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https://reachmd.com/programs/cme/emergency-medicine-and-neurocritical-care-managing-life-threatening-bleeding-in-the-ed/16233/

Released: 10/09/2023
Valid until: 10/09/2024

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Emergency Medicine and Neurocritical Care: Managing Life-Threatening Bleeding in the ED

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

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Dr. Gibler:
Our first speaker, if I could welcome her, is Dr. Natalie Kreitzer. Dr. Kreitzer is an Emergency Physician and a Neurocritical Care Expert with dual training. And she will be speaking to you about managing life-threatening bleeding in the ED and with a focus on ICH. Dr. Kreitzer.

Dr. Kreitzer:
Thank you so much, Dr. Gibler. My name is Natalie Kreitzer. And I'm an Associate Professor of Emergency Medicine and Neurocritical Care at the University of Cincinnati. I want to speak about managing life-threatening bleeding in the emergency department, specifically touching on intracranial hemorrhage, given my focus of neurocritical care, as well as stroke.

I want to begin by just briefly reviewing the pertinent parts of the coagulation cascade that really dictate why there are different reversal or repletion agents for life-threatening hemorrhage in the setting of patients who are anticoagulated. And our vitamin K antagonists, such as warfarin, those have been around for a very long time. And those interact with factors II, VII, IX, and X that the liver produces. So patients who are on warfarin are deficient in those factors. And so, when they require repletion, they're low in those factors, and they require that factor back.

On the other hand, the direct oral anticoagulants which are certainly by far the most common anticoagulant agents being used in the United States now, interact on factors Xa, and those are drugs like apixaban and rivaroxaban, or the direct thrombin inhibitors, such as dabigatran. And those are depicted down here in the bottom parts of the coagulation cascade.

Now when we think about patients who have some type of life-threatening bleed, and in my world that's going to most commonly be those patients with some type of intracranial hemorrhage, we can think about either reversal or repletion to help take care of that anticoagulant effect.

So reversal is going to be agents that such as andexanet alfa for patients who are on factor Xa inhibitors or idarucizumab for those patients on direct thrombin inhibitors.

Now with repletion, there are multiple options for those vitamin K antagonist patients, FFP, PCs. Remember, these are patients who are deplete in those vitamin K-dependent factors II, VII, IX, and X. So those are agents that are approved for warfarin repletion, or off label for DOAC reversal for us in the United States.

Now thinking about the pros and cons. Specifically for intracranial hemorrhage when we think about repletion strategies, for those patients who are on vitamin K antagonists, we can think about FFP, or fresh frozen plasma, versus PCCs, or prothrombin complex concentrates.

Now FFP contains all of the factors necessary for the coagulation cascade. Now that requires large volumes that are often needed 10 to 15 cc/kg. And if you think about a patient who requires that volume repletion, such as a patient with a GI bleed or a patient with some type of major trauma, that may be exactly what you're looking for. But an intracranial hemorrhage, that volume is much smaller, and traditionally, that's not necessary. This takes time to prepare and administer. There's risks of fluid overload as well as transfusion reactions.

When we think about prothrombin complex concentrate for vitamin K antagonists associated intracranial hemorrhage, traditionally, what we have in the United States is a 4-factor, or Kcentra. It can be activated or inactivated, and the dose can be fixed or based on the INR or the weight of the patient. This leads to a faster reversal with less volume administration, but it does come with an increased cost.

Now when we think about the 2 types of reversal strategies for those patients who are on direct oral anticoagulants, again, dabigatran being the direct thrombin inhibitor and apixaban and rivaroxaban being the major factor Xa inhibitors. When we think about dabigatran, we have idarucizumab, which is a monoclonal antibody that binds to dabigatran, usually used if the dose is within the past 12 to 24 hours. And then the labs that you can follow with that are the prothrombin time as well as the thrombin time, and the dose is 5 grams with 2.5 grams twice. We don't see much dabigatran being used, at least in the United States. This is much less common for us. But what's more common for us and certainly what I have seen a lot of and taken care of a lot of these patients who are on factor Xa inhibitors and require andexanet alfa.

Andexanet alfa is a recombinant modified human decoy factor Xa protein. So, it basically behaves like factor Xa. And the factor Xa inhibitor is going to want to bind to that, allowing coagulation to take place and a clot to form. Now, it may be needed if the last dose of the factor Xa inhibitor has been within the past 18 hours. That was what an ANNEXA-4, the large trial which enrolled actively bleeding patients, allowed patients to be enrolled into. There can be a lab to follow, the anti-Xa level. And we'll talk about this a little bit more with some of the panel discussion. This lab is frequently not available and certainly not within a timely fashion at most institutions. And there's a high dose or a low dose and it is dependent on the type of factor Xa inhibitor dose that the patient is on, as well as the time that they last took that dose. It is not based on the severity of hemorrhage or the weight of the patient.

So when I think about a patient who has an anticoagulant-associated intracranial hemorrhage, the things that I like to think about doing are really providing a rapid door-to-needle time in terms of that reverse. So we know that, at least for primary intracerebral hemorrhage, that time when it expands is really within those first few hours. So getting that reversal agent in quickly is key to providing benefit. It helps to also have institutional protocols that include care bundles, which our next speaker will discuss thoroughly, and managing blood pressure and other things that we can be doing simultaneously in addition to reversal.

Things that are good not to do or the idea of prognosticating super early. Certainly, there are going to be some patients who have unsurvivable, very large hemorrhages and those patients may not require the same level of care. But the vast majority of patients we can't know right away how they're going to do, so want to provide the best possible care for them. And then we also want to avoid not reversing small intracranial hemorrhages or waiting for a patient to get worse before we provide that reversal, because that's really where we can make the most impact.

Announcer:
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