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Review Article

Platelet rich plasma—A new revolution in medicine

Vishram Singh[a], Rashi Singh[b,*], Gaurav Singh[c]

[a] Department of Anatomy, Santosh Medical College, India
[b] Department of Paedodontics & Preventive Dentistry, Santosh Dental College & Hospital, India
[c] Section of Dentistry, Springer Nature, India

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ABSTRACT

In the recent years there has been a paradigm shift in consideration of platelets from being just hemostatic cells to actually performing a myrad of diverse functions. The recent use of Platelet Rich Plasma as therapeutic agent is based on its growth factor content and the matrix provided by the platelets themselves. An overview of PRP, its uses in the field of medicine is provided for correct understanding of PRP therapy. Standardization of preparation and administration also remains a challenge due to various variables present. How beneficial are these individually tailored protocols, still remains to be seen.

Blood is mainly liquid plasma containing small solid components such as RBC, WBC and platelets. Platelets contain different growth factors and cytokines contributing to haemostasis and capable of stimulating healing of both bone and soft tissue.

1. Introduction

Platelet rich plasma (PRP) is blood plasma enriched with concentrate of autologous platelets. It was first introduced by Marx et al. in 1998, used in mandibular reconstruction along with cancellous bone marrow grafts. He suggested that addition of PRP accelerated the rate and degree of bone formation.[1]

PRP was made to provide an ideal growth factor delivery system providing the combined effect of fibrin sealing property with growth factors of platelets, at the site of injury.

Growth factors play an essential key role in healing process and tissue formation. Activation of autologous platelet concentrates through thrombin with calcium chloride induces release of growth factors from alpha granules. The various growth factors and cytokines present in PRP include platelet derived growth factor (PDGF), platelet derived angiogenesis factor (PDAF), transforming growth factor beta (TGFβ), fibroblast growth factor, insulin like growth factor 1 (IGF-1), insulin like growth factor 2 (IGF-2), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), interlukin (IL), keratinocyte growth factor, connective tissue growth factor, fibronectin growth factor, CD40L, platelet factor (PF), RANATES.[2] They exhibit chemostatic and mitogenic properties promoting modular cellular functions leading to tissue healing, regeneration and cell proliferation.It also includes three proteins which act as cell adhesion molecules, fibrin, fibronectin and vitronectin.[3]

Platelets directly contribute to formation and synthesis of new tissue through combined effect of platelet growth factors, serotonin, matrix proteinases and tissue inhibitor of metalloproteinase (TIMPS).

The active secretion of growth factors by platelets usually begins within the first 10 min of activation and 95% of presynthesized growth factors are secreted within the first hour.[3]

A platelet count of 10 lakh/ml in 5 ml PRP was proposed as a working definition of PRP by Marx based on the scientific proof of bone and soft tissue healing enhancement.[4] Rugetti et al. studied the relationship between concentrations of platelets in relation to functional activity of human endothelial cells. He thus signified that a PRP platelet has a count of 1 million/ml. This has become the current working definition of PRP. [4]

1.1. Classification

According to the classification proposed by Ehrenfest et al.[5], four main families of preparations can be defined, depending on their cell content and fibrin architecture.[5]

1. **Pure Platelet-Rich Plasma (P-PRP) or leucocyte-poor PRP** products are preparations without leucocytes and with a low-density fibrin network after activation.

* Corresponding author.
E-mail address: drsinghrashi@gmail.com (R. Singh).

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2. **Leucocyte- and PRP (L-PRP)** products are preparations with leucocytes and with a low-density fibrin network after activation. It is in this group that the largest number of commercial or experimental systems exists.
3. **Pure platelet-rich fibrin (P-PRF) or leucocyte-poor platelet-rich fibrin** preparations are without leucocytes and with a high-density fibrin network. They come in a activated gel form, and cannot be injected or used like traditional fibrin glues.
4. **Leucocyte- and platelet-rich fibrin (L-PRF) or second-generation PRP** products are preparations with leucocytes and with a high-density fibrin network.

