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Dabigatran as alternative therapy in prothrombotic immune thrombocytopenia induced by the AstraZeneca SARS-Cov-2 vaccine

Abstract

Reviewing the treatment alternatives for thormbotic thrombocytopenia induced by vaccine (TTIV) after receiving a dose of ChAdOx1 nCov-19 vaccine (AstraZeneca) we observe that dabigatran should be an alternative to be considered since it has several strength points that may be useful in this pathology: Specific antidote, low level of interactions with others drugs and effectiveness in thrombotic events.

Keywords: thrombocytopenia induced, heparin-induced thrombocytopenia, cerebral venous thrombosis, antithrombotic therapy

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Abbreviations: TTIV, thrombotic thrombocytopenia induced by vaccine; HIT, heparin-induced thrombocytopenia; DOAC, direct-acting oral anticoagulants; CVT, cerebral venous thrombosis; SVT, splanchnic venous thrombosis; ISTH, international society on thrombosis and haemostasis; EHRA, european heart rhythm association

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The article by Greinacher et al.[1] in which describe the clinical and analytical characteristics of 11 patients diagnosed with thrombotic thrombocytopenia induced by vaccine (TTIV) after receiving a dose of ChAdOx1 nCov-19 vaccine (Astra Zeneca), pointing out as the etiopathogenic mechanism of this entity. This illness shows a platelet function activating antibodies directed against platelet factor-4, analogously to what occurs in heparin-induced thrombocytopenia (HIT). It has come to our attention, however, that among the drugs anticoagulants that are recommended as an alternative to heparin, direct-acting oral anticoagulants (DOAC) are cited such as rivaroxaban and apixaban, but it is avoided to name dabigatran, the only DOAC with Anti-IIa action. HIT is an acquired hypercoagulative state where, in addition to thrombocytopenia, both arterial and venous thrombotic events could disturb patient's evolution.[2] Dabigatran, together with the DOAC with Anti-Xa action, it has been shown to have an adequate profile of effective and safety in the treatment of this clinical picture.[3,4] Likewise, nine of the patients reported by Greinacher[1] had cerebral venous thrombosis (CVT), and three other of them suffered a splanchnic venous thrombosis (SVT). The use of dabigatran as antithrombotic therapy for both kind of thrombosis, it is well-supported in the medical literature. Specifically, in the RE-SPECT CVT study that included 120 patients diagnosed with CVT, the group treated with dabigatran did not show significant differences in terms of efficacy and safety compared to those who received warfarin therapy.[5] In addition, a work carried out in 330 non-cirrhotic patients with portal thrombosis, showed that the DOAC, as a whole, were safer and more effective than warfarin, observing the highest rate of radiological resolution of thrombosis (75%), in the 8 cases that received dabigatran.[6] In our view, other factor that make dabigatran attractive in the treatment of TTIV is the fact that dabigatran does not use the cytochrome metabolic pathway 450/3A4, which has clinical significance, indeed has a fewer drug interactions and also a reduced risk of liver toxicity. Based on the above, our working group has prepared anticoagulation protocol at discharge in patients admitted for associated pneumonia to SARS-Cov-2 and with atrial fibrillation.[7]

Another point is that the use of corticosteroids in TTIV makes dabigatran an interesting option in the treatment of these patients. This could occur if the platelet count is less than 50x10^3/uL as contemplated by the International Society on Thrombosis and Haemostasis (ISTH) in its provisional guide for the diagnosis and treatment of that entity.[8] However the corticosteroid used in some clinical cases of TTIV, in order to minimize the side effects of intravenous immunoglobulin,[9] may have an impact on DOAC such as rivaroxaban and apixaban, by using both the cytochrome 3A4 pathway and by the induction and competition effect on this metabolic pathway. European Heart Rhythm Association (EHRA) has echoed this problem in the section on drug interactions of its latest practical guide.[10] This interaction is less relevant in case of dabigatran.[10]

If we continue to describe the problem of anticoagulation in TTIV patients, they showed low level of platelet count of approximately 20x10^3/uL in an important group of patients. The EHRA guide before mentioned, contemplates the anticoagulation scenario with DOAC in the presence of thrombocytopenia,[10] nevertheless, in their recommendations for the subgroup of patients with a platelet between 20x10^3/uL and 50x10^3/uL, it would be advocated to act with caution and always from a multidisciplinary and individualized approach. In this context outlined above, use of dabigatran as antithrombotic therapy, which have an agent reverser such as idarucizumab, would provide the patient with an additional guarantee of safety. In light of all the above arguments, we think that dabigatran should be considered as an antithrombotic alternative in patients diagnosed with TTIV.

Conclusion

Dabigatran could be a reasonable option in the treatment of TTIV in the same way of apixaban or rivaroxaban.

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Conflicts of interest

The authors declare do not have conflicts of interest.

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