EDITORIAL

The use of platelet rich plasma in the treatment of soft tissue injuries in professional football: a clinical approach through genetics

El uso de plasma rico en plaquetas en el tratamiento de lesiones de tejidos blandos en el fútbol profesional: un enfoque clínico a través de la genética

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Return to play in professional football is equivalent to players training and competing again with their team after an injury process. For that to happen, there is an individualized way forward, in which the competition needs will surely come under. With the team playing mostly two matches a week during the season, medical teams are forced to seek for different ways to speed up the return to play. Also, competitiveness, social and economic factors may be responsible for a rush in the process. The search for minimally invasive and recovery accelerating treatments of these injuries is of great importance, as it may lead to a reduction in return to play time.

Tissue repair in soft tissue injuries is known to be often a slow and sometimes an incomplete process. Besides, it mostly leaves many sequelae that may affect the player’s performance. Soft tissue injuries have a great impact on elite football players, so that a fast recovery as efficient as possible is of primary importance for the return to play to be fulfilled.

The use of growth factors is thought to be a useful minor invasive treatment in clinical practice because it promotes rapid healing with high-quality tissues and allows a nearly safe and faster return to unrestricted activity. Platelet-rich plasma (PRP) is a simple and minimally invasive way to obtain a natural concentration of autologous growth factors, including IGF, EGF, TGFβ1, FGF2. PRP. It is currently being widely experimented in different fields of medicine due to the thought of its ability to help in the regeneration of tissue with low healing potential. Since PRP was first introduced as topical adjuvant therapy to treat chronic ulcers in the late 1980s,\textsuperscript{1} its use has been extended to many fields of medicine, such as dermatology,\textsuperscript{2} dentistry\textsuperscript{3} and maxillofacial surgery.\textsuperscript{3} Recently, PRP injections have emerged as a non-invasive treatment also in sports medicine,\textsuperscript{4} where they are used to treat acute or chronic tendinopathy,\textsuperscript{5,6} muscle\textsuperscript{7,8} and ligament\textsuperscript{9,10} injuries. Most team medical services from professional disciplines such as American football, basketball, hockey and football use PRP regularly for soft tissue injuries to be treated.\textsuperscript{11,12}

Although PRP are frequently used day to day in professional football teams, the existing literature shows

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promising preclinical results but contradictory clinical findings in individual response to treatment in sports injuries. Nonetheless, there are plenty of studies with contrary results, where no evidence was found in clinical outcomes between PRP and placebo. This contradictory literature may exist due to a lack of agreement when developing PRP clinical studies, leading to a difficult discussion. There is no consensus in needle size, type of injury, specific anatomic location of the injury, injection time or injection frequency. Nevertheless, professional teams seek for the shortest route to recovery and for that, they sometimes choose invasive treatments with few evidence. Also, these contradictions could be due to inter-individual differences in the presence of single nucleotide polymorphisms (SNPs) in genes related to PRP and/or their receptors. These SNPs can determine a greater or lesser response to treatment and consequently a shorter or longer recovery time.

Genetics and individualization: the key of success?

The speed and progression of recovery is under the influence of different elements including the biochemical make-up of the individual. Issues such as the anatomic variability between human beings and a greater understanding on the location and collagen type of the tendon, ligament or muscle injury impacts the efficiency of treatments, and should be considered when using PRP.

The composition of the bioactive molecules that constitute PRP impact the inflammatory, proliferative and remodelling phases associated with healing. Nonetheless individuals are under the influence of its own genetic characteristics, so that success in treatment may be variable. Nowadays genetics has gained importance in the field of sports medicine due to its capability of injury risk severity and recovery time prediction in soft tissue injuries through biomarkers such as HGF, ACTN3 or SOX15. Thus individualization should be mandatory when planning a return to play.

In recent years there has been an increase in research into genes related to soft tissue healing. SNPs in genes that codify for these growth factors could influence treatment effectiveness and explain differences observed in recovery times. Some growth factors such as BMP-2, TGF and FGF have shown promising results improving the tendon-bone healing process related to ACL injuries in vitro. Also, graft remodelling and maturation may be accelerated by the role of PDGF, TGF-b1 and IGF-1. Future literature has to focus on examining the maximum possible number of SNPs in PRP-related genes (or their receptors) in order to identify a gene signature that promotes tissue healing and to determine an objective measurement of an individual’s predisposition to recovery after this specific treatment. (Table 1).

**Table 1** Best genes linked to PRP or their receptors.

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<tr>
<th>Candidate Growth Factors</th>
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<tr>
<td>Insulin like Growth Factor (IGF-1)</td>
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<td>Transforming Growth Factor b1 (TGFb1)</td>
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<td>Endothelial Growth Factor (EGF)</td>
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<td>Fibroblast Growth Factor (FGF)</td>
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<td>Platelet-Derived Growth Factor (PDGF)</td>
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**Conclusions**

Further studies of these SNPs may shed light on the tendency of certain individuals to recover more rapidly and more completely from injuries and may help identify individuals with an enhanced injury repair system. That could be the cornerstone to classify patients within “good or bad responders”. Despite the wide use of PRP injections, research into their clinical efficiency is still in its infancy, and more investigation is required to confirm preliminary results and provide a stronger scientific evidence.

**Compliance with ethical standards**

Conflict of interest: None declared.

**References**

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