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Editorial

Direct oral anticoagulants in antiphospholipid syndrome

Anticoagulantes orais diretos na síndrome antifosfolípide

Antiphospholipid syndrome (APS) is an acquired thrombophilia characterized by thrombosis and/or fetal loss associated or not with the presence of thrombocytopenia in the presence of circulating antiphospholipid antibodies (anticardiolipin, lupus anticoagulant and/or anti-beta2-glycoprotein I). Chronic current treatment of this disease includes the use of vitamin K antagonist oral anticoagulants. There is a good response to treatment with oral anticoagulants; this therapy aims at preventing new thrombotic events; however, re-thrombosis rates of 16% covering a time span of 10 years were described.¹ In this review, the authors found a high rate of re-thrombosis in triple-positive (anticardiolipin, lupus anticoagulant and anti-beta2-glycoprotein I) patients (44% in 10 years). However, these medications are associated with various drug interactions and are greatly influenced by the dietary vitamin K intake.² It is important that adjustments and maintenance controls are carried out, based on prothrombin time (through control of the international normalization ratio – INR) regularly performed throughout the life of the patient, which reduces his/her therapeutic adherence. Moreover, in some cases, the lupus anticoagulant can change the prothrombin time and compromise the patient's monitoring. Another disadvantage is the decrease in C and S proteins, which are natural anticoagulants, with a possible increased risk of thrombosis in the acute phase of anticoagulation.³

Hence, a new class of oral anticoagulant drugs (direct oral anticoagulants) emerged, with the advantage of not requiring a laboratory control, with the added benefit of being very little influenced from food and other medications. Examples of such drugs are dabigatran, which is a direct thrombin inhibitor, and rivaroxaban, apixaban, and edoxaban, which are factor Xa inhibitors. Such drugs are approved by the FDA for use in venous thromboembolic events and in cases of atrial fibrillation in the general population. There are few reports and studies on the use of these medications in patients with APS.

Table 1 summarizes the studies with dabigatran or rivaroxaban in APS.

In the literature, about 85 cases of patients with APS who have taken the new oral anticoagulants were found. Most of these papers are case reports or series of cases, besides two retrospective studies and one prospective study. The median follow-up time ranged from 10 to 19 months and the most widely used medication was rivaroxaban. The recurrence ranged from 0 to 17%, including several arterial events, when only studies that reported the number of recurrences in relation to the number of patients at risk who were followed for a period of time were evaluated. The vast majority of patients included in all studies had suffered previous arterial events or multiple recurrences in the presence of vitamin K antagonists, or discontinued the use of the anticoagulant, or, ultimately, were triple-positive for antiphospholipid antibodies.⁴⁻⁹

Two prospective randomized studies, one of Italian origin (TRAPS) and another English (RAPS),³ currently in a follow-up phase of patients with APS, with a group treated with warfarin versus rivaroxaban, were published. These studies will provide the answers to this question.

Currently, based on available studies and also based on experts opinion of on the subject, one should contraindicate the use of these new oral anticoagulants in patients with triple-positivity of antiphospholipid antibodies, in patients with a history of arterial events, and with recurring events. The opinion of experts in this field is that vitamin K antagonists should remain the basis of anticoagulation in patients with APS; direct oral anticoagulants may be considered in the treatment of APS [the first venous event], if there is refractoriness, allergy or a side effect associated with the use of warfarin; on the other hand, these drugs are not suitable in cases of poor adherence or in cases of thrombotic recurrence, notwithstanding therapeutic levels of anticoagulation.¹⁰

Table 1 – Summary of case series, prospective and retrospective studies on the use of new oral anticoagulants in patients with antiphospholipid syndrome.

Author, year	N	Primary APS	Study type	Follow-up	Previous arterial event	Triple positive	Anticoagulant	Recurrence
Noel et al., 2015 ⁵	26	12/26	Retrospective cohort	19 m	12/26	7/26	Rivaroxaban (n = 15), dabigatran (n = 11)	1 (4%)
Sciascia et al., 2015 ⁶	35		Prospective cohort	10 m	0	ND	Rivaroxaban	0
Son et al., 2015 ⁷	12	8/12	Case series	12 m	2/12	5/12	Rivaroxaban	2 (17%) [2 SLE, 1 previous arterial event, 1 patient discontinued Rivaroxaban 6 d]
Schaefer et al., 2014 ⁸	3	2/3	Retrospective cohort	NA	2/3	1/3	Rivaroxaban (n = 2), dabigatran (n = 1)	3 (100%)
Win et al., 2014 ⁹	3	3/3	Case series	NA	2/3	ND	Rivaroxaban	2 venous, 1 arterial event
Signorelli et al., 2015 ⁴	8	8/8	Case series	NA	2/8	3/8	Rivaroxaban	6 arterial, 2 venous events

NA, not applicable; ND, not determined; SLE, systemic lupus erythematosus.

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Conflicts of interest

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