

Comparison between PRP, PRGF and PRF: lights and shadows in three similar but different protocols

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Abstract. – OBJECTIVE: The main goal of the modern surgery is to get a low invasiveness and a high rate of clinical healing: in the last years, it has been introduced the concept of a “regenerative surgery”, and many techniques has been widely described in the literature. The most used are PRP, PRGF and PRF techniques. Aim of this research is to compare the three protocol of PRP, PRF and PRGF in their essential features, so to suggest to the practitioners the best blood product to use in the regenerative surgery.

DISCUSSION AND CONCLUSIONS: Among the advantages that shows the PRF, compared to PRP and PRGF, we can cite a greater simplicity of production for the absence of manipulation that leads to a reduced possibility of alteration of the protocol due to an error of the operator. The special texture of the PRF and its biological features shows clearly an interesting surgical versatility and all the characteristics that can support a faster tissues regeneration and high-quality clinical outcomes.

Key Words:

PRF, PRP, PRGF, Regenerative medicine.

Introduction

The main goal of the modern surgery is to get a low invasiveness and a high rate of clinical healing: nowadays, it has been widely introduced the concept of the “regenerative surgery”, where in the same surgical access the surgeon combines the demolitive techniques together with the regenerative methodics. Regenerative medicine is nowadays the most interesting field of biotechnology able to combine several aspects of medi-

cine, cell and molecular biology, biomaterials and tissue engineering all aimed to regenerate, repair or replace tissues. The oral surgery and maxillofacial surgery are the medical branches where a tissue loss often means both functional and aesthetic damages: frequently, to rehabilitate these damages, you could use various techniques that have been studied and improved over time¹. In the last years, many techniques has been widely described in the literature. The most used are PRP, PRGF and PRF techniques.

Platelet Rich Plasma

The Platelet Rich Plasma (PRP), also termed autologous platelet gel (Autologous Platelet Gel), is a gel at high concentration of autologous platelets suspended in a small amount of plasma after centrifugation of the blood of the patient. The Platelet-Rich Plasma is a product derived from blood, its characteristic is due to the fact that the platelets present in the PRP release numerous substances that promote tissue repair and affect the behavior of other cells by modulating the inflammation and the formation of new blood vessels. The platelets in fact play a fundamental role in mediating the healing of damaged tissue thanks to the ability to release growth factors, including PDGF, TGF β , VEGF, IGF-1, FGF, and EGF. The granules contained in platelets are also a source of cytokines, chemokines and many other proteins variously involved in stimulating proliferation and cellular maturation, in modulating inflammation and activate other cells by regulating tissue homeostasis and regenerative processes².

Plasma Rich in Growth Factor

Plasma Rich in Growth Factor (or PRGF) is a type of plasma enriched of proteins and circulating growth factors able to aid the bone and soft tissue regeneration. PRGF contains many different cells and cell-types highly concentrated in a gelatinous form which can be placed into the site of the injury: these cells stimulate and accelerate the healing process by forming blood clots and releasing growth factors into the wound. PRGF does not need bovine or human thrombin for coagulation; PRGF includes plasma proteins and coagulative factors and is then more advantageous compared to PRP³. PRGF preparation was carried out by following a previously described protocol. Blood sample was obtained from basilic vein using a large needle to avoid platelet rupture. Sampled blood was combined with anticoagulant (1 ml of 3.8% sodium citrate for 10 ml blood) and centrifuged at 460 G in 8 minutes: after the centrifugation, PRGF was taken from the bottom of the tube. Calcium Chloride was then added to PRGF (0.05 ml per ml): this action promotes the coagulation, usually obtained within at most 10 minutes. At the end of the procedure, we obtained a gelatinous PRGF, to be immediately placed in the surgical site⁴.

Platelet Rich Fibrin

The Platelet Rich Fibrin (PRF) is a quite modern platelet concentrate, it is achieved with a simplified preparation, with no biochemical manipulation of blood.

This technique does not require anticoagulants or bovine thrombin (or any other gelling agent). This feature make this product easily usable, with a low rate of mistakes during the preparation stage⁵.

The blood taken, approximately 10 ml in tubes without anticoagulant, is immediately centrifuged at 3000 rpm for 12 minutes. The absence of anticoagulants allows the activation of platelets in contact with the tube, triggering the coagulation process. The fibrinogen is initially concentrated in the upper part of the tube but, upon the contact with thrombin normally present in the blood, it is converted into fibrin. The platelets are retained into the meshes of fibrin⁶.

A short time between blood collection and its centrifugation is most important to obtain a product clinically valid. Otherwise, in fact, the fibrinogen will be converted to fibrin in a diffuse manner throughout the test tube and, after centrifugation, you can observe a minimal amount of

PRF with poor consistency; thus, it will be unusable.

After performing the centrifugation of the blood, we proceed to the removal, with the use of surgical tweezers, of the result of centrifugation of whitish and yellowish color (PRF), leaving behind the acellular supernatant (PPP) in the test tube. Finally, is separated the layer of PRF from the lower layer rich in red blood cells through the use of scissors. The PRF, compressed between two sterile gauze, gives a membrane in consistency tense-elastic and able to resist the pull of the suture.

The PRF has been studied by many research groups, and it has been shown that it is able to stimulate osteogenesis in bone environment, in addition to angiogenesis; Furthermore, it provides a scaffold consisting of fibrin that allows cellular migration, and these are certainly the fundamental aspects for the process of bone regeneration⁷.

