Rev Esp Cir Ortop Traumatol. 2013;57(4):237–239

Revista Española de Cirugía Ortopédica y Traumatología

www.elsevier.es/rot

LETTER TO THE EDITOR

Therapeutic potential of platelet rich plasma. Reflections on its research and development☆

Potencial terapéutico del plasma rico en plaquetas. Reflexiones sobre la investigación y su desarrollo

Dear Editor,

At present biological therapies represent an area of ongoing research and development in medicine, with a present full of applications and a promising future. Numerous therapeutic techniques have been developed in the field of Traumatology, Orthopedics and Sports Medicine in recent years. The potential applications of platelet rich plasma (PRP) stand out due to the number of publications and different lines of research. There is also considerable controversy regarding its use.[1]

A review of the scientific literature clearly shows the increasing number of publications on this subject. Over 1400 items have been published internationally in relation to the different types of PRP in the past 2 years. The Spanish Journal of Orthopedics and Traumatology has published more than 30 articles. However, this field of research is supported by scarce scientific evidence regarding its benefits, as there are few articles with evidence level I.

A prospective, randomized, double-blind and multicentre article was published in *Arthroscopy* in August 2012, which compared infiltrations with plasma rich in platelet growth factors and hyaluronic acid regarding pain reduction.[2] The results were in favor of the use of plasma. It is worth noting the difficulty in assessing pain, regardless of the rating scales employed, due to the subjective component of perception. In January 2013, this study obtained the award for ''Best article with level I evidence published in *Arthroscopy* in 2012''.

Previously, a meta-analysis of published scientific literature on the different uses of platelet rich plasma (PRP) was conducted in early 2012.[3] In the conclusions section, the authors stated that there was no significant evidence supporting the use of plasma. The study assessed the results of research with various different products (plasma with leukocytic or hematic content, whilst others used plasma containing only platelets), different techniques (ultrasound-guided injections in some studies, whilst others did not use this kind of aid) and diverse locations (tendons, muscles and intra-articular spaces). In other words, the results were hardly comparable.

In Spain, there are various centers and researchers working in the field of biological therapies. These are essential because, regardless of the period of crisis or prosperity, through their efforts and with the support of the institutions, we will be able to discover the benefits of new therapies and to develop applications with extensive social impact.

The position on the use of a therapeutic technique is determined by the degree of scientific evidence regarding its benefits, that is, it must be based on information, on published articles, and evaluate the potential benefits, taking into account that any risks must be minimized.

Novel technique = benefits − risks > 0 (variable: costs)

In my opinion, this position is not so much for or against use, because it is likely that this is not sufficiently supported at the outset. However, we should always be in favor of *research*, seeking the benefit for patients.

Therefore, we must base the use of new techniques on the published literature and the potential benefits, developing research projects and minimizing costs to make them viable, in order to advance.

Symphony of signals

Cells interact with each other as an ''orchestra'', based on a large number of signals, such as the numerous proteins acting as messengers. Small changes in our therapeutic actions can lead to very disparate results. The concentration of chondrocytes implanted in chondral

☆ Please cite this article as: González-Iglesias J. Potencial terapéutico del plasma rico en plaquetas. Reflexiones sobre la investigación y su desarrollo. Rev Esp Cir Ortop Traumatol. 2013;57:237–9.

lesions or the regularization of mechanical stimuli may influence the clinical outcomes of our interventions. It is essential to investigate the underlying biological principles at a cellular and molecular level[4] and thus be able to develop new therapeutic tools for processes such as inflammatory and degenerative cartilage diseases.

Difficulties

At present, there is an excess of indications to be determined. The same set of signals are used for an acute muscle injury (fibrillary injury) and a chronic injury (predominance of fibrosis and cysts). The same signals are used at different times, when muscle repair has a clear temporal pattern (different molecules are predominant at different times). The number of infiltrations into a muscle tear is also variable. If, following a second infiltration, we observe scarce improvement during the third week of recovery, why continue with a third infiltration? If there is no favorable initial evolution, the process is likely to continue its natural course.

