



## REVIEW ARTICLE

## Use of Platelet-Rich Plasma in Autogenous Bone Graft in Implantology

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### Abstract

The use of platelet-rich plasma (PRP) in implantology has potentiated bone regeneration and the healing process, reducing postoperative period, inflammatory process and blood loss. The objective of this study is to verify, based on the literature, the use of PRP in bone regeneration in autogenous grafts, to show its indications and benefits in bone formation and techniques used. A literature review was performed on the efficacy of PRP in autogenous bone grafts in implantology. The databases used were PubMed, Scielo and BVS. In this study, 30 articles from the years 1983 to 2017 were selected demonstrating the effectiveness of the technique. The use of PRP in the dental clinic presents promising results in the regeneration and healing of the tissues, however, more study is needed to verify its long-term efficacy.

### Keywords

Bone graft, Maxillary sinus, Platelet-rich plasma, Growth factors

### Introduction

Plasma Rich in Platelets (PRP) is a blood component with a high concentration of autologous platelets in minimal volume of plasma. The platelets present several cell growth factors, constituted by groups of polypeptides acting as regulators and stimulators of the cellular processes of mitogenesis, chemotaxis, differentiation and metabolism [1,2]. The PRP is performed by autologous blood centrifugation, used to improve the integration of bone, cutaneous, cartilaginous or fragile grafts to stimulate wound healing [3-5].

In recent years there has been a growing interest in the use of platelet-rich plasma because it is a simple and inexpensive procedure and a natural way to accelerate and improve wound healing mechanisms. Several protocols were created with the aim of achieving an optimal platelet count and with a higher growth factor [6]. Therefore, studies on this subject are necessary, this review aims to explain the use of PRP in bone regeneration in autogenous grafts, evidence its indications and benefits in bone formation and techniques used, in order to obtain success of this option therapy.

### Literature Review

The evolution of genetic engineering has promoted improvement in the development of materials that have the capacity to induce bone growth factors or osteoinduction, acting directly on bone osteoblastic activity [7].

Among the materials we can mention the platelet rich plasma (PRP), used since the mid-1990s. It was originally found by Lynch, adopting such appointments as platelet gel, platelet-enriched plasma, platelet-rich autogenous plasma, and plasma rich in growth factors. This gel has been extensively studied in dentistry, being used mainly in small bone grafts in the alveolar region for future dental implants and in periodontal and maxillofacial surgeries, aiming to accelerate the repair of the surgical wound and the bone regeneration. The same was developed with the aim of replacing the

fibrin glue that put the patient at risk of cross infection, since it is a material that depends on the addition of bovine thrombin to be activated and the complexity of the production of its protocols, minimizing the complications resulting from this procedure used for over 60 years [8-10].

PRP is a gel with platelet concentration in a reduced volume of plasma. There are several methods of obtaining it, being able to be used in different scales and time of centrifugation. Generally the platelets are maintained in the plasma at a concentration of about 150,000 to 400,000/mm<sup>3</sup>; in PRP this concentration may increase about 2 or 3 times longer by autologous blood centrifugation [8].

Platelet-rich plasma is an organic, non-toxic, non-immunoreactive product collected in the preoperative period, rich in growth factors and derived from laboratory autogenous blood processing. Plasma gel is a compound derived from the mixture of thrombin and calcium gluconate to PRP. These products, when in the presence of calcium, trigger the organized formation of the clot through the transformation of fibrinogen into fibrin and activation of factor XII, resulting in the gelation of PRP, facilitating its application in surgical management of the grafts [11].

The preparation of the PRP requires aseptic conditions of manipulation of the blood, so as to avoid its contamination, and attention to the materials that are used, requiring a good blood bank infrastructure and a qualified professional [12].

The use of different protocols to obtain PRP is an unfavorable point, since it can induce different biological responses, and should be done with caution and taking into account several factors, such as the number, speed and time of centrifugations used, the number of platelets, the amount of growth factors and concentration of leukocytes and erythrocytes in a manner that provides a satisfactory biological effect and is successful in the preparation [13].

In addition, more research on the effectiveness of PRP should be performed, including the creation of a specific protocol, and patient preparation (use of some medications may interfere with platelet function by altering the properties of the gel), because its benefits have not been fully clarified [14].

## Preparation of PRP

Despite presenting several protocols they follow a general sequence that will first go through the step of collecting the patient's blood [15,16].

Blood collection should preferably be done using plastic syringes and plastic or siliconized tubes to prevent platelet activation and is performed with a needle size equal to or greater than 17 G (1.3 mm) in the median cubital vein to avoid trauma during collection of blood.

Usually are collected between 10 to 60 ml, adjusting the amount to the extent and type of surgery that will be performed. Subsequently the blood is placed in tubes containing anticoagulant (3.2% sodium citrate) [14,16-18].

The blood should then be centrifuged at 1200 rpm for 10 minutes, capable of separating the platelets from the erythrocytes and promoting platelet salvage without any type of damage or lysis that may activate the anticipated secretion of growth factors [16].

Presenting two single and double centrifugation methods, Mazzocca, studied the differences between various systems for obtaining and administering PRP observed that all preparations of PRP resulted in a significant increase of platelets as compared to the normal concentrations present in the current blood. However, comparing the different concentrations obtained with the single centrifugation method and with the double centrifugation method, the author concluded that the double centrifugation method did not reveal significantly higher results in the level of platelet separation compared to the single centrifugation method. These findings support the efficacy of the single centrifugation method in the production of platelet count. In this soft-spin technique, blood is divided into three layers: The first layer consists of some platelets and acellular plasma, also called poor platelet plasma (PPP) or plasma that is poor in growth factors. In the intermediate zone, n° 1 and n° 2, we found a thin and whitish layer known as a "mist zone", consisting mainly of platelets (1<sup>st</sup> layer) and leukocytes (2<sup>nd</sup> layer). In the third layer, there are the erythrocytes which, due to their weight, are deposited in the lower part of the tube [19].

