Platelet-rich plasma: Facts and fallacies.

Platelet-rich plasma (PRP) is defined as plasma with a concentration of platelets above baseline value (peripheral blood). In addition to its main function in securing haemostasis, our understanding of platelets involvement in tissue healing have expanded over the last two decades. Platelets participation in tissue healing occurs via the release of various bioactive molecules (cytokines and growth factors) stored within the α- and dense-granules that occurs upon activation (Table 1) [1].

Table 1:

Bioactive Molecules Found in the α-Granules of Platelets[a]

General Activity Categories	Specific Molecules	Biologic Activities
Growth factors	TGF-β	Promotes matrix synthesis
	PDGF	Chemoattraction, cell proliferation
	IGF-I, II	Cell proliferation, maturation, bone matrix synthesis
	FGF	Angiogenesis, fibroblast proliferation
	EGF	Cell proliferation
	VEGF	Angiogenesis
	ECGF	Endothelial cell proliferation, angiogenesis
Adhesive proteins	Fibrinogen	Blood clotting cascade (fibrin clot formation)
	Fibronectin	Binds to cell-surface integrins, affecting cell adhesion, cell growth, migration, and differentiation
	Vitronectin	Cell adhesion, chemotaxis
	Thrombospondin-1	Inhibition of angiogenesis
Clotting factors	Factor V, factor XI, protein S, antithrombin	All play a role in thrombin activation and eventual fibrin clot formation
Fibrinolytic factors	Plasminogen	Plasmin production (leads to fibrinolysis)
	Plasminogen activator inhibitor	Regulation of plasmin production
	α-2 antiplasmin	Inactivation of plasmin
Proteases and antiproteases	TIMP-4	Regulation of matrix degradation
	Metalloprotease-4	Matrix degradation
	α1-antitrypsin	Inhibits a wide variety of proteases and enzymes
Basic proteins	Platelet factor 4	Inhibition of angiogenesis
	β-thromboglobulin	Platelet activation, inhibition of angiogenesis
	Endostatins	Inhibitors of endothelial cell migration and angiogenesis
Membrane glycoproteins	CD40 ligand	Inflammation, synthesis of interleukins, and integrin production; platelet endothelial cell adhesion, cell signaling, modulation of integrin activation molecule-1 (PECAM-1) on leukocytes
	P-selectin	Vascular cell adhesion molecule, aids in binding and recruitment of leukocytes to inflamed tissue

[a]TGF, transforming growth factor; PDGF, platelet-derived growth factor; IGF, insulin-like growth factor; FGF, fibroblast growth factor; EGF, epidermal growth factor; VEGF, vascular endothelial growth factor; ECGF, endothelial cell growth factor; TIMP-4, tissue inhibitor of metalloprotease-4.

Adopted from Foster et al, (2009)[1]

These cytokines and growth factors influence cellular chemotaxis, cell migration, cellular mitosis, extracellular matrix production, and angiogenesis. Moreover, these bioactive molecules also signal cells to proliferate and influence maturation, differentiation and ultimately tissue repair [2].

More recently, administration of biological substances that is rich in platelets and growth factors has gained a lot of attention. Substances such as autologous blood and blood products including autologous condition serum (ACS), platelet rich plasma (PRP) and platelet-rich in fibrin matrix (PRFM) are currently used for their potential benefits in accelerating soft tissues healing (muscles, tendons and ligaments) despite limited clinical evidence [3].

Our extensive literature review identified only three in vivo laboratory studies, two case reports and one pilot human controlled trial on PRP therapy for muscle injury. Studies vary in their methodology; including type of injectable substance use (ACS, PRP and PRFM), preparation of injectable substance, dosages, frequency of injections, type of muscle injury and the follow-up period.

In vivo laboratory studies reported significantly faster muscle regeneration (myogenesis) demonstrated by immunohistochemical detection of Myogenin and MyoD (markers of muscle regeneration). Moreover animals in the intervention group also demonstrated earlier functional recovery on maximal isometric torque assessment [2,4,5].

The two case reports found athletes treated with autologous platelet rich in growth factors (PRGF) and platelet enriched plasma (PEP) achieved full recovery within a period of one month. Both case reports concluded that application of platelet concentrated plasma is safe and efficacious for grade-II and grade-III muscle injury [6,7].

Only one pilot human controlled trail was available at the time of this review.[4] The study was a non-randomised and non-blinded trial of professional athletes diagnosed with acute second-degree muscle injury. Intervention group received ACS 2.5 ml of ACS injection administered every second day (mean 5.4 injections/athlete) until full recovery was achieved. Even though this study found a significant reduction in DRP among athletes treated with ACS (16.6±0.9 days vs. 22.3±1.2 days, p=0.001), the study design has been question [3,8,9] as it lacks robustness that may restricts

interpretation of the findings with low methodological quality score (PEDro scale = 4/10) [10].

Based on the systematic review conducted, the efficacy of PRP therapy on muscle recovery in humans remained unanswered. There is some evidence to suggest acceleration of muscle recovery (histologically and functionally) with local injection of ACS, PRP and PRFM from in vivo laboratory studies.

At present there is lack of consistency in the preparation, application and dosing methodology in the use of PRP. Therefore the current evidence is insufficient to recommend for or against routinely using PRP in muscle injury. Studies using robust clinical design are needed to evaluate the efficacy of PRP for the treatment of muscle injury.

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