
COMMENTARY & PERSPECTIVE

Platelet-Rich Plasma à la Carte

Commentary on an article by Satoshi Terada, MD, et al.: “Use of an Antifibrotic Agent Improves the Effect of Platelet-Rich Plasma on Muscle Healing After Injury”

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Platelet-rich plasma (PRP) is the latest orthopaedic panacea, administered promiscuously for whatever ails the musculoskeletal system. At the last count this included torn tendons and ligaments, unhealed bones, damaged cartilage, injured muscle, and osteoarthritis. Beyond orthopaedics, use of PRP is associated with treatments for hair loss, wrinkles, and erectile dysfunction. There is only one snag—it may not work, at least not for all of the indications, when using PRP version 1.0.

A detailed meta-analysis, published recently in this journal¹, reported that “use of PRP provided no significant benefit” for treating bone and soft-tissue injuries. Another recent meta-analysis of the use of PRP in wound-healing yielded similar conclusions². Part of the problem in assessing the merits of PRP is the poor quality of the clinical studies^{1,2}. However, there are additional issues.

Several different devices are approved by the FDA (U.S. Food and Drug Administration) in the United States for generating PRP, and these deliver products of diverse composition with regard to the platelet concentration, presence of leukocytes, contamination by erythrocytes, and concentration of certain growth factors. Moreover, repeated PRP preparations from the same individual vary in composition, rendering standardization all the more difficult³. Finally, there is the complexity of the product.

Use of PRP is usually justified by the physician because it contains a “rich cocktail of growth factors.” This may be true, but it contains a lot of other things as well. The platelet secretome has over 300 proteins⁴, including interleukins (ILs), chemokines, proteinases, inhibitors of proteinases, and adhesion molecules. Attention has focused on the proteins present in PRP, but platelets are also a rich source of sphingolipids, thromboxanes, purine nucleotides, serotonin, calcium, and many other mediators. Although PRP is widely thought to have anti-inflammatory properties, several components (such as IL-1, IL-6, and IL-8) are pyrogens, whereas others (such as transforming growth factor-beta [TGF- β]) are pleiotropic. Moreover, ingredients that are an advantage in one setting may be a disadvantage in another. For example, vascular endothelial growth factor (VEGF), a prominent angiogenic component of PRP, might be helpful for bone healing, which has an absolute need for angiogenesis, but a hindrance for repairing cartilage, which is avascular.

Terada et al. address the point that PRP cannot be all things to all tissues. Their solution is to customize PRP for specific indications, an innovative and potentially rewarding concept. They demonstrate the utility of this approach with a murine model of skeletal muscle injury and repair. PRP has the potential to improve healing by enhancing angiogenesis and myoblast proliferation, but the presence of TGF- β impairs healing by promoting fibrosis and inhibiting satellite cell differentiation.

To improve the performance of PRP in their model, the investigators simultaneously treated the injured mice with losartan, an orally active inhibitor of the Smad signaling pathway used by TGF- β . Administration of losartan in this way accelerated the rate of muscle vascularization while inhibiting fibrosis, leading to improved functional recovery. Losartan is already approved by the FDA for the treatment of hypertension and congestive heart failure. This should facilitate the clinical translation of their findings, assuming that short-term use of losartan does not have adverse cardiovascular sequelae in subjects who do not otherwise need it. However, as the authors point out, further work is needed to establish the optimal dose, timing, and frequency of application. This is true of all applications of PRP, bearing in mind that more may not necessarily be better.

More generally, the approach of Terada et al. points the way to further adaptations of PRP for specific uses. In addition to employing the combination therapy of the type exemplified in their article, it is possible to imagine modifying PRP preparations for other particular indications by addition or subtraction. Looking ahead into the era of personalized medicine, there is the potential to customize PRP for individual needs. Advances such as these, coupled with better science and improved clinical trials, could begin a new chapter in the evolution of this tantalizing product.

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*The author did not receive payments or services, either directly or indirectly (i.e., via his institution), from a third party in support of any aspect of this work. He, or his institution, has had a financial relationship, in the thirty-six months prior to submission of this work, with an entity in the biomedical arena that could be perceived to influence or have the potential to influence what is written in this work. The author has not had any other relationships, or engaged in any other activities, that could be perceived to influence or have the potential to influence what is written in this work. The complete **Disclosures of Potential Conflicts of Interest** submitted by authors are always provided with the online version of the article.

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