The first and second layers, just above the red cell layer, occupy the most important segment and must be aspirated together with a pipette, constituting the PRP, which must be deposited in a second tube and added with 10 µl of a solution of calcium chloride to induce coagulation. Once coagulated, the PRP will be ready to fill from the injury site. The entire preparation procedure of PRP should be performed under strictly sterile conditions [20,21].

Relevant aspects for the preparation and characterization of PRP are acceleration and time of centrifugation, particle spacing, amount of blood volume processed, prevention of platelet aggregation and reduction of plasma volume (in the case of double centrifugation). The observation of these aspects ensures the quality of the PRP, allowing the variability of the results to be restricted to the autologous nature of the product [16,22].

Activation of PRP may be through calcium replacement and initiation of the blood coagulation cascade, use of bovine thrombin although this may lead to coagulopathies and by the more preferable method that

utilizes the centrifugal force applied to the separation of PRP, causing the membranes of the platelets are damaged by the high speeds of the centrifugation causing their premature activation. The incubation process for 1 hour at 37 °C can also be taken as an alternative method of PRP activation [17,23,24].

Around 70% of the growth factors are released in 10 minutes and 100% of the growth factors are released in 1 hour. The evaluation of the biological activity of platelet-derived growth factors is complex, so there is no way to evaluate the quality of the gel produced beforehand [25,26].

## The Use of PRP in Implantodontia

PRP can be used during implant placement as a surface treatment to stimulate osseointegration, in maxillary sinus lift, treatment of peri-implant bone defects (after peri-implantitis during placement of an implant with insufficient bone volume) or placement of implants after extraction [27]. Determining a good relation between hard and soft tissues, potentiating its regeneration in implant placement with the balance of fibrin formation and platelet activation, being responsible for the process and performance of the PRP gel [27-29].

## Methodology

A literature review was performed on the efficacy of PRP in autogenous bone grafts in implantology. The databases used were PubMed, Scielo and BVS. In this study 30 papers from the years 1983 to 2017 were selected demonstrating the effectiveness of the technique.

## Discussion

In the first attempts at PRP production, large auto-transfusion equipment was used, but it was necessary to collect bulky blood samples and had a very high cost. Because there is no standard method of obtaining PRP, several protocols have been created in order to obtain better results in relation to the quality of the plasma with a good amount of platelets, through procedures in environments with little technology and that generate a lower cost [6]. As a result, the procedures were more susceptible to errors during preparation, interfering with the quality of the product.

Regardless of the protocol, it is necessary that it is able to increase the platelet count to a concentration well above that found in whole blood, as long as the structure and function of the platelets are preserved, otherwise the platelets may rupture and release the growth, interfering in the therapeutic action of PRP [30]. The blood volume required depends on the protocol used.

Marx [17], created a method that is now used as the basis for the creation of other protocols. The centrifugation was done in two steps, where 400 to 450 ml

(obtained by means of an Electro Medics 500 Medtronic gradient density cell separator) was collected from blood and subjected to a centrifugation of 5600 rpm on the first centrifugation and 2400 on the second, where an approximate platelet enrichment of 338% was obtained, compared to the pre- PRP count in whole blood. F Vendramin, et al. [19] in its study, reached 496%, with a 4.96-fold increase in platelet count in whole blood, applying a force of 300 g in the first centrifugation and 640 g in the second, with bench centrifuge. This indicates that you can get a satisfactory amount of platelets using simpler equipment with a smaller amount of blood, and in the Vendramin study you can suggest that the higher the strength in the second centrifugation, the higher the platelet concentration.

Marx [17] states that a dual-centrifugation protocol is essential so that one can truly concentrate the platelets during the preparation of PRP and that the single-centrifugation protocols do not produce PRP but rather a mixture of PPP and PRP. On the other hand, Anitua [28] recommends a single centrifugation protocol. Although the platelet concentration obtained with this procedure has not been demonstrated. Messori M, et al. made an adaptation of the protocol of Anitua [28] to evaluate the single centrifugation, where he collected 10 ml of blood volume, distributed and stored in vacuum tubes sodium citrate as anticoagulant. From each tube, 0.5 mL of blood was removed for platelet count, where it was then centrifuged at 160 g for 6 minutes, 1 mL of lean plasma from each tube was discarded, followed by collection of PRP, including 1 to 2 mm from the upper portion of the red blood cells, totaling a volume of approximately 1.2 ml per tube. It was found that the low volume of PPP obtained in the centrifuged samples of them did not allow the preparation of PRP therapeutics according to the protocol of single centrifugation. Although blood centrifugation did not provide adequate platelet traction in the PRP samples, the platelet morphology was not affected, suggesting no platelet activation. This favorable aspect reflects an advantage of the single centrifugation protocol used in this study.

## Conclusion

Research has demonstrated the effective use of PRP in the regeneration and tissue healing process, although further research with numbers and controls is needed to prove the quantitative and qualitative effectiveness of PRP, since there are few clinical studies in the literature. Uniformity is also required in the protocols adopted so that there is no discrepancy in the results obtained.

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