



Platelet Concentrates: Review of Evolution and Classification.

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Abstract

Platelets contain a reservoir of growth factors that have numerous biological activities such as assisting in chemotaxis, cell differentiation, proliferation, and angiogenesis which all are pivotal in the wound healing process. From this, platelet concentrates have been described in the literature beginning from the first generation to the second generation both of which have a beneficial impact on the healing of soft and hard tissue following oral surgical procedures. The following review will illustrate the evolution of platelet concentrates and the current classification of the marketed products available.

الخلاصة

تحتوي الصفائح الدموية على مخزون من عوامل النمو التي ترتبط بالعديد من الأنشطة الحياتية مثل المساعدة في الارتباطات الكيميائية، وتنوع الخلايا، والتخصيب وتكوين الأوعية، وتعد عوامل جهرية في التئام الجروح. وعلى هذا الأساس، تم وصف تراكيز الصفائح الدموية في الأدبيات العلمية بدءاً من الجيل الأول إلى الجيل الثاني، وكلاهما له تأثير فعال في شفاء الأنسجة الرخوة والصلبة بعد إجراء العمليات الجراحية الفموية. تقدم المراجعة الحالية تفسيراً لتطور تراكيز الصفائح الدموية وتصنيف المنتجات المتاحة في الأسواق.

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INTRODUCTION

To improve local healing, platelet concentrates as surgical aids in the field of regenerative medicine have been introduced. The typical preparation technique of these concentrates comprises the withdrawal of certain amounts of the patient's peripheral blood and then, centrifuging it with the subsequent selective departure of the liquid and solid components of whole blood ⁽¹⁾. Together the most active components specifically platelets with its growth factor reservoirs like leucocytes and fibrin to prepare them in a clinically usable design. ⁽²⁾ The concentrates come in two forms, either as solutions or gels which can either be injected or directly implanted in the proposed site. ^(3,4) The growth factors contained in the platelets are expected to stimulate the damaged tissues to regulate the local inflammatory processes⁵ through biological mechanisms with the acceleration of angiogenesis peripherally and stimulation of remodeling ^(6,7).

Over the years, two generations of platelet concentrates have evolved; platelet-rich plasma (PRP) to platelet-rich fibrin (PRF) with its modifications as Advanced - PRF, titanium-PRF, injectable -PRF, PRF lysates, and currently concentrated growth factor. Recently, platelet concentrates used are more efficient in terms of biological efficacy ⁽⁸⁾. Platelet life in blood ranges from 7-10 days with younger platelets having a greater functional ability ⁽⁹⁻¹⁴⁾. The main function of platelets is the initiation of haemostatic mechanisms that arrest bleeding following vascular injury ⁽¹⁵⁻¹⁷⁾. In addition to numerous processes ranging from fighting

infection through modulating inflammatory response, enhancing wound healing, promoting tumor angiogenesis and metastasis, etc. ⁽¹⁸⁻²⁷⁾ In the resting state, platelets are non-thrombogenic and require a stimulus to become more potent and active such as thrombin in which a change in its shape takes place from a disc to a compact sphere having pseudopodia. ²⁸⁻³⁰ Platelets contain a reservoir of growth factors that have numerous biological activities like assisting in chemotaxis, cell differentiation and proliferation, and angiogenesis which all are pivotal in the wound healing process ^(31,32).

Evolution of Platelet Concentrates:

Platelet concentrates are defined as autologous biological products that are extracted from peripheral blood by centrifugation with different centrifugal speeds resulting in various types of platelet concentrates with specific biological content and action ⁽³³⁾ In the 1900s, fibrin was investigated in the form of a blood clot that applied to a wound. For nerve anastomosis, an autologous plasma glue rich in fibrinogen and thrombin were used in 1940 ⁽³⁴⁾. The impression of platelet concentrates was coined in the 1970s for the treatment of hemorrhagic disorders, to be more precise leukemia and thrombocytopenia, and as a replacement therapy following blood loss ⁽³⁵⁻³⁹⁾. The use of human plasma derivatives (fibrin glues, fibrin tissue adhesive, or sealants) as surgical adjuncts was described by Matras ⁽⁴⁰⁾. In the 1970s. Due to the risk of cross-infection with commercial adhesives, autologous fibrin sealants were developed. However, its manufacture led to rheological

qualities that were less repeatable or adequate⁽⁴¹⁾. Numerous kinds of research were continued in their investigations through 1975-1978, which proposed enhanced healing by a mixture of platelet fibrinogen and thrombin in the design of foam gel⁽⁴²⁾. In 1980, Niekisch has reported the use of fibrin glue for managing bleeding disorders in oral and maxillofacial surgery⁽⁴³⁾. In 1986, Knighton and colleagues were the first who termed the platelet concentrates by Platelet-Derived Wound Healing Factors (PDWHF)", because of their successful promote healing, especially in necrotic lesions⁽⁴⁴⁾. The first generation of platelet concentrates; Platelet-rich plasma (PRP), was advocated by Whitman et al in 1997 in oral surgery⁽⁴⁵⁾. In the blood, the platelet count ranges from 150,000/ μ l to 350,000/ μ l. Lesser quantities haven't been found to improve wound healing, and higher concentrations haven't been proven to do so either⁽⁴⁶⁾. Marx and colleagues applied PRP in numerous soft and hard tissue surgery to enhance bone formation and increase density⁽⁴⁷⁾. Anitua⁽⁴⁸⁾ introduced a new variety of these concentrates in 1999, dubbed Platelet Rich in Growth Factors (PRGF), but it is no longer used due to its difficult and time-consuming manufacturing procedure. The second generation of platelet concentrates is Choukroun's platelet-rich fibrin (PRF) which is a natural autologous biomaterial containing platelets, and leukocytes embedded in a network of rich fibrin. Compared to PRP, there is no need for an anticoagulant⁽⁴⁹⁾. PRF is made up of a platelet concentration and white blood cells entangled in a fibrin matrix. They originally formed platelet-rich fibrin (named L-

