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USE OF PLATELET-RICH FIBRIN IN MAXILLOFACIAL SURGERY

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Abstract: Platelet Rich Fibrin (PRF) is autologous biomaterial which is the second-generation platelet concentrate. It has a favorable biological properties that accelerate healing of soft tissue, and bone, giveing a wide range of applications found in oral and maxillofacial surgery and other surgical fields.

PRF technique was developed by Choukroun et al in 2001 and it represents a second generation of autologous platelet concentrate, which is used to accelerate the healing of soft and hard tissue. In contrast to the PRP, the PRF is composed of autologous fibrin matrix in which a large amount of platelets and their growth factors are embedded. PRF-graft is used in augmentative techniques residual bone defects, alone or in combination with biomaterials. When the alveolar ridge augmentation technique GBR, the PRF membranes can be used for protection and stabilization of bone compensation. PRF accelerates the healing of soft tissue and reduces the possibility of dehiscence and exposure of the membrane.

Keywords: platelet rich fibrin, growth factors, wound healing.

1. INTRODUCTION

Platelet-rich fibrin (PRF) is an autologous biomaterial which presents the second generation of thrombocyte concentrates. It possesses favourable biological characteristics which accelerate both soft tissue and bone healing, due to which fact it is extensively used in oral and maxillofacial surgery, as well as other surgical specialties [1,2]. It is the successor of platelet-rich plasma (PRP), having multiple benefits [3]. The greatest benefits of working with PRF are simple preparation, availability for every patient and minimal trauma. Several works related to the issue of the use of PRP and PRF in periodontal, oral, maxillofacial and plastic surgery as well as in otorhinolaryngology have been published [4]. Some of the application areas are: sinus augmentation after maxillary sinus floor lift, alveolar ridge preservation after tooth extraction, guided bone regeneration, guided tissue regeneration and soft tissue healing in mucogingival surgery.

Platelet Rich Plasma or PRP and Platelet Rich Fibrin or PRF are autologous preparations which are produced after the patient's blood sample is placed in a centrifuge and they consist of thrombocytes and plasma. A human blood clot consists of approximately 95% of erythrocytes, 5% of thrombocytes and less than 1% of leukocytes. Contrary to that, PRP/PRF clot consists of 4% of erythrocytes, 95% of thrombocytes and 1% of leukocytes.

Tissue damage and the disrupted continuity of blood vessel walls stimulate the creation of the thrombocyte stopper and blood clot, as well as the secretion of several growth factors. Alpha granules, which are found in thrombocytes contain specific growth factors: growth factor originating from thrombocytes (PDGF), the transforming growth factor β (TGF-β, including isomers TGΦ-β-1 TGΦ-β-2), vascular endothelial growth factor (VEGF), epidermal growth factor from thrombocytes (PD-EGF) and insulin-like growth factor (IGF-1) which is found in plasma. Upon the activation of the thrombocytes, α-granules merge with the cell membrane and secrete the active forms of growth factors.

During the wound healing process thrombocytes secrete the above-mentioned growth factors which control the proliferation, chemotaxis, the synthesis of the extracellular matrix and tissue morphogenesis. By using PRF and PRP it is possible to achieve multiple increase in the concentration of the growth factor and accelerate the healing process by stimulating the fibroblast proliferation and bone healing, the increase of the tissue vascularisation and the creation of collagen and mitosis of mesenchymal stem cells and osteoblast [5].

PRF technique was developed in 2001 by Choukroun et al., and it presents the second generation of autologous thrombocyte concentrate used for accelerating the soft and hard tissue healing. Contrary to PRP, PRF consists of the autologous

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fibrin matrix, into which a large amount of thrombocytes and their growth factors were built in. During the period of 7-11 days after the application, the fibrin net is degraded, while the growth factors are progressively released. With PRP there is no fibrin net and that is why the growth factors are released only once and in an uncontrolled manner during the PRP preparation and application period. Growth factors have a limited time of operation, after which they are deactivated and dissolved. Wound healing is a complex process which demands the interaction of different cells over time. Due to that, releasing the growth factor only once directly influences only the initial stadium of the wound healing process, lacking the extended effect which is important for the soft tissue and bone regeneration. Because of that extended effect, fibrin net plays an important role in the regenerative characteristics of PRF.

