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Assessing Anticoagulants & Antiplatelets During GI Bleeding

Dr. Buch:
Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch. And joining us today to talk about the management of anticoagulants and antiplatelets during acute gastrointestinal bleeding and the periendoscopic period is Dr. Neena Abraham. In addition to being the Associate Medical Director for Mayo's Clinic Center for the Science of Health Care Delivery in Arizona, she's also the lead author of the joint American College of Gastroenterology and Canadian Association of Gastroenterology Clinical Practice Guideline on this exact topic, which was published in the *American Journal of Gastroenterology* in April 2022.

Dr. Abraham, welcome to the program.

Dr. Abraham:
Thank you so much, Dr. Buch. I appreciate the invitation to join you.

Dr. Buch:
So let's dive right in, Dr. Abraham. Why is prothrombin complex concentrate preferred to fresh frozen plasma for patients who are bleeding while on warfarin?

Dr. Abraham:
So that's an excellent question and an important paradigm shift. For patients who are on warfarin with a GI bleed, the first thing to know is that reversal with an agent such as prothrombin complex concentrate is not necessary unless the INR is significantly supratherapeutic or the patient is having a life-threatening hemorrhage. In that situation, the use of PCC is preferred over fresh frozen plasma because of a more favorable risk-benefit profile and the more favorable physiologic effects in the setting of life-threatening GI bleeding including a decreased volume of administration and the absence of transfusion-related, adverse events, such as pulmonary edema and transfusion-related congestive heart failure, that often accompanies the large volume of fresh frozen plasma that would need to be transfused to actually reduce a patient's INR significantly.

Dr. Buch:
Very helpful. Which patients on dabigatran with GI bleeding should be considered for the administration of idarucizumab?

Dr. Abraham:
Yeah. So, when it comes to all of these direct oral anticoagulant agents and their reversal agents, the most important thing to understand is our review of the clinical evidence does not support its routine use, so you shouldn't be ordering reversal agents in the setting of GI bleeding related to any direct oral anticoagulant routinely. However, if the patient does have life-threatening hemorrhage, then that may be appropriate, and so what I really want physicians to know, particularly in the emergency room setting or in the pre-endoscopic setting, what constitutes a life-threatening hemorrhage. So these are folks who have major clinically overt or apparent bleeding causing hypovolemic shock, severe hypotension requiring pressors or surgery, or associated with a decrease in hemoglobin greater than 5 grams per deciliter. They often require transfusions greater than 5 units of packed red blood cells and are at high risk of death, so it's a much more severe level of GI bleeding than I think most people are dealing with. It's only in the setting of life-threatening hemorrhage would any of the direct oral anticoagulant reversal agents be appropriate, so in this case idarucizumab for dabigatran.

Dr. Buch:
Thank you. And what's your advice regarding aspirin use and GI bleeding?

Dr. Abraham:
Yes. So we spent a fair bit of time looking at the evidence surrounding that, and the key thing to remember is that cardiac aspirin, so

aspirin that's been prescribed to patients who have already had a heart attack or stroke, so it's cardiac prophylaxis for the, for the second event, is very important. And the patients who are on these drugs are often on this drug in concert with another antiplatelet agent, such as a P2Y12 inhibitor agent, clopidogrel, prasugrel or ticagrelor. In that setting of dual antiplatelet therapy, we certainly recommend discontinuation of the P2Y12 inhibitor, but the aspirin really doesn't need to be discontinued because the antiplatelet effect will actually persist, even if it's discontinued at the time the patient hits the emergency room based on the pharmacodynamics of the drug. And since the current practice, best practice for endoscopy is to perform emergent endoscopy in the setting of GI bleeding within 24 hours, 48 at the absolute most, continuing the aspirin is just fine because the benefit to the heart, is more important, and stopping it is not going to have any significant impact on the endoscopist's success at hemostasis.

Dr. Buch:
Another very important highlight for our listeners. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Neena Abraham about the management of anticoagulants and antiplatelets during acute gastrointestinal bleeding and the periendoscopic period.

So, Dr. Abraham, let's continue our discussion by focusing on various situations encountered with warfarin. First, when is it safe to continue warfarin for elective endoscopic procedures?

Dr. Abraham:
Yes. That's a very important question. And remember that currently in the literature we only have, at best, empiric estimates of endoscopic procedural bleeding risk off of off of these antithrombotic agents, so certainly, whatever estimates we have now which are guiding our data and our recommendations are going to be magnified in the setting of someone who's a regular antithrombotic user, such as a warfarin user. So, if you are not doing a high-risk bleeding procedure, then it would be perfectly appropriate to do your endoscopic procedure on the warfarin.

