



Review article

Optimisation of platelet concentrates therapy: Composition, localisation, and duration of action

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Abstract

Platelet concentrates (PC) generally refers to a group of products that are prepared from autologous blood intended to enhance healing activities. PC therapy is now very popular in treating musculoskeletal injuries; however, inconsistent clinical results urge the need to understand the working mechanism of PC. It is generally believed that the platelet-derived bioactive factors are the active constituents, and their bioavailability in the vicinity of the lesion sites determines the treatment efficacies. Therefore, the composition, localisation, and duration of the action of PC would be key determinants. In this review, we discuss how different preparations and delivery methods of PC would affect the treatment outcomes with respect to clinical evidence about PC therapy for osteoarthritis, tendinopathies, rotator cuff tears, anterior cruciate ligament injuries, and bone fractures. This review can be used as a quick guide for the use of PC therapy and provide insights for the further optimisation of the therapy in the near future.

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Introduction

Platelet concentrates (PC) has currently attracted much attention in the field of regenerative medicine, with its high-safety profile, ease of preparation, and broad-application profile. The most common form of PC is platelet-rich plasma (PRP). In theory, the concept of PRP is to harness and concentrate the platelets, which have self-healing potential and are present in everyone's blood.

After wounding, platelet activation is regarded as the first line of events responding to injuries and initiating the healing

responses, which involve release of sufficient bioactive factors that orchestrate various processes like angiogenesis and recruitment of healing cells to the lesion sites. PC therapy involves triggering the general natural healing process with a supplement of highly concentrated bioactive factors, regardless to the pathological processes or injury mechanisms. Thus, various forms of PC are used to boost up self-healing in a wide spectrum of musculoskeletal disorders or injuries, including osteoarthritis (OA), tendinopathies, rotator cuff tears, anterior cruciate ligament (ACL) injuries, and bone fractures. However, due to large variations in the preparation and administration methods, the clinical outcomes of PC therapies for musculoskeletal disorders or injuries are inconsistent.^{1–5} Factors that may affect its treatment efficacies are as follows: (1) composition of PC; (2) localisation of PC to the region of interest; and (3) keeping PC *in situ* for sufficient duration to achieve the

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therapeutic effect. In the following sections, we will explore how different preparations and delivery methods of PC would affect these factors and examine whether these factors have been addressed in the currently available best clinical evidences about the PC therapy for OA, tendinopathies, rotator cuff tears, ACL injuries, and bone fractures.

Previous reviews or systematic reviews about PRP or PC chiefly covered the biology of PRP, preparation of PRP, or effects of PRP on particular type of soft tissue injuries. This review combined an overview of PRP and a systematic review of its treatment effect on five major applications in order to evaluate the operational factors that may affect treatment effects. While previous reviews chiefly focused on the issues of composition and activation of PRP, this is the first review addressing the importance of localisation and duration of action of PRP.

Composition of PC

Forms of PC

Numerous preparations of PC were developed, but the terminology and classification have not been standardised yet. Three classification systems for PC were proposed including four families,⁶ PAW,⁷ and DEPA systems,⁸ which are primarily based on composition (platelet, fibrin, activators, leucocytes, erythrocytes),^{6,7} injecting dosage,⁷ or preparation efficiency into account.⁸ PAW and DEPA systems involve grading of PC according to the platelet count and preparation efficiency; however, there is still no clear indication of the platelet dose that offers the best treatment effect. Therefore, we prefer to follow the classification simply based on the presence of individual components suggested by the four-family system (Table 1). The most common form of PC is PRP: pure (P-PRP) and leucocyte PRP (L-PRP), which are prepared by centrifuging whole blood with anticoagulants and optionally supplementing with platelet activators (Ca²⁺ or thrombin) before use. These PRP preparations are liquid and therefore injectable; however, activation will lead to the formation of blood clot. Alternatively, PC could be prepared in solid form as platelet-rich fibrin (L-PRF, P-LRF) which are only useful for topical application⁹ or surgical implantation.¹⁰

Preparation methods for PC

With the injectable nature and ease of preparation, PRP are most commonly used, and there are a number of commercially

available PRP preparation devices (Table 2). Indeed, most commercially available devices are for PRP preparation, and fewer devices are available for PRF preparation. For PRP preparation, most of the devices involve the use of centrifugation to concentrate the platelets from blood with anticoagulants, and platelet activator is added before use. In some devices, special accessory to reduce the leucocyte counts is included. Most of the preparations use either closed or semi-closed systems. Compositional analyses of different PRP preparations revealed large variations in platelet and leucocyte counts. In order to determine the best kinds of preparations, further examination of the roles of individual components of PRP is necessary.

Commercial systems such as Cascade are commonly used for to generate P-PRF; while L-PRF is usually “homemade” by common centrifuge.¹⁸ Many commercial systems such as Magellan, Gravitational Platelet Sequestration System⁶ are developed to prepare PC as PRP. Their uses are more flexible since they can be applied by coating or immersion to the graft,²⁴ by spraying topically to the wound,²⁵ (e.g., with applicators CoAxial Spray Kit, Biomet Biologics), and most popularly by injection.

Constituents of PC

Platelet counts

The idea of using platelet supplementation to treat musculoskeletal injuries or disorder is primarily based on the ability of platelets to trigger healing response; however, the number of platelets required for efficacy remains unknown. A study of the concentration effect of platelet on ACL graft healing showed that the enhancement did not differ with 5-fold or 3-fold platelet concentration.²⁶ The inhibitory effect on proliferation of dog alveolar bone cells²⁷ and human oral fibroblasts and osteoblasts²⁸ was even observed with high dose of platelets. Moreover, the required number of platelets may vary according to the tissue types,²⁹ lesion size, and pathological conditions. Thus, it is difficult to define the quality standards for PRP simply based on platelet counts. As thrombocytopenia may not have direct impact on dermal healing³⁰ or tendon healing,³¹ it is very likely that the absolute platelet count may not be the sole determinant for healing outcomes. It should also be noted that for PC to take a positive biological effect on different clinical conditions, the requirement for platelet conditions may be different. Other factors such as localisation and activation status should also be taken into considerations.

Leucocytes

As leucocytes express proinflammatory properties, their presence in PC is regarded as unfavourable, and it is speculated that L-PRP or L-PRF would have negative effects, especially for clinical conditions with chronic inflammation such as OA^{32,33} and tendinopathies.³⁴ Moreover, L-PRP was found to be less effective than P-PRP in bone repair.³⁵ In contrast, the putative antibacterial function of leucocytes is regarded as favourable for wound healing³⁶; however, it

Table 1
Composition of different platelet-rich products modified based on the four-family system.

Type of platelet concentrates	Contain leucocytes?	Need activation?	Status
Leucocyte platelet-rich plasma	Yes	Yes/No	Gel/liquid
Leucocyte platelet-rich fibrin	Yes	Yes	Solid
Pure platelet-rich plasma	No	Yes/No	Gel/liquid
Pure platelet-rich fibrin	No	Yes	Solid

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