Letter by Moll Regarding Article, “Hemostatic Therapy in Experimental Intracerebral Hemorrhage Associated With the Direct Thrombin Inhibitor Dabigatran”

To the Editor:

No published data exist on how to best manage patients who have major bleeding at the time of being treated with dabigatran. Several management algorithms have been proposed, but suggestions for use of prothrombin complex concentrates (PCC), recombinant factor VIIa, or fresh-frozen plasma are based on ex vivo reversal of abnormal coagulation tests, animal data, and a study of human volunteers. In view of the vacuum of clinical data the study by Zhou et al and its conclusion that “the study provides strong evidence that PCC prevent excess intracerebral hematoma expansion” captures, of course, the clinician’s interest.

Although one cannot highlight enough that this is “only” a mouse model study, the data are, nonetheless, interesting, particularly because this study’s finding that PCC prevented excess intracerebral hematoma expansion is contrary to a recent human volunteer study, which showed that PCC was not effective in reversing the coagulation test abnormalities caused by dabigatran.

Why these discrepant results? Was it because the mice received twice as high a dose of PCC? Was it because different PCCs were studied? The mouse model study used 100 U/kg of Beriplex and the human volunteer study 50 U/kg Cofact. Considering that the activity of PCCs is measured based on their factor IX content and that the content of the other vitamin K-dependent coagulation factors varies between products, the mice still received approximately double the dose of factor II as the human volunteers. However, the dabigatran plasma levels in the mice were also at least 3 times as high as those in the human volunteers. It remains unclear why PCCs were effective in the mouse model study but not in the human volunteer study.

What is clear, however, is this: (1) based on the very limited published data so far, the clinician cannot count on PCCs having any effect in decreasing the bleeding in dabigatran-associated major bleeding; and (2) to understand what intervention might be helpful in the patient who bleeds on dabigatran, clinical data are needed. A useful next step would be a publication of the data from the large clinical trials as to how patients who had major bleeding on dabigatran were managed and what their outcomes were. The enthusiastic conclusion of Zhou et al that “there is strong evidence that PCC prevent excess intracerebral hematoma expansion” applies only to mice.

Disclosures

None.

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