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Platelet Rich Fibrin Application in Maxillo Facial Surgery: Literature Review

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ABSTRACT

Platelet rich fibrin is being tried in different fields of medicine and dentistry. Its clinical application and use has recently been increased. Its novel applications in clinical dentistry isbeing reported widely in the literature. This literature review discusses in detail the biology, preparation and applications of platelet rich fibrin in various fields of oral and maxillofacial surgery.

Keywords: Fibrin, graft, growth factors, platelet richfibrin, wound healing

Introduction:

The success of oral and maxillofacial surgery depends not only in diagnosis, and skill of the surgeon, but also depends on proper wound healing, tissue regeneration and repair. Though there are various soft and hard tissue repair and regenerative materials available, autologous bone grafts and blood products are the gold standard biomaterials. Tissue healing is carried out by various intra and extra cellular events for restoring the integrity of injured tissues guided by protein signals. During the process of wound healing, initially blood clot formation occurs, platelets are released, which in turn promotes the release of growth factors like platelet derived

growth factor (PDGF), vascular endothelial growth factor (VEGF), transforming growth factor-β1 (TGF-β1), transforming growth factor- β2(TGF-β2), insulin like growth factor (IGF) and bone morphogenic protein.

In recent years the application of platelet concentrates namely platelet rich plasma (PRP) and platelet rich fibrin (PRF) have flourished . Whitman et al [1]in 1997 was the first person to introduce the platelet rich plasma (PRP) in oral surgical procedures since it increased the osteoprogenitor cells in the recipient bone. But the use of PRP is restricted due to additives used like bovine thrombin. This has been found to be carcinogenic and causes potential coagulative disorders. Later PRF was introduced by Choukroun et al[2]in2001. It is very popular for its ease of preparation, lack of chemical additives and remarkable handling properties. Basically platelet rich fibrin isbroadly classified into six major types, namely L-PRF, I-PRF, T-PRF , P-PRF , A-PRF and S-PRF.

Background:

In platelets various growth factors such as chemokines, coagulation factors, cytokinesand adhesion molecules are present in abundant numbers. Cytokines play a vital role in the biology of this biomaterial in which the fibrin matrix forms the skeletal framework[3]. The 3D architecture of the fibrin matrix provides the PRF membrane with great flexibility , density , elasticity , and strength which are excellently suited for manipulation , handling , suturing.

Few eminently distinct characteristics of healing such as angiogenesis, immune control, harnessing the circulating stem cells and wound protection by epithelial cover are considered to comprehend the biologic effect of fibrin matrix which serves in healing andmaturation of soft tissues[4]. The entire process of angiogenesis is supported by the three dimensional structure of the fibrin gel of PRF in the presence of cytokines entrapped in the fibrin meshes.

Incorporating PRF membrane along with graft material instigates the rapid wound healing process since PRF acts as a biological bridge connecting the various constituents of the graft promoting angiogenesis, stem cell capture and osteoprogenitor cell migration to the graft site.

Dohan Ehrenfest et al. [5] classified the generic PRP into pure PRP, leukocyte-PRP, pure platelet-rich Fibrin (P-PRF) and leukocyte-PRF (L-PRF).

Platelet Rich Fibrin Preparation

PRF preparation protocol is simple and similar to that of PRP preparation. It includes collection of whole venous blood from patient's median cubital vein of approximately 5ml each in sterile vacutainer tubes (6ml) without any additives like anticoagulants or bovine thrombin. Even though there are different types of centrifuges available throughout the world. Intra-Spin centrifuge and Intra-Lock centrifuge are commercially approved by CE and FDA. The other three types of commercially approved centrifuges are A-PRF 12 (Advanced PRF, Process), LW-UPD8 (LW Scientific) and Salvin 1310 (Salvin Dental).In India some of the common types of laboratory

centrifuges used are (DUOS®, Remi 8C® and Remi C854®)[6].In these centrifuges vacutainer tubes are used for the preparation of different forms of platelet concentrates. These vacutainer tubes are balanced and placed in centrifugal machine at 3000rpm for 10 minutes. Due to the difference in weight and gravity three layers formation are formedvizUpper straw colored

a-cellular plasma , Middle layer of fibrin clot and lower layer containing red blood cells. Upper straw colored layer is removed. The fibrin clot or the middle layer thus collected 2mm below to the lower dividing line is called the platelet rich fibrin [7].

Mechanism:

The venous blood is collected in the vacutainer tubes. After collection of the venous blood centrifugation process starts. The fibrinogen concentrated in the upper part of the tube mixes with the circulating thrombin due to the centrifugation process to form fibrin . Then the fibrin clot is formed in the middle layer between the red corpuscles at the bottom and a-cellular plasma at the top. Thus, the middle layer is rich in platelets trapped massively in fibrin meshes [8].

