

PRP: more words than facts...

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The use of platelet concentrates is not a new concept in medicine, but it is relatively new for clinical applications in orthopaedics and sports medicine [9].

Interest in this biological approach has been aroused in these fields in recent years, after the comparative trial on the treatment of chronic elbow tendinosis published by Mishra et al. [6], which showed promising results, but even more so after anecdotal reports by the media at the beginning of 2009. This increasing interest is supported at different levels: in fact, the market on this blood derived product was evaluated 45 million \$ in 2009 and is expected to reach more than 120 million \$ in 2016 [3], and the literature also recorded an impressive number of new articles on this treatment. The attractive possibility of using patients' own growth factors, concentrated and in physiologic proportions, to enhance reparative processes in tissues with low healing potential and promising preliminary clinical findings and their safety explain the wide use of PRP. A PubMed research on platelet-rich plasma, platelet gel, or platelet concentrate in human studies in orthopaedics and sports medicine found 109 articles, of which 82 published from 2010. Numerous and heterogeneous applications have been documented, ranging from tendinopathies to early osteoarthritis, from bone healing to muscle regeneration, and aiming to manage different clinical aspects, from the management of pain to tissue regeneration in both acute and chronic clinical settings, as minimally invasive standalone treatment or as augmentation

procedure during surgical procedures [4]. However, although the popularity of PRP has reached a peak, the scientific evidence for this procedure is still in its infancy: most of the studies have poor quality, and the real potential of PRP is far from being proven [4].

It is interesting to notice that of the published articles selected on this topic using the previously mentioned research criteria, less than half were clinical trials, whereas 58 were just literature analyses of the available evidence on PRP. This means that to date there is more talk than real attempts to understand how this treatment could be useful in the clinical practice. Recently, even a meta-analysis has been published trying to understand the quality of the trials and the evidence for PRP use in musculoskeletal lesions [7]. Despite the effort of the authors to use this scientifically sound methodology in the hope of identifying patterns among study results or other interesting relationships that may come to light in the context of multiple studies, results were predictably disappointing, underlying the limits of the current literature. The point is that a meta-analysis is a statistical procedure that integrates the results of several independent studies considered to be "combinable" [2], but unfortunately to date there are not enough studies to be compared.

In fact, the variables differing among studies are countless: first of all the clinical condition, the type and phase of the pathology, the minimally invasive or surgical application, the combination with different invasive or conservative treatments, but also the differences in what is called PRP. This acronym includes different procedures that produce different platelet concentrates, which we could try to summarize in macro-categories [1], but the truth is that every single product differs in aspects that could markedly influence the clinical application, such as blood volume harvested, use of anticoagulant, number and

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speed of centrifugations, volume of PRP obtained and injected, activation method, integrity of platelets, cryo-preservation, presence of other cells, etc. Also in the application modality, there is no homogeneity, with different amounts, timing and modality of PRP delivery, and post treatment management and evaluation methods differ as well. Even the definition of PRP itself is still far from being established thus questioning which products can really be called “PRP” (concentrate more than 2 times? More than 4 times? More than 1 million platelets? With or without leucocytes? ...). The difficulties in this field are further increased by recent findings showing the extreme variability in the growth factors obtained not only by different procedures [8] but even from the same subject with the same procedure during different blood samples [5].

Taking this into consideration, it appears clear that systematic reviews or even more meta-analyses are of limited usefulness in this phase. Whereas the desire to communicate one’s own point of view on such a fashionable topic is understandable, basic and clinical researchers should spend more effort in answering the many questions still open on this field, documenting the clinical experience and performing more preclinical and clinical high level studies to demonstrate the real potential of this biological approach. Finally, considering the high number of variables that make the literature confusing and hinder the progress in this field, we suggest performing more trials with direct comparison of different platelet concentrates to clearly demonstrate benefits, limits and indications of each product for every specific clinical application.

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