

Letter to the Editor

Plasma rich in growth factors: The pioneering autologous technology for tissue regeneration

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In their last letter to the editor, Dohan et al.¹ tried to clarify some important aspects related to the terminology, classification, and commercialization of platelet rich plasma products. Unfortunately, they dedicate nearly half of the letter to criticize with poor arguments, the technology developed by our research group: the plasma rich in growth factors (PRGF), also known as Endoret: endogenous regenerative technology.²

It is not our aim to use this scientific journal to fuel a commercial battle that the "platelet rich fibrin" (PRF) group composed by Choukroun and Dohan started against PRGF technology a couple of years ago. On the contrary, we only pretend to shed light on some important issues related to these types of technologies.

PRGF-Endoret is the pioneering autologous technology for accelerating wound healing and tissue regeneration. In 1999, we published for the first time in the literature, a 100% autologous protocol to obtain different therapeutic plasma-based formulations from small blood volumes (~40 mL).³ Until then, the way of obtaining platelet rich plasma required large initial blood volumes (400–500 mL) and the use of bovine thrombin as activator. Both issues clearly hampered the progress of this approach due to technical and biosafety reasons. Therefore, it is always necessary to remember the past and see that the developments reported by our group more than a decade ago opened the door to routine use of these types of technologies, including the relatively young PRF.

Some of the arguments of Dohan and coworkers, especially those related to the commercialism, have not a scientific basis. The term PRGF-Endoret was adopted to distinguish this autologous technology from other nonautologous platelet rich plasma products that differ in composition and quality and consequently may lead to different biological effects. It is interesting to read that Choukroun and Dohan criticize an approach that has been also followed by them to commercialize their PRF many years later.

The aim of this letter is not to describe in detail the similarities and differences between PRGF and PRF. However, it is easy to understand the potential of each approach in just few examples. First, PRF is mainly a variation of the original protocol reported by our group more than a decade ago. Second, PRF is only a fibrin product that is difficult to manipulate and control as the release of growth factors from platelets starts just in the centrifugation step. Apart from its poor reproducibility, the protocol from Choukroun and Dohan does not allow to separate the red blood cells and leukocytes from the fibrin scaffold. On the contrary, PRGF is a reproducible protocol to

obtain a leukocyte and red blood cell-free platelet rich plasma.⁴ The big difference is that our approach allows you technically to obtain or not those cell fractions if you wish.

PRGF-Endoret is a real technology, as almost four different formulations (and not only one) with therapeutic potential can be obtained from the same patient's blood depending on the coagulation and activation degree of the samples.⁵ More importantly, the clinician controls the technology and not in other way round (as PRF). In our approach, the platelet-derived growth factors will only be delivered once the clinician adds the calcium chloride to the PRGF. The latter will facilitate the handling and administration of the different formulations.

Last but not least, it is our opinion and even our suggestion for the PRF group of Choukroun and Dohan to avoid losing time and energy in criticizing the PRGF-Endoret technology. Maybe, it will be more interesting for the scientific community to dedicate your efforts, as we have done with PRGF, in demonstrating for the first time the biosafety and efficacy of your product by means of a randomized clinical trial. Until then, PRF should only be considered as one of nearly 40 similar products that have been marketed in the last few years, always in the shadow of the pioneering technologies.

Eduardo Anitua¹

Mikel Sánchez²

Roberto Prado¹

Gorka Orive¹

¹*Biotechnology Institute I MAS D*

c/ San Antonio 15, 01005 Vitoria, Spain

²*Unidad de Cirugía Artroscópica, UCA, Clínica USP La Esperanza, 01002 Vitoria, Spain*

REFERENCES

1. Dohan DM, Bielecki T, Del Corso M, Inchingolo F, Sammartino G. 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. *J Biomed Mater Res A* 2010;95:1280–1282.
2. Anitua E, Sánchez M, Orive G. Potential of endogenous regenerative technology for in situ regenerative medicine. *Adv Drug Deliv Rev* 2010;62:741–52.
3. Anitua E. Plasma rich in growth factors: preliminary results of use in the preparation of future sites for implants. *Int J Oral Maxillofac Implants* 1999;14:529–35.
4. Anitua E, Sánchez M, Orive G, Andia I. Delivering growth factors for therapeutics. *Trends Pharmacol Sci* 2008;29:37–41.
5. Anitua E, Sánchez M, Orive G, Andia I. The potential impact of the preparation rich in growth factors (PRGF) in different medical fields. *Biomaterials* 2007;28:4551–4560.