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Emergency Medicine Perspectives: Targeted vs. Nonspecific Approaches to Anticoagulation Reversal in Real World Analyses for ICH or GI Bleeds

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Fermann:
Hello, my name is Greg Fermann. I currently serve as Professor and Executive Vice Chair in the Department of Medicine at the University of Cincinnati College of Medicine. And my talk today is described as targeted versus nonspecific approaches to anticoagulation reverse.

These are my disclosures.

In terms of context, the primary adverse event associated with oral anticoagulant use is hemorrhage. Most oral anticoagulated-related hemorrhage is minor, although some are not. Our task as emergency physicians is to resuscitate when necessary, to differentiate major from minor bleeding, and to decide if reversal or repletion is part of our therapeutic strategy. We also have to acknowledge that reversal returns patients to their pretreatment thrombotic risk.

We turn to the four R's when we talk about managing DOAC-associated hemorrhage. First, we review the timing of the last dose, comorbidities, the source of bleeding, and baseline labs. We simultaneously resuscitate our unstable patients. We try to remove from the GI tract and the offending agents. We then turn our attention to repair, which largely a source control, we assess the need for surgery, interventional radiology, or endoscopy. And then finally, we turn our attention to reversal with nonspecific or targeted reversal strategies.

What do we mean by targeted versus nonspecific? Well, targeted generally refers to molecules that are specifically designed for a specific class of oral anticoagulant. For instance a factor Xa inhibitor such as apixaban or rivaroxaban, we have andexanet alfa. For a direct thrombin inhibitor, we have etaracizumab. A nonspecific approach would deploy, for instance, a four-factor PCC, which is in essence, a lyophilized, vitamin K-dependent factors of 2, 7, 9, 10, protein C, and protein S. This agent is approved for warfarin repletion. But it's often used off label for DOAC reversal.

What about real-world evidence comparing these two strategies? First, we turn to a multicenter retrospective chart review presented at the Research Forum of the American College of Emergency Physicians in San Francisco in October of 2022. The objective of this trial was to compare in-hospital mortality in patients hospitalized with oral factor Xa inhibitor or enoxaparin-related intracranial hemorrhage, or GI hemorrhage, who were treated with andexanet alfa or four-factor PCCs.

Baseline characteristics are on this panel. But I call your attention first and foremost to the size of this comparison. Andexanet alfa group was over 1,300 subjects, in the four-factor PCC group was over 1,400 subjects, the average age was about 65, with males being about

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55% of the dataset. Apixaban was seen in about 40% of the subjects, rivaroxaban in about 25 to 26% of the subjects, a small number of edoxaban treated patients, and a relatively sizable enoxaparin treated dataset. About 60% of patients were treated for GI hemorrhage, and about 25 to 26% were ICH hemorrhage patients.

Among patients with ICH, the in-hospital mortality was significantly lower with andexanet alfa compared to four-factor PCCs, 13.6% versus 19.8%. With respect to GI bleeds, among patients with GI bleeds, the incidence of in-hospital mortality was 2.5% in andexanet alfa treated subjects, and 3.6% in those treated with four-factor PCCs. There is about an equal weight and distribution of upper and lower GI bleeds. And about 40% or so of subjects had endoscopy or colonoscopy. Treatment with andexanet alfa demonstrated a 33% lower likelihood of in-hospital mortality compared to four-factor PCCs, even after adjustment for the type of anticoagulant use, the time since the dose, the bleed type, traumatic versus spontaneous, age, sex, systolic blood pressure, mental status, and DNR status, and comorbidities.

In conclusion, in this large retrospective dataset comparing patients that are on oral factor Xa inhibitors or enoxaparin that were treated with andexanet alfa versus four-factor PCCs, we saw a 33% reduction in the odds of in-hospital mortality. And this signal was maintained across both ICH and GI bleeds as well as spontaneous and traumatic ICH. The limitations of this dataset are inherent to any retrospective design chart review data. Thankfully, we're going to assess another 1,500 subjects, and this is in peer review.

Thank you for your attention.

Announcer:
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