

PRP in periodontics: Myth or reality?

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ABSTRACT

The goal of periodontal therapy is to protect and maintain the patient's natural dentition for his or her lifetime. More specifically, after periodontal regenerative surgery, the aim is to achieve complete wound healing and regeneration of the periodontal unit. Platelet-rich plasma (PRP), a concentrated suspension of the growth factors found in platelets, which are involved in wound healing and are postulated as promoters of tissue regeneration. The review focuses on the clinical benefits of PRP and the step-by-step preparation of PRP and of its mechanisms of action and benefits, as well as the controversy regarding its use i.e. myth or reality!

Introduction

The goal of periodontal therapy is to improve periodontal health and thereby to satisfy the patient's esthetic and functional needs or demands. To achieve this goal, most periodontal treatments aim to reduce probing depths and maintain or improve attachment levels and these parameters are used as surrogates of improved tooth retention. Conventional periodontal therapy includes non-surgical treatment as well as a variety of surgical approaches. In such treatments, histologic analysis revealed that periodontal healing occurs with repair rather than regeneration¹. In repair, long junctional epithelium exists between the treated root surface and alveolar bone.^[1,2]

The first evolutionary stage of periodontal regeneration focused on using a variety of bone graft materials. Since these techniques have had limited success, more effective regenerative approaches have been suggested such as GTR, EMD, Polypeptide growth factors, PDGF, PRP and PRF that utilize tissue-engineering techniques.^[3]

Platelet-rich plasma (PRP) is an evolving, versatile component of regenerative human and veterinary medicine by providing a concentrated growth-factor cocktail and a provisional matrix to facilitate healing. Platelet-based therapy began in the early 1990's after multiple growth factors were identified in platelet alpha granules.^[4]

Marx first reported the applications and clinical benefits of platelet rich plasma in 1998. He noted that PRP is a volume of autologous plasma that has a platelet concentration above baseline.^[5] Typically, to achieve therapeutic effects, a 400% to 500% increase in platelet concentration is required to reach the recommended PRP platelet count of 1,000,000/²L in a 5-mL volume.^[6]

What is PRP in Relation to Recombinant Growth Factors?

Within PRP, the increased number of platelets delivers an increased number of growth factors to the surgical area. The seven known growth factors in PRP are:

1. Platelet derived growth factor as (PDGF_{aa}), PDGF_{bb}, PDGF_{ab},
2. Transforming growth factor beta-, (TGF- β), TGF- α ,
3. Vascular endothelial growth factor (VEGF), and
4. Epithelial growth factor (EGF).

Recombinant growth factors are pure human growth factors, but they are not native growth factors.^[7] PRP is the combination of seven native growth factors within a normal clot as the carrier. The clot is composed of fibrin, fibronectin, and vitronectin, which are cell adhesion molecules required for cell migration such as is seen in osteoconduction, wound epithelialization, and osseointegration. Platelet Rich Plasma is also not osteoinductive. PRP acts on healing capable cells to increase their number (mitogenesis) and stimulate vascular ingrowth (angiogenesis). Therefore, it is unlikely to significantly promote bone substitutes and other non-cellular graft materials.

How is PRP Prepared?

PRP can be prepared by two techniques.

1. General-purpose cell separators
2. Platelet-concentrating cell separators

1. General-purpose cell separators:

It requires large quantities of blood (450 ml) and generally requires to be operated in a hospital setting. Blood is drawn into a collection bag containing citrate-phosphate-dextrose anticoagulant. It is first

centrifuged at 5,600 rpm to separate RBCs from platelet-poor plasma (PPP) and PRP. The centrifugation speed is then reduced to 2,400 rpm to get a final separation of about 30 ml of PRP from the RBCs.[8]

2. Platelet-concentrating cell separators:

It requires small quantity of blood and can be prepared by using certain equipments in a dental clinic set up. Currently, two such systems are approved by FDA and commercially available:

1. Smart PreP (Harvest Technologies, Plymouth, MA, USA)
2. Platelet Concentrate Collection System (PCCS; 3i Implant Innovations, Inc, West Palm Beach, FL, USA).

A study conducted by Marx et al⁸ indicated that of all of the devices tested, these 2 PRP devices approved by FDA, produced greatest platelet concentrates and most important, release of therapeutic level of bioactive growth factors.

