Comments on the Editorial "Antiphospholypid Syndrome: New Clinical and Therapeutic Perspectives"

To the Editor: We congratulate you on the publication of the editorial titled "Antiphospholypid Syndrome: New Clinical and Therapeutic Perspectives," by Cervera et al,[1] which updates in a clear and concise manner aspects of an entity with which it is necessary to be familiarized, given its growing importance in the field of the systemic autoimmune disease. Precisely due to this, we would like to point out some aspects relating to the treatment of thrombosis in this group of patients.

It is difficult to establish a single recommendation for every case given the diverse nature of the clinical presentation of the antiphospholypid syndrome (APS). We also have important limitations in the current studies, such as their retrospective character[2-5] or the fact that no control group is available[4-7] or limited only[6,7] or almost only[8] to patients with venous thrombosis or in which the high degree of anticoagulation pretended in one of the treatment arms was not achieved[8]. The case that clearly exemplifies this paradigm is the APASS, published in JAMA in 2004[9] in which the control group was formed by individuals with cerebrovascular accidents in which the presence of antiphospholypid antibodies was, in the majority of cases, and epiphenomenon.[10]

Therefore their conclusions should not be extended to patients with defined APS according to the criteria in use currently.[10] The reference that Cervera et al make to the high risk of bleeding according to the international normalized rate (INR) >3.5 is adequate in general; nonetheless, it could not be applicable to all of the patients in this group, generally young patients without additional risk of hemorrhage. In fact, the incidence of severe bleeding has been low in all of the series[2,3,5,8]: a more concerning phenomenon is the presence of thrombosis with an INR 2-3 than the hemorrhages present with an INR intensity between 3 and 4.[5,8]

We definitely share the belief of Cervera et al in the need for a prolonged (or indefinite) anticoagulation in patients with APS and thrombosis. The intensity of anticoagulant treatment should take into account the individual risk for bleeding, limited by the presence of previous events and the risk factors associated such as an older age, lesions that could potentially bleed (ie, leukoaraiosis) and the use of several, simultaneous medications. The patients that have had episodes o venous thromboembolism without severe pulmonary embolism could be candidates to a standard anticoagulation regiment, that is, with an INR 2-3. But those with a more serious presentation, especially those that present cerebrovascular accidents are, in our opinion, candidates to an early, more intense anticoagulation, with an INR >3.[10] The presence of lupus anticoagulant and/or persistent high titer IgG anticardiolypin antibodies should also be considered an indicative factor of the danger of relapse and should therefore predispose to a more aggressive treatment.

As commented by Cervera et al, the control of other risk factors is fundamental. We must lastly point out the potential role that aspirin (or other antiplatelet drugs) or hidroxycloroquine have, associated to the anticoagulant treatment in the management of patients with refractory forms of APS.

Guillermo Ruiz-Irastorza[a] and Munther A. Khamashta[b]

[a]Servicio de Medicina Interna, Hospital de Cruces, Universidad del País Vasco, Barakaldo, Vizcaya, Spain
[b]Lupus Research Unit, Guy´s, King´s, and St Thomas´ Medical School, The Rayne Institute, St. Thomas´ Hospital, London, United Kingdom

References

1. Cervera R, Asherson RA. Síndrome antifosfolipídico: nuevas perspectivas clínicas y terapéuticas. Reumatol Clin. 2005;1:183-6.
2. Rosove MH, Brewer PMC. Antiphospholipid thrombosis: clinical course after the first thrombotic event in 70 patients. Ann Intern Med. 1992;117:303-8.
3. Khamashta MA, Cuadrado MJ, Mujic F, Taub NA, Hunt BJ, Hughes GRV. The management of thrombosis in the antiphospholipid-antibody syndrome. N Engl J Med. 1995;332:993-7.
4. Krnic-Barrie S, O´Connor CR, Looney SW, Pierangeli SS, Harris EN. A retrospective review of 61 patients with antiphospholipid syndrome. Analysis of factors influencing recurrent thrombosis. Arch Intern Med. 1997;157:2101-8.
5. Ruiz-Irastorza G, Khamashta MA, Hunt BJ, Escudero A, Cuadrado MJ, Hughes GRV. Bleeding and recurrent thrombosis in definite antiphospholipid syndrome: analysis of a series of 66 patients treated with oral anticoagulation to a target INR of 3.5. Arch Intern Med. 2002;162:1164-9.
6. Schulman S, Svenungsson E, Granqvist S and the Duration of Anticoagulation Study Group. Anticardiolipin antibodies predict early recurrence in thromboembolism and death among patients with venous thromboembolism following anticoagulant therapy. Am J Med. 1998;104:332-8.
7. Kearon C, Gent M, Hirsh J, Weitz J, Kovacs MJ, Anderson DR, et al. A comparison of three months of anticoagulation with extended anticoagulation for a first episode of idiopathic venous thromboembolism. N Engl J Med. 1999;340:901-7.
8. Crowther MA, Ginsberg JS, Julian J, Denburg J, Hirsh J, Douketis J, et al. A comparison of two intensities of warfarin for the prevention of recurrent thrombosis in patients with the antiphospholipid syndrome. N Engl J Med. 2003;349:1133-8.
9. Levine SR, Brey RL, Tilley BC, Thompson JL, Sacco RL, Sciacca RR, et al. Antiphospholipid antibodies and subsequent thrombo-occlusive events in patients with ischemic stroke. JAMA. 2004;291:576-84.
10. Ruiz-Irastorza G, Khamashta MA. Stroke and antiphospholipid syndrome: the treatment debate. Rheumatology (Oxford). 2005;44:971-4.