

Letters to the Editor



Platelet-Rich Plasma Therapy and Antithrombotic Drugs

TO THE EDITOR:

We have read with great interest the recent article entitled "Timing of Platelet Rich Plasma Injections During Antithrombotic Therapy" by Ramsook and Danesh (1). In this interesting review the authors discuss the timing to use or discontinue the use of platelet-rich plasma (PRP) treatments in patients who are medicated with antithrombotic drugs, namely those that affect to the platelets and to blood coagulation (2). This issue is in the spotlight as more than six million patients in the United States are currently on medication with antithrombotic drugs to prevent thromboembolism (3).

The authors argue that for an effective PRP treatment in patients with concomitant antithrombotic therapy, these drugs must be suspended prior to applying the PRP treatment. They also stress the need for establishing clinical practice guidelines that can cover the PRP treatment for this type of patients. We do agree in this latter point; however, there are some points that we would like to clarify, since the authors state that literature guiding the timing of PRP injections during antithrombotic therapy is severely lacking (1).

It is true that the literature on this subject is scarce, but our group has recently published two articles assessing the PRP of patients that are on medication with different drugs that affect both platelets and blood coagulation (4,5). We guess that these two articles should have been cited in the review because, to the best of our knowledge, they are the only ones that characterize both the PRP and its in vitro biological effect in patients undergoing antithrombotic therapy. Specifically, we studied plasma rich in growth factors (PRGF), a PRP classified as a pure PRP (P-PRP) and characterized by a moderate enrichment of platelets and by the absence of both leukocytes and erythrocytes. The PRGF obtained from patients taking acetylsalicylic acid, acenocoumarol or glucosamine sulfate, as well as from a control group who were taking no medication, was analyzed (4,5).

In this study several features of the PRGF were observed including determination of clot formation and

retraction time, platelet activation by flow cytometry (both spontaneous and activation following stimulation with ADP) and quantification of main growth factors present in platelets (PDGF-AB, VEGF, TGF- β 1) and plasma (IGF-1 and HGF). With respect to all these parameters, the only statistically significant difference found was an increased clot formation time in the group of patients treated with antiplatelet drugs (acetylsalicylic acid) (5). For the rest of the aforementioned parameters no differences were found.

Following the characterization of the PRGF, a careful evaluation of its in vitro biological effects was carried out. The experimental model was a primary culture of both gingival (4) and tendon fibroblasts (5). We studied cell proliferation and migration, as well as the synthesis of growth factors (HGF, VEGF and IGF-1) and extracellular matrix components (procollagen type I, fibronectin and hyaluronic acid) by such cells. The only negative results were a decrease in the synthesis of VEGF, fibronectin and hyaluronic acid by human tenocytes exposed to PRGF from donors medicated with acenocoumarol.

One of the limitations of both studies (4,5) is the low number of patients and the need to test more types of antithrombotic drugs. However, we believe that these pioneering studies, along with the clinical evidence, should be taken into account when developing clinical practice guidelines for the treatment of these patients.

Recently, Di Matteo et al (6) have published a case report of the successful knee osteoarthritis treatment with PRP in a patient medicated for 9 years with acetylsalicylic acid due to severe coronary disease without interrupting antiplatelet therapy. Despite being a case report, it is an example of how patients under antithrombotic therapy can benefit from treatment with PRP.

An important issue that should not be neglected is that the effectiveness of PRP therapy is not only due to platelets, since there are more actors responsible for

this efficacy that are present in the plasma fraction and not in platelets, as fibronectin, growth factors such as IGF-1 and HGF, and other bioactive molecules of plas-matic origin (7). It would be appropriate to observe whether molecules in the plasma are affected by the antithrombotic therapy, since our group has only exam-ined HGF and IGF-1 with no differences found with the control group.

In summary, we believe it is necessary to deepen in the study of the PRP of patients medicated with antithrombotic drugs, both at pre-clinical and clinical levels. Hence, a better understanding of the molecular mechanisms underlying the effectiveness of PRP will be the keystone to extend this treatment to patients with antithrombotic therapy.

Conflict of interest

E.A. is the Scientific Director of and G.O. and R.P. are scientists at BTI-Biotechnology Institute, a dental implant company that investigates in the fields of oral implantology and PRGF-Endoret technology.

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