Bleeding news

Comparison of 4-factor prothrombin complex concentrate and andexanet alfa for reversal of apixaban and rivaroxaban in the setting of intracranial hemorrhage

Michelle Lipski, Stacy Pasciolla, Kevin Wojcik, Brian Jankowitz, Lauren A Igneri

J Thromb Thrombolysis. 2023 Apr;55(3):519-526. doi: 10.1007/s11239-022-02752-z.

Four-factor prothrombin complex concentrate for the treatment of oral factor Xa inhibitor-associated bleeding: a meta-analysis of fixed versus variable dosing

Thita Chiasakul, Mark Crowther, Adam Cuker

Res Pract Thromb Haemost. 2023 Mar 10;7(2):100-107. doi: 10.1016/j.rpth.2023.100107

Author of the comment: *Dra. Raquel Ferrandis Comes.* *Anesthesiology and Resuscitation. Hospital Universitari i Politècnic La Fe, Valencia. Member of the SEDAR-COVID working group.*

Urgent management of direct anti-Xa anticoagulant drugs (xabans) is still a controverted issue, given the absence of a specific reversal agent approved in our field, since andexanet alfa is not yet available, although approved by the FDA in May 2018, based on ANNEXA-A study. Andexanet alfa, unlike idarucizumab (reversal agent of dabigatran), is a modified Xa factor that removes the drug following a competitive mechanism, thus achieving–according to several authors–a hemostatic efficiency close to 80%.

In this context, the authors of our first article present a retrospective study on 70 patients with intracerebral hemorrhage, 47 of which are treated with 4-factor prothrombin complex (4F-PCC), and 23 with andexanet alfa. The assessment of hemostatic efficiency was defined according to the increase of hematoma in control CT after 12 hours. Efficiency was deemed excellent if the increase was less than 20%, and good if between 20 and 35%. Following this criterion, both groups achieved excellent or good hemostatic efficiency in 70% of the cases, similarly to what is described in the literature. No differences were either observed in secondary outcomes approached as efficacy (need for re-operation, use of other hemostatic agents, prognosis or neurological recovery scales). It must be noted that the number of recorded thrombotic events, even though not achieving statistical significance, was higher in the andexanet (22%) group than the 4F-PCC group (17%).

Therefore, in our field, urgent management of bleeding in xaban-anticoagulated patients is based on provision of hemostatic agents, such as 4F-PCC. However, the originally recommended dose in the main guides was 50 UI/kg, a value which, apparently, is progressively decreasing, although it is not yet established.

Bleeding news

The second article we would like to discuss this month provides a systematic literature review, comprising 25 studies with over 1,700 patients. These studies are grouped together based on whether variable—on average, 38 UI/kg—or fixed—on average, 38 UI/kg—4F-PCC doses have been used. Although criteria assessing hemostatic efficacy differ, the overview provided by the meta-analysis is that hemostatic efficacy is achieved in 74-79% of the cases. Furthermore, recorded thrombotic events were on average 4 and 3%.

A conclusion can be drawn from this study that the doses derived from a weigh-based strategy are higher and way more variable than fixed doses. Nevertheless, in a logistic regression analysis of the data, no benefit is observed from that dose increase. These results are similar to the ones described for AVK reversion with 4F-PCC.

All in all, and still with a significant lack of evidence, the use of 4F-PCC with doses of 25-30 UI/kg, as a hemostatic agent in xaban-anticoagulated bleeding patients, might be effective and safe.