2. MATERIALS AND METHODS

Several works related to the issue of the PRP and PRF use in periodontal, oral, maxillofacial and plastic surgery as well as in otorhinolaryngology have been published. Some of the application areas are: sinus augmentation after maxillary sinus floor lift, alveolar ridge preservation after tooth extraction, guided bone regeneration, guided tissue regeneration and soft tissue healing in mucogingival surgery [6−19].

2.1. PRP preparation

Blood collected for PRP preparation is immediately mixed with an anticoagulant (citric dextrose ACD): 2 ml of ACD and 20 ml of blood or 7 ml of ACD and 60 ml of blood, in order to prevent the activation of thrombocytes. During the first centrifugation procedure, blood is separated into three layers: at the bottom of the test tube there is the erythrocytes layer, in the middle is the layer rich in thrombocytes and on the top there is acellular plasma rich in plasmatic molecules (fibrinogen) called Platelet Poor Plasma, PPP. The first two top layers and a little bit of the erythrocyte layer are aspirated by a sterile syringe and they go through the centrifugation procedure again, this time without anticoagulants. The second centrifugation procedure uses faster spinnig and lasts longer than the first one. After the second centrifugation procedure it is possible to collect the PRP layer. Immediately before the PRP application, it is necessary to polymerize the thrombocyte concentrate by using calcium chloride and bovine thrombin. Polymerization occurs in 6−10 seconds.

2.2. PRF preparation

PRF is the material produced through the centrifugation process of the patient's blood, without using any extra additives. Due to that fact, no anticoagulants or bovine thrombin are necessary for its preparation. To prepare PRF a centrifuge (PC-02 table centrifuge, figure 1) and a blood-taking set consisting of a butterfly needle (24G), 9 ml test tube and a tourniquet are needed.

Figure 1

PRF protocol is simple: after veinpuncture, 20–60 ml of blood are taken and put in several 9 ml test tubes (figure 2) without anticoagulants, and it immediately goes through the centrifugation process at 3000 per minute, for fourteen minutes.

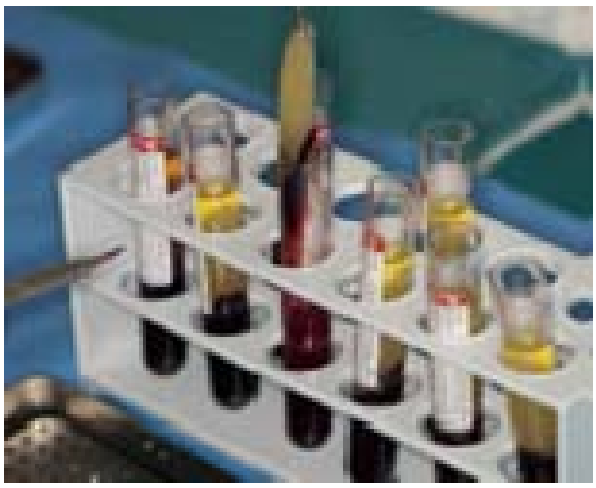

Figure 2

Due to the absence of anticoagulants, the coagulation cascade is initiated, fibrinogen changes into fibrin which is multiply cross-linked, creating a dense fibrin net (figure 3). In that way fibrin clot containing a half of leucocytes and almost all active thrombocytes present in the collected blood sample is created. For the PRF preparation it is important how quickly the blood is collected and how soon the centrifugation process begins.

