Treatment rapidly reverses the effect of blood thinner dabigatran

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At least 28 million prescriptions for blood thinners are filled by pharmacists yearly for the irregular heartbeat of atrial fibrillation, deep vein thrombosis, and other indications, according to the Department of Health and Human Services. However, on rare occasions, anticoagulants can present risks of accidental bleeding and hemorrhage or can delay emergency surgery. A newly completed phase III clinical study demonstrates the safety and efficacy of idarucizumab, a novel therapy that acts as an antidote to the blood thinner dabigatran.

"Prior to idarucizumab, there was no rapid, reliable, and effective method for reversing dabigatran and other orally administered blood thinners, which otherwise may take at least 12 to 24 hours to clear from the body," says first and corresponding author Charles Pollack, M.D., Professor of Emergency Medicine at Sidney Kimmel Medical College of Thomas Jefferson University. Dr. Pollack also serves as Associate Provost of Thomas Jefferson University. "Physicians will now have a potentially life-saving option for treating patients at risk of uncontrolled bleeding or in need of emergency surgery."

The results of the RE-VERSE AD clinical trial were published in *The New England Journal of Medicine* on July 11.

The study enrolled 503 patients taking dabigatran in 39 countries between 2014 and 2016, who had an urgent medical need to reverse the blood thinner. Patients were grouped by those who had uncontrolled bleeding or hemorrhage and those who required emergency surgery that could not be safely performed under anticoagulation. All patients received one dose of five grams of idarucizumab; only nine received a second dose. The researchers checked the blood for various measures of clotting ability before the reversal agent was administered and then at six time points afterwards to assess the therapy's speed and efficacy.

Idarucizumab was able to return patients to normal clotting function within minutes of administration (the first tested time point was between 10-30 minutes after therapy was given). The researchers saw that in patients with uncontrolled bleeding, idarucizumab was able to stop the bleeding within a median of 2.5 hours. Those requiring surgery were able to begin the procedure at a median of 1.6 hours.

The therapy, idarucizumab, from Boehringer Ingelheim Pharmaceuticals, is made from an antibody segment that functions by binding tightly and specifically to dabigatran and preventing the anticoagulant from working. As such, the therapy is only an effective antidote to dabigatran and not other anticoagulants.

Interim results of this study were published in 2015 and included the analysis of results from 90 patients. Based on those results and consistent findings from pre-clinical studies, the US Food and Drug Administration and the European Medicines Agency both granted approval for use of the drug in emergency settings. The current study confirms and strengthens the interim findings.

"For the first time we have the ability to turn off oral anticoagulation like a light switch," says Dr. Pollack. "In the past, we haven't had the ability to do that."

More information: Charles V. Pollack et al, Idarucizumab for Dabigatran Reversal—Full Cohort Analysis, *New England Journal of Medicine* (2017). DOI: 10.1056/NEJMoa1707278

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