So, who makes up that group of low to moderate bleeding-risk patients who are undergoing these procedures? These are procedures such as EGD with and without biopsy, colonoscopy with or without biopsy, flex-sig with or without biopsy, ERCP with biliary or pancreatic stent placement or papillary dilation without sphincterotomy tissue sampling or treatment of choledocholithiasis, EUS without FNA, push enteroscopy and diagnostic balloon-assisted enteroscopy. You can also safely do enteral stent deployment, argon plasma coagulation, balloon dilation and polypectomy of small lesions greater—less than one centimeter on warfarin. Once you start getting into therapeutic maneuvers, then the risk of bleeding after the endoscopic procedure goes up, and in those patients we would recommend temporary interruption of the antithrombotic agent.

Dr. Buch:
So, in other words, there will be some situations where we may be doing a colonoscopy on a patient on warfarin and find that there's a large polyp and then have to do another procedure at a future time.

Dr. Abraham:
Yes, and it really depends on your practice setting, so for example, where I practice at the Mayo Clinic in Phoenix, Arizona, we have an open access endoscopy unit, and so, as part of the ordering process for patients, it's flagged to our scheduling team if the patient is on warfarin, and we recommend temporary interruption of warfarin in almost all our patients because our intent is therapeutic. In other words, if we're doing a colonoscopy and we see polyps, we don't want to have anything to—anything in the way of removing all the polyps regardless of size. Now, if you are not in that kind of setting and you have the ability to do procedures over if you come face-to-face with a lesion that is going to require a procedure that is of higher bleeding risk and you can do the procedure over, that's fine, but what we've found is that most patients would like to be one and done.

And the other thing to remember that is—something people forget is elective procedures should not be done when these cardiac patients are at highest risk for an adverse thromboembolic event. Right? So we know now which patients on anticoagulants are at highest risk of, uh, periprocedural thromboembolism. In those patients we recommend deferring an elective procedure like a, a colonoscopy for polyp removal until after that patient is out of that window of time where their risk of thromboembolism exceeds the benefit of removing the polyp.

Dr. Buch:
Thanks for that excellent clarification. Our next question is, when stopping warfarin, which patient should receive low molecular weight heparin bridging?

Dr. Abraham:
So, patients at the highest risk of thromboembolism are folks with mechanical heart valve, or atrial fibrillation with CHADS scores greater than 5 or 6, CHADS-VASc scores greater than 7, and recent venous thromboembolism, within 6 months.

Now, the other thing that is important to know is you really shouldn't be doing elective procedures in these folks, but if they have conditions that are not going to go away, such as mitral valve pros—prosthesis, then you should be doing the procedure with a heparin bridge or a Lovenox bridge.

Dr. Buch:
Thank you. And if we think about patients who are undergoing elective endoscopic GI procedures whose warfarin was interrupted, can you discuss why a recommendation could not be reached regarding when to resume warfarin?

Dr. Abraham:
Yes. When need to back up a little and understand the rigor with which the process and the rigor with which this guideline was conceived and developed. We followed an extraordinarily rigorous GRADE approach, involving 2 GRADE methodologists from each country, both leaders in the field, and more importantly, we didn't cut corners.

In the situation of resumption of these drugs, we've—the committee fell into the same problem and the same, with all of them, which is the absence of good quality evidence and literature to inform the clinical question. Now, GRADE also requires you to define the clinical questions before you do the literature search, and these are called PICO questions. And the way we defined our PICO questions for resumption of anticoagulants or even antiplatelet drugs was resumption within 1 to 7 days after the procedure, so that gave us the window of time within which we looked for high-quality literature to answer the question. And when it came to warfarin, the evidence to support a specific timing was lacking. However, with this guideline is published a companion dissemination tool. And I'd really like the highlight the importance of reading that dissemination tool for folks who are practicing endoscopy. And in that dissemination tool we explain that warfarin or any other anticoagulant be started, with immediate hemostasis. And in the case of direct oral anticoagulants, it's the day after the procedure, and in warfarin, day of procedure with good endoscopic hemostasis.

Dr. Buch:
Before we conclude, are there any other thoughts you'd like to share with our audience today?

Dr. Abraham:
Yeah. I think the most important thing for the audience to understand is this is not cookbook medicine. You really need to read the companion piece that's in the *American Journal of Gastroenterology's* "Red Section" authored by, first authored by Alan Barkun, who was the second author on the Guideline, to really appreciate the context of how you should use these recommendations. And then again, that additional clinical context is provided in the accompanying dissemination tool. That's why this guideline was designed the way it was, to have these extra pieces to make this actionable for clinicians given the fact that there's a lot of nuance to managing these patients.

Dr. Buch:
Those were some great insights. And I want to thank my guest, Dr. Neena Abraham, for an excellent, superb, spectacular discussion. Dr. Abraham, it was a pleasure speaking with you today.

Dr. Abraham:
Thank you so much.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit reachmd.com/giinsights where you can be Part of the Knowledge. Thanks for listening, and see you next time.