

Platelet Rich Plasma

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Platelet-rich plasma (PRP) has long been used in maxillofacial and general surgery. There is heightened public awareness and a broadening desire to explore its applications in regenerative medicine. Treatment of injuries of high profile athletes with PRP has been extensively covered with testimonials in the lay press, but evidence-based scientific literature is rare.

Platelet Rich Plasma (PRP): Key Points

- Well characterized as a bioadhesive
- Basic science supports role of platelet-derived growth factors in tissue repair and regeneration
- Lack of Level 1 evidence of efficacy; few randomized controlled trials, conflicting results
- Heterogeneity of PRP Preparations
 - Variable yields and activity; Interfering factors not well characterized
- Optimal "dose"/regimen unknown
 - Single vs. multiple treatments
 - Is optimal dose tissue dependent?

Basic science suggests that PRP might augment healing and repair. In addition to their primary role in hemostasis, platelets are circulating reservoirs of growth factors. Platelet granule release upon activation results in the delivery of platelet-derived growth factor (PDGF), transforming growth factor (TGF) β , vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), fibroblast growth factor (FGF), and epidermal growth factor (EGF). These stimulate cell proliferation

and collagen production, and initiate angiogenesis and cell differentiation, all important factors in wound repair.¹ However, their physiological role, efficacy and optimal concentrations for regeneration in disparate tissues (bone, tendon, muscle, skin, etc.)

with different pathological profiles (acute vs. chronic injury, degenerative disease) is unknown.

One challenge in characterizing the in vivo effects of PRP is the highly variable nature of autologous preparations from different individuals and the different growth factor yields in products made from similar platelet concentrations using the same methods. Comparison of growth factor yields across technologies, even those utilizing the same basic methods, shows even greater variability.² The actual growth factor "dose" may be affected by premature platelet activation during manipulation, presence of growth factor absorbing proteins (fibrin monomers, thrombospondin), variation in procedures and other factors associated with the biodynamic properties of the applied matrix. Thrombin and calcium chloride are often used to activate platelets upon application. In short, platelet count and measurement of growth factor yields may not be predictive of the actual growth factor delivery and ultimate biofunction. The environment in which PRP is prepared (blood bank, OR, physician office) and the expertise of associated personnel in the particular method used may also influence product quality.

While there is a plethora of literature exhorting the benefits of applications of PRP, the vast majority consists of case reports and anecdotal evidence. Randomized controlled clinical trials yielding Level 1 evidence are rare, many studies are underpowered, and they often produced conflicting results. For example, several clinical trials with PRP injections in sports medicine have been conducted. A study by de Vos et al. published in JAMA compared the effectiveness of PRP injection with that of saline combined with eccentric exercises in chronic Achilles tendinopathy and found no difference in pain improvement and activity.³ Conversely, Peerbooms et al. concluded that treatment of patients with chronic lateral epicondylitis with PRP reduced pain and significantly increased function as compared to corticosteroid injection (but no placebo group).⁴ Unfortunately, the quality and quantity of activated growth factors contained in these injections were neither controlled nor known.



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Recently, Driver et al. performed a small prospective, randomized, controlled, blinded multicenter trial of PRP for the treatment of diabetic foot ulcers. PRP was prepared using a compact point-of-care system suited to the clinic environment. Platelet content and growth factor yield were not measured, and “healing” was determined by measurements of wound size and clinical observations (exudates, tunneling, odor, necrotic tissue, and granulation) for 12 weeks. Bovine thrombin was used to activate the PRP. The authors concluded that PRP gel treated

wounds were significantly more likely to heal than control (saline) gel treated wounds. Further, they observed that exposure to the bovine thrombin did not cause Factor V inhibition, nor did the repeated withdrawal of the small amount of blood required to manufacture PRP affect the patient’s hemoglobin, hematocrit or platelet count. However, the sample size was

small, post-hoc reanalysis was required to achieve significance, and additional work is needed to evaluate more complex diabetic foot ulcers, such as those with exposed tendon or bone, or in patients with more advanced vascular disease.⁵

Patient factors such as age, comorbidities, and intake of prescription and over-the-counter medications may also influence the overall results of PRP therapy. Some pathologic processes in selected tissues may not be corrected, even with application of the appropriate growth factors. For example, fibroblasts present in chronic ulcers respond poorly to PDGF, FGF and EGF, even though adequate numbers of growth factor receptors are present.⁶ The mechanism of such suppression is not understood, but delivery of a “mega dose” of platelet-derived growth factors is unlikely to resolve the lesion.

Variable Factors in PRP Preparations

- Platelet concentration
- Method of preparation and activation
- Presence of growth factor absorbing proteins
- Tissue to be treated, added grafting materials
- Pathophysiologic process of lesion
- Patient-specific factors (comorbidities, medications)

For acute injuries, the question remains whether use of PRP for pain control and expedited healing might lead to premature return to activity and more injury, especially in athletes. Certainly, the pathophysiology of acute injury differs from that of chronic injury. Concerns about stimulation of fibrosis or promotion of tumor cell growth due to mitogenic effects also need to be addressed,⁷ which will require long term clinical follow-up.

In conclusion, while robust evidence demonstrates the ability of growth factors to affect tissue regeneration, definitive evidence of their benefit as delivered by specific PRP preparations in clinical situations is lacking. More study is required to define benefit for specific preparations, pathologies and patients. It is unlikely that PRP will prove to be a regenerative panacea for all patients and in all tissues. More Level I evidence and process standards are needed before this therapy can be considered mainstream.

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