schoeffler C, Vervelle A. Une opportunite´ en paro-implantologie: le PRF. Implantodontie 2000;42:55–62.
2. Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (PPRP) to leucocyte- and platelet-rich fibrin (L-PRF). Trends Biotechnol 2009;27 (3):158–67.
3. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, Gogly B. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part II: platelet-related biologic features. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101(3):e45–50.
4. Pirraco RP, Reis RL, Marques AP. Effect of monocytes/macrophages on the early osteogenic differentiation of hBMSCs. J Tissue Eng Regen Med 2013;7(5):392–400.
5. Dohan Ehrenfest DM, Del Corso M, Diss A, Mouhyi J, Charrier JB. Three-dimensional architecture and cell composition of a Choukroun's platelet-rich fibrin clot and membrane. J Periodontol 2010;81(4):546– 55
6. Ehrenfest DM, Andia I, Zumstein MA, Zhang CQ, Pinto NR, Bielecki T. Classification of platelet concentrates (Platelet-Rich Plasma-PRP, Platelet-Rich Fibrin-PRF) for topical and infiltrative use in orthopedic and sports medicine: current consensus, clinical implications and perspectives. Muscles, ligaments and tendons journal. 2014 Jan;4(1):3.
7. Sclafani AP. Safety, efficacy, and utility of platelet-rich fibrin matrix in facial plastic surgery. Archives of facial plastic surgery. 2011 Jul 18;13(4):247-51.
8. Raja VS, Naidu EM. Platelet-rich fibrin: evolution of a second-generation platelet concentrate. Indian Journal of Dental Research. 2008 Jan 1;19(1):42.
9. Meshram VS, Lambade PN, Meshram PV, Kadu A, Tiwari MS. The autologous platelet rich fibrin: A novel approach in osseous regeneration after cystic enucleation: A pilot study. Indian Journal of Dental Research. 2015 Nov 1;26(6):560.
10. Canellas J, Medeiros PJ, Figueredo C, Fischer RG, Ritto FG. Platelet-rich fibrin in oral surgical procedures: a systematic review and meta-analysis. International journal of oral and maxillofacial surgery. 2018 Jul 30.
11. Temmerman A, Vandessel J, Castro A, Jacobs R, Teughels W, Pinto N, Quirynen M. The use of leucocyte and platelet-rich fibrin in socket management and ridge preservation: a split-mouth, randomized, controlled clinical trial. J Clin Periodontol 2016;43(11):990–9.
12. Thakkar DJ, Deshpande NC, Dave DH, Narayankar SD. A comparative evaluation of extraction socket preservation with demineralized freeze-dried bone allograft alone and along with platelet-rich fibrin: a clinical and radiographic study. Contemp Clin Dent 2016;7(3):371–6.
13. Gurler G, DelilbaSi C. Effects of leukocyte platelet rich fibrin on postoperative complications of direct sinus lifting. Minerva Stomatol 2016;65(4):207–12.
14. Sclafani AP. Platelet-rich fibrin matrix for improvement of deep nasolabial folds. Journal of cosmetic dermatology. 2010 Mar;9(1):66-71.