During centrifugation artificial haemostatic and inflammatory phenomenon occurs, which causes the release of cytokines. There are various cytokines released during this process of centrifugation of which four different cytokines are of prime importance in the inflammatory phenomenon. They are Three pro-inflammatory cytokines (IL-1β, IL-6e TNFα), and one anti-inflammatory cytokine (IL-4). Activated platelets discharge a wide range of growth factors and proteins like Platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF), transforming growth factor-β1 (TGF-β1), transforming growth factor-β2(TGF-β2), insulin-like growth factor(IGF) and bone morphogenic protein (BMP). Transforming growth factors β1 and β2 play a vital role in new bone matrix formation and bone healing [9]. Undifferentiated mesenchymal cells are attracted towards the injured site and they facilitate chemotaxis, angiogenesis and cell proliferation. The synthesis and degradation of extracellular matrix proteins are controlled by these factors.

PRF has the capability of serving as a guide to three main factors of healing such as angiogenesis, immunity and epithelial cover. The 3D structure of the fibrin gel meshwork with the action of entrapped cytokines constitute the fibrin matrix responsible for the property of angiogenesis. The fibrin gel encases various major angiogenesis factors such as b-FGF, VEGF and PDGF [10]. The edifice and rigid consistency of the fibrin matrix plays a key role in supporting the endothelial cells for the capillary production as a consequence of stimulation of growth factors; such as VEGF and basic fibroblast growth factor (b-FGF). The neutrophil migration and the membrane's expression of complement receptors (CD11c/CD18) exacerbation are provoked by fibrin and fibrin degradation factors[11].

CD11c/CD18 receptors function in phagocytosis, cell migration and cytokine production by monocytes/macrophages as well as induction of T-cell proliferation by Langerhans cells [12]. This increased CD11c/CD18 receptors allows the binding of neutrophils to the endothelium and fibrinogen. Also, the fibrinogen degradation products (FDP) regulate the neutrophil engulfment and enzymatic degradation therefore fibrin too comes into play in immunity control. PRF is able to regulate inflammation and to stimulate the immune process of chemotaxis [13].

Since PRF possess all these robust consequences of repair and regeneration[14]; it is proved to be beneficial in the oral and maxillofacial surgeries and also proves to be surpassing the collagen in the multiplication of periosteal cells in human beings and aids in quick wound healing sans pain, desiccation and purulent discharges.

Handling:

Success of this technique purely depends on the time gap between the autologous blood sample collection and its transfer to the centrifuge through the vacutainer tubes in negligible time gap. Since the vacutainer tubes are devoid of anticoagulants, the PRF layer starts to coagulate almost immediately upon contact with the glass. Strictly following the protocol is the key to obtain a good PRF clot charged with serum and platelets[15].Thick autologous PRF membranes may be obtained by driving out the fluids trapped in fibrin matrix.

Role of Platelet Rich Fibrin in Oral andMaxillofacial Surgery:

It was in 1990s that theoral maxillofacial surgery community's attention was drawn by a chain of scientific papers which claimed that PRF could be used for achieving both bone grafting and hemostasis. Later they found that the use of additives like bovine thrombin may produce antibodies to the factor-V, factor-XIand also may cause fatal coagulopathies.PRFcan be used in various other surgical procedures like alveolar ridge height preservation in multiple extractions, reduction of probing depth in case of periodontal bone defects, as a potential framework in pulp revascularization[16,17].PRFis the good graft material of choice because of its adequate quantity, quality and availability[18].

Impaction:

Third molar removal is one of the most common procedures performed in the field of oral and maxillofacial surgery.The success of oral and maxillofacial surgery not only depends on the diagnosis, investigations, skill of the surgeon or techniques used, but also rely on the proper wound healing, tissue regeneration and repair

Surgical removal of mandibular third molars is usually accompanied by pain, swelling, trismus and delayed healing of the sockets which may affect the patients quality of life. Meticulous

surgical technique and scrupulous pre-operative care can reduce the risk of complications and limit their severity. Various medical and\or surgical modifications have been used to improve patients quality of life. Platelet Rich Fibrin (PRF) is an autologous soluble biologic material devoid of foreign material which is best suited for the surgical site. PRF which comprises of platelet, cytokines, leucocytes and circulating stem cells that are entangled by a complex fibrin matrix. These unique components in PRF makes it a good healing biomaterial that permits optimal healing [19].The slow release of cytokines –transforming growth factor from alpha granules, vascular endothelial growth factor, epidermal growth factor and platelet derived growth factor are the key factors which play an important role in neoangiogenesis, tissue healing makes this particular material very uniqueL-PRF is used postoperatively in these cases in order to reduce pain, facial swelling and soft tissue healing.

Sinus Augmentation by PRF:

In posterior maxilla prosthetic rehabilitation depends the quality and quantity of residual alveolar bone relies on bone resorption following extraction, presence of enlarged maxillary sinus and normal age changes of the maxilla. Tatum et al in 1980's introduced sinus lift procedure which was about creating a space between the maxillary alveolar process and the elevated schneiderian membrane, which is filled with graft materials to maintain the space. PRF's strength comes from promoting the vascularization of bone tissue, improving scaffold mechanics, reducing tissue inflammation and accelerating new bone formation[20].Histological examination of the grafted site was done 24 months after the surgery which revealed distinctly mature bone tissue and newly formed lamellar bone surrounding the woven bone[21].Simonpieri et al and Diss et al also showed the use of PRF as the only graft material which demonstrated the formation of substantial new bone. Mazor et al in his study found that 6 months after sinus augmentation surgery histologically high volume of natural bone with osteoblasts and osteocytes were present in the newly formed tissue.

