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Life-Threatening GI Bleeds and Anticoagulation Reversal in the ED

Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.

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Dr. Gibler:

Our next speaker is Dr. Rich Body. And Rich is Professor at the University of Manchester in Manchester, United Kingdom. And he is an expert in the early diagnosis of acute coronary syndrome. So, you have probably seen many of his manuscripts from those efforts. But I asked Rich to talk about something that I think is very important and fits very nicely because of the United Kingdom and their views on this particular therapy for patients with GI bleeding. Dr. Body.

Dr. Body:

Thanks very much everyone, and thanks Brian for the introduction. Hello to everyone who's watching virtually. So, I'm going to talk about how we manage a patient who's on oral anticoagulants, who presents to the emergency department with a life-threatening gastrointestinal bleed. So, I'm going to go through our approach to managing that patient from start to finish, and then I'm going to illustrate that, with a case study at the end. And that's based on a real case, but I've changed some details just to protect the patient's confidentiality. So here are my disclosures.

Okay, so let's talk about the case. We've got a life-threatening gastrointestinal hemorrhage in an anticoagulated patient. What are we going to do about it? Well, we're going to do the same thing as we would for every single patient, we're going to resuscitate them. So, we're going to go through our ABCDE approach, but there are some special considerations around that, for patients who have a life-threatening GI hemorrhage. So, when we come to assess the airway for this patient, there are some important things. If this is an upper GI bleed and a patient is vomiting, they may well have airway compromised. So, consider early intubation, they can vomit massive amounts of blood and it can really threaten the airway. You don't want them to aspirate that, so we've got to be prepared to intubate them very early on, and that's a difficult thing to do. You may want to decompress the stomach before going ahead with intubation. So, an NG tube prior to RSI is often used in order to make sure that we minimize that risk of aspiration. And you may be aware of the SALAD approach. The SALAD is one of a few different approaches that have been described, that essentially use suction to prepare you for intubation. So, with SALAD you'll go in essentially with your laryngoscope, with your left hand and the suction catheter. You can even buy a custom made one, not that we have them in Manchester, with your right hand. And then switch hands, you keep the suction catheter with the laryngoscope down and then you intubate. And that, because of course as you're intubating, you can get an impaired view with the blood. A head-up approach is useful, because these patients are often hemodynamically unstable, we may want a lower dose of induction agents, but a high dose of the paralytic. We want experienced hands for this, so get your most experienced support for managing the airway.

We'd call our anesthetic colleagues to try and help with this. When it comes to managing the circulation, there are some other specific considerations. So just like we would in trauma, replace blood loss with blood products. If the platelet count drops below 50, replace the platelets. If your prothrombin time goes above one and a half times normal, give the patient FFP, and monitor the fibrinogen, if their

fibrinogen is below 1.5 grams per liter despite the FFP cryoprecipitates indicated. And then the other thing is looking at exposure, make sure we correct hypothermia. It's very easy for these patients to become hypothermic. Often if there's bleeding they might be wet which compromises their temperature, and with hypothermia of course, it's not a great mix with bleeding, it increases your coagulopathy, so make sure you maintain normothermia.

Once we've done our initial resuscitation, we're then going to have to think about what's caused this situation in the first place. So, if we've got an upper GI bleed, the first and most important thing to consider is, this is the disastrous diagnosis, aortoenteric fistula. If it is, then we're really in trouble. Because it's a very serious thing, Those patients will have a massive hemorrhage, typically. Consider this in patients who known to have aortic pathology. If you suspect it, these patients are going to be going straight to theater with the cardiothoracic surgeons. So be aware of that one, that's the very rare one, but important that we recognize it and go straight to theater with those patients. For the rest, we then going to divide them into variceal and non-variceal causes of GI bleeding. So, for a variceal bleeding there's good evidence for terlipressin or octreotide which can give you the vasoconstriction and reduce the bleeding. Ceftriaxone, antibiotics have been shown to reduce mortality quite dramatically in patients with variceal bleeding.