1. Venous blood is drawn into a tube containing an anticoagulant to avoid platelet activation and degranulation.
2. The first centrifugation is called "soft spin", which allows blood separation into three layers, namely bottom-most RBC layer (55% of total volume), topmost acellular plasma layer called PPP (40% of total volume), and an intermediate PRP layer (5% of total volume) called the "buffy coat".
3. Using a sterile syringe, the operator transfers PPP, PRP and some RBCs into another tube without an anticoagulant.
4. This tube will now undergo a second centrifugation, which is longer and faster than the first, called "hard spin". This allows the platelets (PRP) to settle at the bottom of the tube with a very few RBCs, which explains the red tinge of the final PRP preparation. The acellular plasma, PPP (80% of the volume), is found at the top.
5. Most of the PPP is removed with a syringe and discarded, and the remaining PRP is shaken well.
6. This PRP is then mixed with bovine thrombin and calcium chloride at the time of application. This results in gelling of the platelet concentrate. Calcium chloride nullifies the effect of the citrate anticoagulant used, and thrombin helps in activating the fibrinogen, which is converted to fibrin and cross-linked.[9] Blood should be drawn immediately before the initiation of surgery.[7] Blood cannot be drawn and stored ahead of time.

How Does PRP Work?

PRP is an autologous concentration of eight growth factors: PDGF-aa, PDGF-bb, PDGF-ab, transforming growth factor (TGF- 1, TGF- 2), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and insulinlike growth factor (ILGF-1). These growth factors are stored within platelet alpha granules, and initiation of their release begins within 10 minutes of blood clotting.[10,11] After 1 hour, 95% of these factors are released, and the platelets then continue to synthesize and release additional growth factors over the next 7 to 8 days. The secreted growth factors immediately bind to the external surface of cell membranes of cells in the graft, flap, or wound via transmembrane receptors. These

transmembrane receptors in turn induce activation of an endogenous internal signal protein, which causes the expression of (unlocks) a normal gene sequence of the cell such as cellular proliferation, matrix formation, osteoid production, collagen synthesis etc. thus PRP growth factors act through the stimulation of normal healing, just much faster.[12,13]

Clinical applications of PRP

Because PRP enhances osteoprogenitor cells in the host bone and in bone grafts[10], it has found clinical applications in,

1. Continuity defects [10]
2. Sinus lift augmentation grafting [14]
3. Horizontal and vertical ridge augmentations [15]
4. Ridge preservation Graftings [16]
5. Periodontal/Peri- implant defects [17]
6. Cyst enucleations/Periapical surgeries
7. Healing of Extraction wounds
8. Endodontic surgeries and Retrograde procedures
9. Ablative surgeries of the Maxillo-Facial region

Why the Controversy?

Kevy and Jacobson [18] compared the efficacy of a number of PRP preparation systems and found that the SmartPreP® (Harvest Technologies Corp, Plymouth, MA), a dual-spin, variable revolutions per minute PRP preparation system, produced both, the greatest percentage of platelet yield and the least coefficient of variability. Marx [7] suggested that PRP systems failing to use dual-spin technology do not produce the necessary platelet concentration to achieve therapeutic effects.

Safety Concerns of PRP

Because it is an autogenous preparation, PRP is inherently safe and therefore free from concerns over transmissible diseases such as HIV, Hepatitis.[8] However, Sanchez et al [19] have elaborated on the potential risks associated with the use of PRP. The preparation of PRP involves the isolation of PRP after which gel formation is accelerated using calcium chloride and bovine thrombin. It has been discovered that the use of bovine thrombin may be associated with the development of antibodies to the factors V, XI and thrombin, resulting in the risk of life threatening coagulopathies. Bovine Platelet Concentrates thrombin preparations have been shown to contain factor V, which could result in the stimulation of the immune system when challenged with a foreign protein. Marx et al stated that the second set of bleeding episodes in the patients who developed coagulopathies were not due to antibodies against bovine thrombin or human thrombin but instead due to antibodies that developed to bovine factor Va that was a contaminant in certain bovine thrombin commercial preparations. Other methods for safer preparation of PRP include the utilization of recombinant human thrombin, autologous thrombin or perhaps extra-purified thrombin.

What are the advantages of PRP?

The main advantages of PRP are its autologous nature, non-invasive collection process, and rapid preparation. PRP is generally more cost-effective and time-saving than stem cell processing and treatment and can be prepared without specialized equipment, using a standard centrifuge. It can be modified into various forms according to whether an "open" (i.e. surgical) or "closed" (i.e. percutaneous) application is desired. PRP can provide a matrix/scaffold and growth factor concentrate to enhance stem cell treatment of a lesion.

Conclusion

PRP is a new application of tissue engineering and a developing area for clinicians and researchers. Although the growth factors and the mechanisms involved are still poorly understood, the ease of applying PRP in the dental clinic and its beneficial outcomes, including reduction of bleeding and rapid healing, hold promise for further procedures. More well designed and properly controlled studies are needed to provide solid evidence of PRP's capacity for and impact on wound healing, soft-tissue reconstruction and (in combination with bone grafts) augmentation procedures, especially in oral and periodontal therapy.

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