PRF) constituting 97 percent platelets with more than 50 percent leukocytes embedded in a dense fibrin network. The absence of an anticoagulant gives the advantage of rapid handling between blood collection and centrifugation.⁽⁴⁹⁻⁵³⁾ In 2006, Concentrated Growth Factors (CGF) was coined by Sacco which is the most current platelet concentrate. In this technique, once the blood is collected in non-anticoagulant tubes, it is immediately centrifuged in a specifically designed centrifuge (Medifuge; Italy) with a pre-programmed centrifugation cycle and as follows: an acceleration cycle of x 30", 2,700 rpm x 2', 2,400 rpm x 4', 2,700 rpm x 4', 3,000 rpm x 3' followed by a deceleration down to x 36" and end of the cycle⁽⁵⁴⁾. This centrifugation protocol produces a high-density complex three-dimensional architecture of a fibrin matrix rich in growth factors and has more regeneration ability than the other previous platelet concentrates⁽⁵⁴⁻⁵⁶⁾. As a modification from the standard Choukroun's PRF described in 2000 (S-PRF) in which the centrifugation protocol is 3000 rpm / 10 minutes, various low-speed centrifugation protocols are currently being used to prepare PRF:

- 1- Leukocyte- and PRF (L-PRF) by Dohan Ehrenfest with a centrifuge speed of 2700 rpm for 12 minutes.⁽⁵⁰⁾
- 2- Advanced PRF (A-PRF) Choukroun with a centrifuge speed of 1300 rpm for 8 minutes.⁽⁵⁷⁾
- 3- Injectable PRF (i-PRF) by Choukroun with a centrifuge speed of 700 rpm for 3 minutes is the most current protocol described in the literature concerning second-generation

platelet concentrates. The difference between the i-prf protocol, when compared to its predecessors mentioned above, is time which is shorter. In this protocol, only the separation of blood components is required and this takes place in the first 2-4 minutes. For success, the use of plastic tubes is recommended since they have a hydrophobic surface that does not trigger the coagulation process and as such, under the centrifugation forces, all the blood constituents necessary to form a good platelet concentrate will be located at the top of the tube in 2-4 minutes⁵⁸. Another modification for PRF preparation was described by Tunalli et al called Titanium prepared PRF (T-PRF). In this protocol, the collected blood is centrifuged in titanium tubes at a speed of 2800 RPM for 12 minutes. It has been shown that the fibrin clot formed is more compactly woven with thicker fibrin when compared with the orthodox L-PRF since titanium has been shown to have an enhanced hemocompatibility when compared to glass leading to the formation of a more polymerized fibrin.⁽⁵⁹⁾

Classification System of Platelet Concentrates:

With the literature concerning PRP developed and the misinterpretations and conflicts on this topic, there was a need for more accurate global terminology and classification system for all platelet concentrates which include the neglected parameters of healing (fibrin architecture and leucocyte content). A classification system was established and published in the first international consensus paper. Currently, whatever they are in form or

content, all products available fall under the term "platelet concentrates"^(3, 5, 53). The most current classification of platelet concentrates forms a foundation for future terminology evolutions and approvals for clinical use has been recommended by the POSEIDO organization. The leukocyte content and fibrin architecture in these available products must be highlighted referring to a unique biological activity^(5, 60, 61). Based on their leukocyte (L) and fibrin content, the four main families are highlighted as follows:

- Platelet-rich plasma (PRP) prior activation in liquid form: L-PRP and "pure platelet-rich plasma" (P-PRP). On the other hand, « P-PRP gel » and « L-PRP gel » represent the activated counterpart of P-PRP and L-PRP respectively.⁽³⁾
- **Platelet-rich fibrin (PRF)** in a solid state containing a strong fibrin network; pure platelet-rich fibrin" (P-PRF) and platelet-rich Fibrin" (L-PRF)^(62, 63).

CONCLUSION

In this context, several bioactive surgical additives have been developed and explored for enhanced wound healing. One of which is platelet concentrates. Within its specific granules, platelets contain high concentrations of essential growth factors that stimulate cell migration and proliferation which support wound healing. Due to this favorable property, autologous platelet concentrates have been introduced and evolved as a therapeutic modality for accelerating healing. The POSEIDO principles are based on published platelet concentrate classifications and serve as

a framework for future nomenclature and clinical use. Simple and free systems, such as Choukroun's PRF and its variants, are currently the most extensively employed in dentistry, with promising outcomes in both soft and hard tissue healing.

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