



## Would you have an injection without knowing its formula? New challenges in platelet-rich plasma therapy

Theodorakys Marín Fermín<sup>1</sup> · Marius M. Scarlat<sup>2</sup> · Markus Wilhelm Laupheimer<sup>1</sup>

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After developing vaccines for COVID-19, the general population raised many concerns regarding the nature and composition of this valuable tool in controlling the pandemic. A sector of the people refused to vaccinate, worried about long-term side effects, raising questions about alterations of their genomics, among others. On other register, many patients seeking injection therapies for cosmetic purposes or degenerative joint diseases rarely question the composition of orthobiologics and consent to their treatment with vague or unspecific responses from their physicians with the explanation of its autologous nature.

It has been well documented that most published literature lacks the minimum reporting guidelines for platelet-rich plasma (PRP) therapy. In a systematic review by DeClercq et al. [1], including 19 studies on PRP for rotator cuff repair, only 58.5% of the items on the Minimum Information for Studies Evaluating Biologics in Orthopaedics (MIBO) guidelines were fulfilled. Of the 47 items comprising this reporting guideline, 22 were reported in half of the studies. And details regarding whole blood and PRP processing and characteristics were reported inconsistently. This is also true for studies on professional soccer players, in which only 26.13% of the studies reported relevant information [2]. The lack of this data compromises the principle of reproducibility, one of the foundations of the scientific method, and explains the contrasting outcomes of PRP implementation in different musculoskeletal pathologies.

PRP products and commercial devices have shown high variability in the composition of the concentrate to inject. Each device shows different blood volumes collected for centrifugation, spin protocols, platelet and leukocyte concentration, and PRP volume. Yet, the most relevant factor in the treatment, the final platelet dose, is seldomly reported.

Most commercial products indicate their effectiveness by stating that it achieves superior platelet concentrations followed by a number and an X, the so-called increase factor (e.g., 2.5X, referring that it yields 2.5 times baseline platelet concentration). Concentration itself does not correspond to dosage; it creates an illusion. A valid concentration calculation should be accompanied by the baseline platelet concentration (which varies among patients), the collected blood volume, and the final PRP product volume. The dose should be standardized, referring to the absolute number of platelets and any other PRP component delivered per injection, like in any other therapeutic drug. Magalon et al. [3] reviewed 50 PRP commercial devices, revealing a wide range of theoretical platelet dosages for delivery from 300 million to 12.8 billion platelets. Moreover, only 14 of those devices have been appropriately described in the literature to characterize their PRP product.

The quest for the ideal platelet dose in PRP injections, and other relevant components, such as leukocytes, will help to elucidate its efficacy in future clinical trials. Recent studies suggest a minimum 10 billion platelet dose for sustained therapeutic effect in treating knee osteoarthritis with significant improvement of IKDC and WOMAC scores at one year follow-up [4]. However, only five devices reviewed in Magalon et al. [3] study can yield such a dose.

Despite the inconsistencies in the PRP formulations and commercial devices, a survey from the American Orthopaedic Society for Sports Medicine revealed that 66.1% of the respondent members used orthobiologics in their practice, and 71.6% were expecting an increase in their implementation [5].

✉ Marius M. Scarlat  
mscarlat@gmail.com

<sup>1</sup> Aspetar Orthopaedic and Sports Medicine Hospital,  
Sports City Street, Inside Aspire Zone, Al Buwairda St,  
29222 Doha, Qatar

<sup>2</sup> Groupe ELSAN, Clinique Chirurgicale St Michel, Toulon,  
France

Scientific journals play a crucial role in high-quality standard practices on orthobiologics, which show promising results but remain inconsistent within the studies. In fact, an analysis of the top 50 cited articles (mean number of citations  $241 \pm 94$ , range 151–625) on orthobiologics revealed a high level of evidence and fair methodological quality [6]. Nevertheless, no significant improvement in the quality of the studies was noted in recent publications. As a scientific community driven by excellence, we shall aim to improve the methodological quality of our clinical trials and fill the void needed to adopt the conscious use of orthobiologics among our colleagues. In this regard, many initiatives have been conducted that deserve to be highlighted again, such as the MIBO [7] or the DEPA classification (dose of injected platelets, efficiency of production, purity of the PRP, activation of the PRP) [8]. Implementing mandatory reporting guidelines to review submitted manuscripts would help increase the quality of publications while assuring its evidence-based implementation.

Our Journal publishes regularly new research in orthobiologics [9–11]. The quality of information is one of our paramount criteria for selection. As scientists, we have to report truth and evidence. However, as citizens, we still have this question “Are we sure about what we have in the box?”.

Knowing precisely what we inject into our patient is mandatory.

## Declarations

**Ethics approval** No ethics approval was required for the presented study.

**Conflict of interest** The authors declare no competing interests.

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