The specific benefits may cause conflicts of interest and produce biases in studies or highlight differences with scarce statistical significance in favor of or against a particular technique.

The difficulty in comparing studies is characteristic of many novel biological therapies. Homogenizing the type of products, doses, techniques and application times requires considerable research. How can we compare the results of a study where PRP is applied in a tendon with those of another study applying plasma with different cell lines, that is, with different biological signals? Let us maintain the perspective. We do not even know the different protein concentrates being introduced in the lesion. These are not previously analyzed and these concentrations can vary greatly from one person to another, and even within the same person at different times.

Controversy

In November 2009, Nin et al. published an article in *Arthroscopy* evaluating the use of PRP on autogenous grafts used in anterior cruciate ligament reconstruction.[5] In the conclusions, they did not indicate any clinical or biomechanical variations from the use of PRP with the methodology employed. They emphasized the need for further clinical studies to show the effectiveness of PRP in this type of surgery. The article led to an interesting exchange of views in June 2010 in the same journal (Letters to the Editor), which reviewed important issues such as the process of obtaining PRP and the protocol for application of plasma during surgery, highlighting the need for prospective, randomized, double-blind studies with level I evidence.

Present and future

This is a constantly evolving field and one where recent studies conducted in our country have had considerable international impact. Patients come to us with questions that arise after news items related to biological therapies appear in the press and on television. Our duty is to *know the different therapeutic possibilities*, to seek and analyze the articles with *the highest level of scientific evidence*, and to use the treatments which can offer the greatest benefit for our patients.

We must encourage and develop research, from the laboratory to clinical practice, and legislation plays a major role in this regard. The next law which considers plasma rich in platelet growth factors as a *special medication* must help to regulate its use and to compare different studies.

In coming years, research lines which achieve greater development will be those where *combination therapies* are prominent, going from the repair of tissues to their regeneration. The use of biological signals, such as platelet growth factors, along with the culture of different cell lines, will lead to significant advances with a great impact on the quality of life of our patients.

Level of evidence

Level of evidence v.

Ethical responsibilities

Protection of people and animals. The authors declare that this investigation did not require experiments on humans or animals.

Confidentiality of data. The authors declare that this work does not reflect any patient data.

Right to privacy and informed consent. The authors declare that this work does not reflect any patient data.

Conflict of interests

The authors have no conflict of interests to declare.

References

1. Nguyen RT, Borg-Stein J, Mclnnis K. Applications of platelet-rich plasma in musculoskeletal and spots medicine: An evidence-based approach. Am Acad Phys Med Rehabil. 2011;3:226–50.
2. Sánchez M, Fiz N, Azofra J, Usabiaga J, Aduriz Recalde E, Garcia Gutierrez A, et al. A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) Versus hyaluronic acid in the short-term treatment of symptomatic knee osteoartritis. Arthroscopy. 2012;28:1070–8.
3. Sheth U, Simunovic N, Klein G, Fu F, Einhorn TA, Schemitsch E, et al. Efficacy of autologous platelet-rich plasma use for orthopaedic indications: A meta-analysis. J Bone Joint Surg. 2012;94:298–307.

4. Goldring MB, Marcu KB. Cartilage homeostasis in health and rheumatic diseases. Arthritis Res Ther. 2009;11:224, http://dx.doi.org/10.1186/ar2592. Online.
5. Valenti Nin JR, Mora Gasque G, Valentí Azcárate A, Dámaso Aquerreta Beola J, Hernandez Gonzalez M. Has platelet-rich plasma any role in anterior cruciate ligament allograft healing? Arthroscopy. 2009;25:1206–13.

J. González-Iglesias

Unidad de Terapias Biológicas, Hospital San Juan de Dios, Santurce, Vizcaya, Spain

E-mail addresses: javi.g.iglesias@gmail.com, jgiglesias@hsjd.es