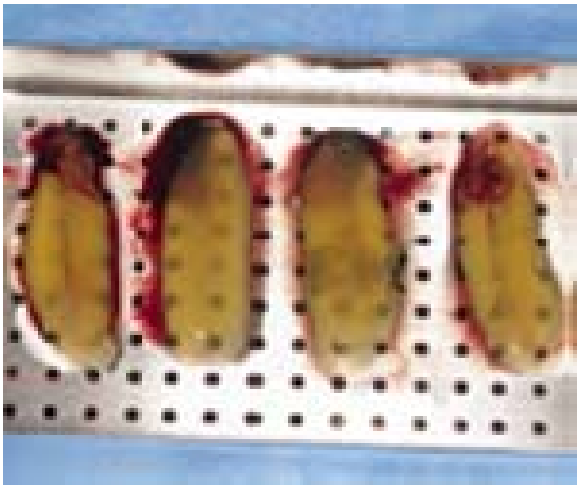

Figure 3

In PRF technique fibrin is polymerized naturally and slowly during the centrifugation process, which enables the creation of a homogenous 3D structure containing built-in growth factors and thrombocytes. Besides that, the fibrin structure makes the skeleton (mold) in which endothelial cells, osteoblast and other cells migrate during the tissue healing process. The presence of the fibrin net organized in that way accelerates the angiogenesis of the wound at the beginning of the wound healing process, which enables faster migration of osteoblast and the beginning of bone formation. In their study done in *in vitro* conditions Carol et al. proved that six growth factors are released from PRF in an unchanged concentration over seven days.

PRF Box (Process, France) is the instrumentarium used for creating the membranes and cylinders from PRF. After the deposition of the fresh PRF clot within the PRF Box, the membranes of equal thickness are obtained. Multiply cross-linked fibrin structure stabilizes the clot, creates the consistence which resists 'displacement', maintains space, prevents the invasion of soft tissue and at the same time progressively releases growth factors. Serum exudate, which is rich in vitronectine, is extruded from the fibrin net and deposited at the bottom of the box during compression. It can be used for the hydration of the bone graft, surgical wounds or for preserving an autologuous bone graft.

PRF cylinders are used for preserving post-extraction alveoli and with the transalveolar technique of lifting the maxillary sinus floor by using osteotomes. PRF is placed within PRF Box cylinder and while the piston gradually makes pressure, a small disc of 1 cm in diameter is formed. The disc can easily be placed in the post extraction alveola or within the surgically formed window during the process of the sinus floor lift by applying the transcrestal osteotomy technique.

PRF is used with the lateral sinus lift approach intervention, as well as with the transcrestal approach to sinus cavity [20−24].

2.3. PRF application (alongside with bone graft)

After the centrifugation procedure, PRF clot is cut into small pieces with special sterile scissors and mixed with the selected grafts (figure 4). In case when a xenogene or aloplastic graft is used, PRF will intensify the osteoinductive characteristics of the graft by affecting the proliferation and chemotaxis of osteoblasts within the neighbouring sinus walls, the improved mitigation and the setting of the bone on graft particles. Clinically a faster mineralization of graft can be expected. Apart from that, the positive effect of PRF on soft tissues related to accelerated healing and dehiscence of a wound will be observed.

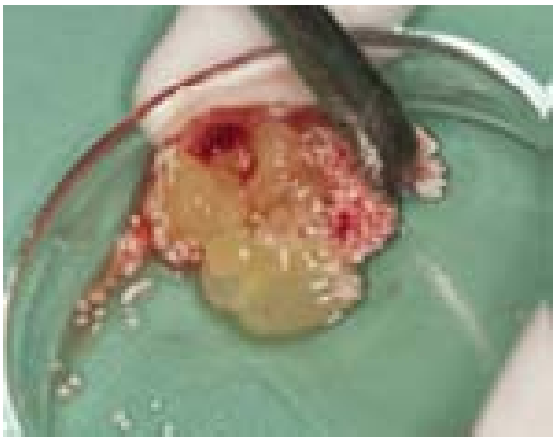

Figure 4

2.4. Applying PRF membrane on Schneiderian membrane

PRF membrane acts as a mechanical and biological protection of the Schneiderian membrane, protecting it from perforations which can occur while pushing in the graft granules into the sinus cavity. PRF membrane can be used for repairing the

existing perforations, while growth factors can accelerate its healing. Besides that, the bone graft around the top of the implant can be stabilized.

2.5. Applying PRF membrane over the lateral window

PRF membrane can be applied instead of the resorbable collagen membrane through the lateral window in order to prevent the invagination of the mucogingival tissue. It is beneficial because of being economically acceptable as an autologous biomaterial and because of being biologically active since it releases growth factors which accelerate soft tissue and bone healing.

