Outcomes associated with 4-factor prothrombin complex concentrate administration to reverse oral factor Xa inhibitors in bleeding patients

Emily A. Highsmith, Celia Morton, Sara Varnado, Kevin R. Donahue, Suraj Sulhan, Annette Lista

J Clin Pharmacol. 2020 Oct 23 [Epub ahead of print]

Author of the commentary: *Dr Joan Cid.* Apheresis Unit, Department of Hemotherapy and Hemostasis, ICMHO, Hospital Clinic, Barcelona

Compared with vitamin K antagonists (VKAs), oral factor Xa inhibitors (FXaIs) are associated with at least equivalent efficacy and a lower incidence of major bleeding. Despite this benefit, bleeding remains the most common adverse event. Prior to the approval of andexanet alfa, alternative agents such as 4-factor prothrombin complex concentrate (4F-PCC) were used for reversal of anticoagulation.

In this article the authors conducted a retrospective, descriptive study on patients ≥18 years of age who received 4F-PCC for reversal of bleeding associated with oral FXaIs. Patients were excluded if they received a VKA or dabigatran in the previous 48 hours. A subgroup analysis comparing 4F-PCC with andexanet alfa was performed on patients who met the inclusion and exclusion criteria of the ANNEXA-4 trial.

The primary endpoint of this study was to evaluate the incidence of haemostasis and associated dosing strategies in patients receiving 4F-PCC for reversal of bleeding associated with oral FXaIs. Thirty-eight patients were included and 28 patients (74%) achieved haemostasis. In patients who achieved haemostasis, the median 4F-PCC dose was 50 units/kg, and in those who did not achieve haemostasis, the median dose was 30 units/kg. Within the subgroup analysis, there were no differences in overall rates of haemostasis between the groups who received 4F-PCC and andexanet alfa.

To conclude, based on the results presented in this study, 4F-PCC remains a reasonable option to use for reversal of oral FXaIs, especially when andexanet alfa is unavailable, with 50 units/kg appearing to be the most effective dose to achieve haemostasis.