Letter by Marlu et al Regarding Article, “Reversal of Rivaroxaban and Dabigatran by Prothrombin Complex Concentrate: A Randomized, Placebo-Controlled, Crossover Study in Healthy Subjects”

To the Editor:

Eerenberg et al.1 recently published a very interesting article on the reversal of rivaroxaban and dabigatran anticoagulation by prothrombin complex concentrate (PCC). In their study, the authors reported that a single bolus of a high dose of PCC (50 IU/kg) was responsible for the normalization of both rivaroxaban-induced prothrombin time (PT) and endogenous thrombin potential (ETP) alteration and thereby for a complete reversion of the anticoagulation effect. These results concerning the reversion efficacy based on correction of hemostatic tests PT and ETP should be interpreted with caution. First, the effect on PT reduction does not prejudge the hemostatic effectiveness of the treatment. For example, recombinant activated factor VII, which was described as able to dramatically reduce PT, has been reported to be ineffective in the case of cerebral hemorrhage,2 and its ability to correct coagulopathy in severe trauma remains questionable. Second, although rivaroxaban was shown to induce a concentration-dependent prolongation of PT, this increase in clotting time varied, depending on the thromboplastin reagent used,3 and could be responsible for divergent results in terms of reversion. Finally, some experimental data do not support a correlation between hemostatic tests such as PT or ETP and clinical efficacy. For example, Godier et al.4 recently described the use of PCC in a rabbit hepatosplenic hemorrhagic model. Although this was an animal model, Godier et al showed that PCC 40 U/kg was ineffective in reducing blood loss; however, PCC significantly increased ETP. Similarly, Eerenberg et al suggest that PCC was unable to reverse dabigatran because PCC did not correct either dabigatran-induced prolongation of activated partial thromboplastin time or the ETP lag time.5 In contrast, in an intracerebral hemorrhagic mouse model using dabigatran, PCC 50 U/kg dramatically reduced hematoma growth and decreased the 24-hour mortality after intracerebral hemorrhagic.6

Therefore, because of the absence of a clinically based efficacy analysis in humans, these conflicting results make it difficult to assess the potential true reversal effect of PCC and currently to propose its use in rivaroxaban-anticoagulated patients.

Disclosures

Dr Pernod was principal investigator for the oral direct factor Xa inhibitor rivaroxaban in patients with acute symptomatic deep-vein thrombosis or pulmonary embolism (EINSTEIN) Study using rivaroxaban. The other authors report no conflicts.

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