Implants:

PRF is used in immediate implant placement to accelerate the healing of both soft and hard tissues. One of the major complication after implant placement is marginal bone loss which is inevitable. Various biomaterials and growth factors have been substituted traditionally. Diverse researches in the recent era clearly indicates that L-PRF(Leucocytes-Platelet Rich Fibrin) significantly enhances wound healing in both hard and soft tissues. PRF consists of an autogenous Leucocyte Platelet Rich Fibrin matrix composed of a tetramolecular structure with platelets, cytokines and stem cells which acts as a bio-degradable scaffold and favours micro vascularization through neoangiogenesis. L-PRF is unique in its nature because of the slow and gradual release of growth factor from one week to four weeks[22].The natural fibrin mesh framework allows growth factors to be active for a relatively longer period and promotes tissue

regeneration factor. With the use of L-PRF, satisfactory preservation of marginal bone structures has been achieved.

Oroantral Fistula:

Oroantral communication may form immediately after extraction that may get epithelized .Monolayer technique of closure was developed in 1939 by Wassmund and was modified in 1948 by Borusiewicz. Recently bilayer method of closure using buccal fat pad with vascular pedicle is the treatment of choice. The residual alveolar ridge formation is very much minimal by using the above techniques. To overcome this problem single stage alveolar augmentation with autogenous bone graft and PRF has been used.PRF as a graft material is beneficial for increasing bone mineral density, shortening healing time and no donor site morbidity[23].

Mandibular Reconstruction:

Platelet Rich Fibrin in oral and maxillofacial surgery improves bone healing in Mandibular Reconstruction. Autologous platelet rich fibrin is considered to be a healing biomaterial. The use of platelet rich fibrin recently shows good promising results. One of the greatest challenge of clinical research was development of bioactive surgical additives which has been used to regulate inflammation and increase the speed of the healing process. Platelet Rich Fibrin (PRF) regulates the healing process of both soft and hard tissues. It is known that platelet play a critical role not only in hemostasis, but also in wound healing process [24].

Surgical Repair of Alveolar Clefts:

Reconstruction of alveolar ridge in patients with cleft lip and cleft palate is a challenging procedure. The treatment algorithm includes stabilization of the dental arch and orthodontic tooth movement in the area of cleft. Platelet rich fibrin acts as an autogenous membrane and stimulates healing of both hard and soft tissues. by acting as a physical barrier[25]. Commonly alveolar bone grafts are used to close the defects. In some cases the failure of bone grafts occurs due to contamination of graft after exposure to the nasal cavity. So here PRF membrane protects the grafted area and allows new bone formation.

Advantages of Platelet Rich Fibrin:

1. Cost effective and simplified process.
2. Gradual and natural polymerization leads to favorable feeling.
3. Additives are not required - bovine thrombin and anticoagulants
4. Autologous chances of graft infection or rejection are not there.
5. Can be used in different forms like gel, membrane and sheet.

6. Can be sandwiched between donor and recipient bone.
7. Minimized blood manipulation.
8. It can be used solely or in combination with bone grafts, depending on the purpose.

Disadvantages of Platelet Rich Fibrin:

1. Tincture of time is crucial.
2. Requirement of vacutainer tubes to achieve clot formation.
3. Possible refusal for vein puncture.
4. The final quantity available is low because it is autologous blood.

Other Clinical Application:

1. Probing depth reduction in periodontal bone defects.
2. Reduction in localized osteitis in extraction sockets.
3. In free gingival graft as an adjunct to palatal wound healing.
4. To preserve alveolar residual ridge height.
5. After ablative surgeries in reconstruction of large bone defects.

Discussion:

Dohan et al in 2005 compared the growth factors available in PRF and PRP and found that PRF has increased tissue vascularity, increased rate of collagen formation, increased rateof mitosis of mesenchymal stem cells when compared to PRP. Several authors have demonstrated that the fibrin in the platelet rich fibrin provides an optimal support to mesenchymal stem cells.Benefits of using PRF includes ease of preparation and lack of biochemical handling, adhesive nature of PRF and good tensile strength for clot stabilization and maturation.Because of the above powerful effects on tissue regeneration and repair, enormous amount of human clinical studies have recommended the use of PRF in reconstructive oral and maxillofacial surgery, during placement of dental implants, sinus grafting and periodontal surgeries.

Conclusion:

The biologic activity of fibrin molecule in PRF is good enough to prove its efficacy in new bone formation. Gradual polymerization of PRF membrane favors physiological meshwork support to the healing process. Since PRF produced using autologous blood the risk of disease transmission is nil. PRF production technique is minimally invasive and has good satisfactory clinical proven results.

Ethical Clearance: Not required

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Conflict of Interest: NIL

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