So don't forget your antibiotics. And consider whether you might need something like a Blakemore/Segstaken tube to try and tamponade the bleeding from those variceals, even if it's just a temporary measure. For patients with non-variceal bleeding. So, you may not completely understand which one of these, which side of the algorithm you're going down, variceal versus non-variceal. But you're going to know whether the patient has risk factors for variceal bleeding, stigmata of chronic liver disease, high alcohol intake, et cetera, known viruses. For the rest that are non-variceal. You might be tempted to use proton pump inhibitors 'cause it makes sense, but the trials consistently show no evidence of benefit, and one big macroanalysis showed no evidence of benefit, prior to endoscopy. After endoscopy it's different, but prior to endoscopy no evidence of benefit. So, you're wasting your time with proton pump inhibitors. There's no evidence of benefit with terlipressin or octreotide in non-variceal bleeding either, and there's no evidence of benefit with tranexamic acid. The trial in the UK, big multi-center trial, randomized patients to TXA or placebo and found no benefits. So, you might as well use homeopathy than use any of those treatments. So, concentrate on other things that are going to make a difference to the patient, not those in non-variceal bleeding.

If it's a lower GI bleed, the most common cause of a massive bleed is a diverticular bleed. But there are some others, even hemorrhoids can present with very large bleeds. You can get angiodysplasia, you can even get cancers that are odd vessels in the bowel, and present with massive bleeds especially in your anticoagulated patients. So, what's our approach to the patient with a lower GI bleed? Well endoscopy is not the first line for these patients it's CT angiography would be the first line for such a patient. If you don't find a lower GI source on the CT angiogram have a think about whether this bleed presenting as lower GI could actually have an upper GI source, because sometimes the bleeding is so profuse it doesn't present with Molina or it comes out with bright red blood but it's an upper GI source. And surgeries generally reserved for cases that can't be solved with radiological or endoscopic means. So it's usually last resort.

So those are our specific things, and we do all of that first. And then we're going to think about reversal and repletion. You might do some of this in parallel but those are the most important priorities. And then of course, 'cause this patient's anticoagulate we need a strategy for reversing or replacing the patient. So just as Barbara mentioned, if the patient's on a coumarin or warfarin, then we're going to give them 4-factor prothrombin concentrate and vitamin K. If they're on a DOAC. So, dabigatran, apixaban, edoxaban, rivaroxban, we're going to give them specific reversal agent. So, for the factor Xa inhibitors, that's all of the the DOACs with Xa in the name rivaroxban, edoxaban, apixaban, and we're going to give Andexanet alfa, and if it's a factor two B inhibitor the only one is dabigatran, idarucizumab is agents of choice. So, let's have a little look at the reversal agents, Andexanet alfa first of all.

So, this is a specific reversal agent for factor Xa inhibitors. It was evaluated in the ANNEXA-4 trial. So this is not a randomized trial, all of the patients in the trial were anticoagulated, they had massive bleeding, and they were all given on Andexanet alfa, and followed through to see how well this reversal agent actually sorted out their coagulation parameters. 82% of patients achieved excellent or good hemostasis at 12 hours. NICE in the UK, the National Institute for Health and Care Excellence has given this a recommendation for gastrointestinal bleeding. So, it is recommended in the UK. The caveats are, there is a small number of patients in the ANNEXA-4 trial, so the subgroup with GI bleeding is only 62 patients. So, it's relatively small, and of course there was no control group in this trial. It's the best evidence that we've got hence the nice recommendation. But you know, there's still a few unanswered questions. And remember it is an expensive treatment so make sure your patient does fit the indications. If they do, it's a really important treatment 'cause these patients have a high risk of mortality but it is expensive treatment.

And then for the factor two B inhibitors, similarly we've got idarucizumab and this was evaluated in a very similar trial called RE-VERSE AD. It's again, a specific reversal agent. The trial again, had no control group, everyone in the trial had an idarucizumab and they measured coagulation perimeters. The median reversal of dabigatran was 100% and they got normal periprocedural hemostasis in 93%

of patients. Again, in the UK, NICE recommends this treatment. So, caveats, again it's a relatively small group that was in the trial, 137 patients, no control group. And it's still a relatively expensive treatment, although cost has come down a lot, it's been out for a few years now.

So, in summary, our approach to managing an anticoagulated patient who's got a life threatening GI bleed is to resuscitate first. And remember those specific considerations around the airway, the circulation, and the temperature control. Think about the cause, cause that's going to affect how we manage the patient. Is it upper GI bleed? Is it variceal or non-variceal? Could it be an aortoenteric fistula? What it could, if it's a lower GI bleed think about CT angiography, and then reverse or replete the patient to correct their anticoagulation.

Announcer:

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