This classification system was largely cited, advocated, and validated by a multi-disciplinary consensus conference published in 2012.[6]

1.2. Preparation of platelet rich plasma

The source of PRP is blood obtained from the patient, containing limited amount of plasma enriched platelets. It can be prepared by two methodologies based on technique:

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

In general purpose cell separators the volume of blood required is more, around 450 ml and thus are generally used in a hospital set-up environment. Whereas in platelet concentrating cell separators volume of blood required is less thus they can be used in individual setups. The preparation process is similar for both techniques though the anticoagulant used and speed and duration of centrifuge may differ for different systems.

Traditionally a double spin technique is used. The process is as follows:

- Venous blood is drawn from the subject into a vacuumed tube containing anticoagulant, to prevent platelet activation and degranulation.
- The first spin of Centrifugation "Soft spin" causes separation of blood into three layers:
  - Red blood cells (RBC's) -bottom most layer (55% of total volume)
  - Platelet rich plasma (PRP) – an intermediate layer (5% of total volume), known as the buffy coat and is rich in WBCs,
  - Platelet poor plasma(PPP)- top most layer (40% of total volume)
- This is followed by a second cycle of "Hard spin" centrifugation. It is faster and longer than the first spin and allows the setting down of PRP at the bottom of the tube with very few RBC's. An acellular plasma layer (PPP) 80% by volume is found at the top.
- Most of PPP is removed and discarded and PRP is obtained for application.
- A platelet activator/agonist (topical bovine thrombin and 10% calcium chloride) is added to activate the clotting cascade just prior to application, to produce a platelet gel. Calcium chloride nullifies the effect of the anticoagulant used.
- The whole process takes approximately 12 min.

However, in preparation of PRP, there may be a certain risk associated with the use of bovine thrombin which may lead to development of antibodies to factor V, XI & thrombin resulting in life threatening coagulopathies likes stimulating the immune system when challenged with foreign protein. Therefore, other safer method used for formation of PRP is utilization of recombinant human thrombin, autologous thrombin or extra purified thrombin.[7,8]

1.3. Applications

PRP is one such material which is biologically compatible, non toxic,providing scaffold for angiogenesis & new bone growth, osteogenic, resorbable, microporous & easy to handle and is therefore, used for treatment of:

1. Multiple musculoskeletal disorders & regeneration & healing of tissues.
2. In soft connective tissue injuries: Autologous growth plasma being a good source of growth factors is an effective way to induce tissue repair & regeneration.
3. Tissue engineering & cell therapy
4. Facial plastic surgery, eye surgery & cosmetic surgery

PRP yields adequate hemostasis with use of PPP to create a seal to hault bleeding.

1.4. Dental application

1. Oral Implant surgeries
2. PRP is used in combination techniques with bone grafts for guided tissue regeneration as periodontal therapy for intrabony defects in humans.
3. In sinus lift procedures: accelerates healing & reduces healing time with stable bone growth.
4. socket preservation to maintain alveolar bone height.

PRP improves graft incorporation in maxillary & mandibular bone reconstruction. It accelerates the rate in degree of bone formation.

The regenerative potential of PRP was related to strong clinical results such as reduction of pocket depth & gaining attachment with bony grafts.[9,10]

1.5. Conclusion

PRP offers many advantages in different fields in itself & in combination with other materials & techniques. Its uses can be seen in orthopaedic & maxillofacial surgeries, bone reconstruction, tissue engineering, facial & cosmetic surgeries, dental implantology, periodontology & also in various other branches. It facilitates a more rapid soft tissue healing, decreases frequency of intra & post operative bleeding at both donor & recipient sites, aids in initial stability of graft tissue, promotes rapid vascularisation of healing tissue by delivering growth factors inducing regeneration.

PRP proves to be an interesting tool for tissue engineering & developing new area for clinicians & researchers more well designed & properly controlled studies are needed to provide solid evidence for impact of PRP in tissue healing capacity.

Conflicts of interest

None.

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