2.6. Applyng PRF instead of bone graft

PRF, as a substitute for a bone graft, can be used both with the lateral approach technique and crestal approach by using osteotomes. During the lateral approach and after the elevation of the Schneiderian membrane, PRF membrane is placed over it to protect and close the existing perforations. After placing the implant, the sinus cavity is filled with several PRF cylinders and the window is covered with one or two PRF membranes in order to prevent the invagination of the soft tissue into the sinus cavity.

When a vertical technique is used, PRF plug is applied inside the sinus by using an osteotome as a substitute for a bone graft.

PRF graft is used in augmentative techniques of bone defects, on its own or in combination with biomaterial. During the augmentation of the alveolar ridge by using GBR technique, PRF membrane can be used to protect and stabilize the bone compensations. PRF will accelerate the soft tissue healing and reduce the likelihood of membrane dehiscence and exposition.

PRF clot can be chopped up into smaller pieces by using scissors and added to the graft which will better interconnect the graft into a whole, stimulate the neoangiogenesis, proliferation and chemotaxis of the osteoprogenitor cells.

Contrary to commercial resorptive or non-resorptive membranes, PRF membrane is economically more acceptable, reducing the patient's expenses.

PRF can be used on its own in alveolar preservation techniques in order to preserve the dimensions and accelerate bone and soft tissue healing. After the four-month healing period, post-extraction alveoli are filled with a mature bone, without any soft tissue invagination. The dimensions of the alveolar ridges are almost preserved, with the minimal ridge width loss of 7.38% and height loss of 7.13%. In the studies in which resorbable membranes and bone grafts were used, resorption values of 17.79% of height and 11.59% of width were identified, in some studies even higher.

3. CONCLUSION

Platelet-rich fibrin (PRF) is an autologous biomaterial which presents the second generation of thrombocyte concentrates. Due to its favourable biological characteristics which accelerate both soft tissue and bone healing it is used in oral and maxillofacial surgery, as well as other surgical specialties. PRF graft is used in augmentative techniques of bone defects, on its own or in combination with biomaterial. During the augmentation of the alveolar ridge by applying the GBR technique, PRF membrane can be used to protect and stabilize a bone graft. PRF will accelerate soft tissue healing and reduce the likelihood of membrane dehiscence and exposition.

The greatest benefit of working with PRF is the simplicity of the preparation development, availability for every patient and minimal trauma.

PRF can be divided into two categories, depending on the leukocyte content: L-PRF and P-PRF.

PRF can be used on its own in the alveolar ridge preservation techniques to preserve its dimension and accelerate bone and soft tissue healing.

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ПРИМЕНА ФИБРИНА ОБОГАЋЕНОГ ТРОМБОЦИТИМА
У МАКСИЛОФАЦИЈАЛНОЈ ХИРУРГИЈИ

Сажетак: Тромбоцитима обогаћен фибрин (PRF) аутологни је биоматеријал који представља другу генерацију тромбоцитних концентрата. Има повољна биолошка својства која убрзавају мекоткивно те коштано зарастање, због чега широко подручје примене налази у оралној и максилофацијалној хирургији, те другим хируршким гранама.

Технику PRF-а су 2001. године развили Choukroun и сарадници, и представља другу генерацију аутологног концентрата тромбоцита која се користи за убрзање зарастања меког и тврдог ткива. За разлику од PRP-а, PRF се састоји од матрикса аутологног фибрина у који су уграђене велике количине тромбоцита и њихових фактора раста. PRF-графт користи се у аугментативним техникама заосталих коштаних дефеката, самостално или у комбинацији с биоматеријалом. Приликом аугментације алвеоларног гребена техником GBR-а, PRF-мембрана се може користити за заштиту и стабилизацију коштане надокнаде. PRF убрзава зарастање меког ткива, те смањује могућност дехисцијенције и експозиције мембране.

Кључне речи: тромбоцитима обогаћен фибрин, фактори раста, зарастање рана.