Aim of this research is to compare the three protocol of PRP, PRF and PRGF in their essential features, so to suggest to the practitioners the best blood product to use in the regenerative surgery.

Discussion

The PRF protocol achieves the gel without any manipulation of the blood: this method, therefore, totally respects the European directive 2004/23/EC, while both the PRP and the PRGF require the addition of biochemical additives in order to be obtained.

With the technique of the PRF, immediately after the blood sample, the tube is placed in the centrifuge without anti-coagulants, so there are no limitations to the use of this blood product, provided that the centrifuge is conforms to 2000/70/EC.

Among the advantages that shows the PRF, compared to PRP and PRGF, we can cite a greater simplicity of production for the absence of manipulation that leads to a reduced possibility of alteration of the protocol due to an error of the operator (Table I). Furthermore, the technique of the PRF has the advantage of producing a larger share of blood product over the share of blood taken: in fact, in the PRGF using only a share of 20% of the blood collected⁸.

Following the centrifugation, the clot of PRF obtained contains:

Table I. Overview table comparing the three blood products about their most important characteristics.

Blood products	PRF (2004)	PRGF (2001)	PRP (1998)
Protocol	Easy	Complex	Very complex
Speed-rate	Fast	Very Slow	Slow
Reproducibility	No Bias	Possible Bias	Possible Bias
Use of anticoagulants	No	Yes	Yes
Amount obtainable	Good	Poor	Enough
Costs of the protocol	Low	High	Moderate
Amount of fibrin obtainable	High	Low	Low
Speed of fibrin formation	Physiological	High	High
Fibrin morphology	Trimolecular	Tetramolecular	Tetramolecular
Leukocytes amount	65%	0%	0-50%
Immunomodulatory properties	Yes	No	Poor
Neo-angiogenic potential	+++++	++	+
Osteoconductive potential (scaffolding)	High	Poor	Poor
Mechanical properties (sol-gel-membrane)	Good	Poor	Enough
Presence of MSCs	Yes	Yes	Yes

1. The highest values of platelets
2. The highest values of the growth factors PDGF, VEGF and TGF
3. A share extremely representative of fibrin, fibronectin and vitronectin
4. About 65% of leukocytes

The PRF is the technique that provides more white blood cells after centrifugation, in comparison with the technique of PRGF that no quotas representative of white blood cells⁶, or with respect to the technique of PRP which provides shares less than 50%.

Important studies have found that the PRF can be a node on the local immune regulation, with ability to show a feedback control of the local inflammation. This notion may explain the reduction of postoperative infections when the PRF is used as an additive surgery⁹.

Despite the leukocytes present fibrinolytic activity, we would suggest the use of this blood product since it improves undoubtedly the immune activity of leukocytes in the surgical site.

One major difference between the other blood derivatives and the PRF is attributable to the mode of gelification. The PRP and the PRGF need to interact with thrombin and calcium chloride to initiate the last phase of coagulation and fibrin polymerization. These two additives, therefore, influence the speed and mode of gelification, resulting indispensable in the preparation of these products. In the early stages of polymerization of the PRF thrombin definitely has an important role but, being present in physiological concentrations since there is no addition, this allows the formation of a fibrin matrix in a slow and

physiological way: this timing of the process of formation of the fibrin is crucial for the three-dimensional organization of the fibrin network¹⁰.

During the early stages of gelification, fibrin fibrils can be assembled together in two different ways: as tetra-molecular structures condensed, as happens in the processes of the protocol of the PRP and the PRGF, or as trimolecular connected structures, as typically occurs in the process of PRF formation.

The bilateral conjunctions are formed with high concentrations of thrombin that allow the thickening of the polymers of fibrin; this biological process results in the formation of a rigid network which disadvantages the entrapment of cytokines and cell migration, but precisely this rigidity, favors the sealing of biological tissues. This happens in preparations blood such as PRP or PRGF. Low concentrations of thrombin, as in PRF protocol, determine the formation of a flexible network, and capable of favoring the entrapment of cytokines and cell migration. We can also add that this organization will give great flexibility to the three-dimensional fibrin matrix: in fact, this conformation of fibrin is rapidly invaded by leucocytes, highly present in the PRF, which are the first cells to start the neo-angiogenesis, the white blood cells, in fact, contain the VEGF that acts as a potent vascular growth factor. The platelet-derived growth factors (PDGF) promote neo-vascularization and fibrin serves as a tissue matrix for local regeneration.

The spatial conformation of fibrin obtained by the method of the PRF serves as the substrate for platelets and acts as a chemotactic signal for stem cells that would, therefore, be concentrated

in the surgical site: this MSCs recruitment configures the PRF as a good environment for MSCs growth and differentiation towards others specific tissues such as bone, muscles and nerves¹¹.

Conclusions

The special texture of the PRF, thus, allows clinical use in the amorphous form but also in the membranous form, after a slight compression of the gel between two sterile gauze: this membranous form will be used to cover and protect a large tissue graft. The biological features of PRF shows clearly an interesting surgical versatility and all the characteristics that can support a faster tissues regeneration and high-quality clinical outcomes. All these features support the conclusion that the PRF is the best blood product able to better enhance the healing of soft and hard tissue, comparing to other similar blood product.

Consent Statement

No patient has been involved in this research.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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