Letter to the Editor

Shedding light in the controversial terminology for platelet-rich products: Platelet-rich plasma (PRP), platelet-rich fibrin (PRF), platelet-leukocyte gel (PLG), preparation rich in growth factors (PRGF), classification and commercialism

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A recent series of letters were published in JBMR-A[1,2] about platelet concentrates for surgical use, where both terminology and content of these materials were hotly debated. The definition and classification of the platelet concentrate products are indeed very important issues, as many misunderstandings are widely spread in the large literature on this topic.[3] These techniques were initially gathered under the name "platelet-rich plasma (PRP),"[4] in reference to the generic term used in transfusion hematology, but this name is too general for the qualification of the many products developed now.

In the first letter, Everts et al.[1] insisted on the presence of leukocytes in most platelet preparations for surgical use. These authors explained a very important truth that many PRPs were in fact leukocyte- and platelet-rich plasmas (L-PRPs), and that the presence of leukocytes in these surgical adjuvants may be highly beneficial. They thus, introduced the term of "platelet-leukocyte–rich plasma (P-LRP)." Moreover, they pointed out that the two activation forms of the product (liquid platelet suspension or gelified fibrin-platelet clot) have different characteristics, and that the concentrates activated with a fibrinogen-cleaving agent (thrombin, batroxobin) should be named in fact as "platelet-leukocyte gels (PLG)." In this letter, these authors resumed the clarification process of the platelet concentrate definitions started in 2006.[5] However, their proposals for terminology were not complete and have been improved and systematized in the recent publication of a wide classification system for these products.[3]

The first concern is that all PRPs do not contain leukocytes. Many PRPs obtained from cell separator units or from the Anitua's preparation rich in growth factors (PRGF) subfamilies do not contain leukocytes and were classified as pure PRP (P-PRP).[3] On the contrary, PRPs containing leukocytes were classified as L-PRP: this acronym seems obviously more logical and reader-friendly than P-LRP, but we agree that a consensus should be found to solve this issue once for good.

The second issue is related to the gel form terminology. "Platelet gel" and "PLG" are too general terms. Indeed, products with a high-density fibrin network also exist and were classified as "platelet-rich fibrin (PRF)," some with leukocytes [leukocyte- and platelet-rich fibrin (L-PRF)] and some without leukocytes [pure platelet-rich fibrin (P-PRF)].[3] All these PRFs are only available in the form of a very dense fibrin gel,[6] while PRP gels are never so strong and dense.[7] We thus believe that the activated form of P-PRP or L-PRP should simply be named "P-PRP gel" and "L-PRP gel" to differentiate them from the products of the PRF families.

In the second letter, Anitua et al.[2] agreed that the recent development of many different techniques with various platelet and leukocyte contents led to a confusing jungle of terms and products. This notion of "jungle of platelet concentrates" was already pointed out some years ago,[8] when the main confusion between PRPs and the first PRF appeared. Anitua et al. were right in their call for the definition of a relevant terminology but their approach was unfortunately partisan.

First, Anitua et al. claimed that leukocytes should be avoided in platelet concentrates for surgical use, to avoid the proinflammatory effects of the proteases and acid hydrolases contained in white blood cells, particularly when injected in tendons. However, these authors did not justify their statement with scientific evidence; to sustain their claim, Anitua et al. cited Ref. 9 describing very positive anabolic effects on tendon cells obtained with a PRP, . . . but the PRP described in this study was in fact a leukocyte-rich PRP.

This question of the leukocyte content within platelet concentrates for surgical use is in fact an old debate. There is however actually no proof that the leukocytes within these surgical preparations might have undesirable side effects. On the contrary, several studies showed that L-PRPs have antimicrobial effects,[10,11] but no undesirable inflammatory reactions have been observed with L-PRPs

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up to now, even in immune sensitive applications.[9,12–15] From our standpoint, the influence of leukocytes injected with surgical platelet concentrates is actually a relevant way of research,[16–18] and no author can claim that their influence is negative. All statements on this matter should be carefully and scientifically discussed and proven.

The second controversial statement is related to the term "PRGF" used to define Dr. Anitua's products and is a good illustration of the confusion induced by the superposition of trademarks and terminology. Described in 1999 by Anitua, the PRGF (plasma[19] or preparation[20] rich in growth factors) protocol is a manual procedure for the production of a P-PRP with a moderate platelet concentration increase.[21] The PRGF trademarks and associated patents are the proprietary of Dr. Anitua and Biotechnology Institute (BTI, a dental implant company, the "BTI" trademark being the proprietary of Dr. Anitua also), as it was published in the international trademark and patent database of the World Intellectual Property Organization. Whatever the conflict of interest, it is obvious that the PRGF technology, with the different possible variations described by Anitua et al., generates products with a light fibrin network and no leukocyte, and thus clearly belongs to the P-PRP family.[3] We agree with Dr. Anitua that giving a specific name to a specific product such as PRGF is of great help to identify techniques and the associated literature. However, we also believe that this commercial strategic approach should remain reasonable and evidence based. It is not possible to consider PRGF as something fundamentally different from the other P-PRP without true scientific justification other than the claims of the company. When a trademark is used without caution as a scientific denomination, it induces confusion and raises suspicion of commercialism. The risk is then to discredit the whole database produced by Dr. Anitua about his P-PRP, while these data are very interesting for a better understanding of the biological differences between the four main classified families of products.[3]

As a conclusion, it is now very important to find a terminology consensus on platelet concentrates technologies, to avoid confusions in this wide and complex field of research, particularly concerning the role of leukocytes and the fibrin architecture. In many articles, the lack of characterization of the tested products (such as the leukocyte content) made the literature in this field very difficult to sort and interpret. Without a consensus, this field will remain opaque and this situation will considerably restrain its development.

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