Managing Antithrombotic Agents in the Setting of Acute Gastrointestinal Bleeding

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KEYWORDS

• Antithrombotic agents • Gastrointestinal bleeding • Anticoagulants

KEY POINTS

- In general, if hemostasis is certain, antithrombotics should be resumed as soon as possible.
- This is because the outcome of a thrombotic event is usually far worse than a recurrent gastrointestinal (GI) bleeding event.
- Dilemmas arise when the clinician is not confident in whether hemostasis has been achieved.
- This is when the thrombotic risk assessment is required before a decision is made to withhold further antithrombotics.
- When the thrombotic risk is higher than the risk of recurrent GI bleeding, the antithrombotic agent should be continued.

INTRODUCTION

Antithrombotic-associated gastrointestinal (GI) bleeding is an increasing burden due to the growing population of advanced age, with multiple medical comorbidities, and the use of combinations of antiplatelet agents and anticoagulants.[1] GI bleeding in antithrombotic users is associated with subsequent increase in short-term and long-term mortality.[2] This increased mortality risk can be due to the disruption of antithrombotic or myocardial ischemia resulting from severe anemia or hemodynamic shock.

Although there may be consensus on ceasing anticoagulant and antiplatelet agents during an acute GI bleeding episode, debate remains concerning the appropriate approach to restarting these agents.[3–7] Clearer guidance is still needed on (1) under what circumstances each of the antiplatelet agents or anticoagulants should be stopped and (2) under what circumstances each of the antiplatelets or anticoagulants

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should be resumed, together with a time frame. This article provides the available evidence for the optimal management strategy of antithrombotics in the setting of acute GI bleeding and highlights areas weak in evidence in which future studies will be valuable.

GENERAL APPROACH TO THE MANAGEMENT OF ANTITHROMBOTICS

The following general approach can be adopted when faced with a patient with antithrombotic-associated bleeding:

1. Preendoscopy: (1) Resuscitation with fluids and blood, (2) assessing the need for reversing anticoagulant effects, and (3) early endoscopy.
2. Postendoscopy: An assessment should be made whether to continue or disrupt the antithrombotic based on a risk assessment: (1) What is the risk of recurrent bleeding after the endoscopic procedure? (2) What is the risk of a thrombotic event if the antithrombotic is disrupted?

MANAGEMENT OF ANTICOAGULANTS IN ACUTE GASTROINTESTINAL BLEEDING

Patients Receiving Warfarin

Summary

- Fresh frozen plasma (FFP) or prothrombin complex concentrate (PCC) should be the first-line reversal treatment of warfarin-associated bleeding.
- There are no randomized trials to assess whether or when warfarin should be resumed. The authors propose that in patients at high-risk for thrombosis (mechanical mitral valve, atrial fibrillation [AF] with $CHADS_2$ [congestive heart failure, hypertension, age $\geq$75 years, diabetes mellitus, stroke (double weight)] score 5 or 6, AF with rheumatic valvular heart disease, venous thromboembolism [VTE] within 3 months) warfarin should be resumed when definitive endoscopic hemostasis has been achieved. Concurrent heparin bridging therapy should be used until therapeutic INR have been achieved.
- When there is uncertainty concerning definitive endoscopic hemostasis, a second-look endoscopy can aid the decision on resumption of an antithrombotic agent.
- With the lack of high-quality evidence, it remains difficult to determine the time frame between thrombus formation and the subsequent clinical event and cessation of anticoagulant. Further research is required to identify the optimal duration of warfarin interruption after a GI bleeding episode.

Reversing the anticoagulant effects of warfarin

The most commonly used anticoagulant remains warfarin. The half-life of warfarin is approximately 40 hours. If the INR is between 2.0 and 3.0, it will require 4 days for the INR to reduce to 1.5 after withdrawal.[8]

Warfarin anticoagulant effect can be reversed with intravenous (IV) vitamin K or FFP or PCC. Vitamin K promotes the synthesis of new clotting factors II, VII, IX, and X. The INR will decrease within 2 to 4 hours following IV vitamin K infusion and normalize within 24 hours. FFP is a blood product made from the liquid portion of whole blood. The recommended adult therapeutic dose is 12 to 15 mL/kg. The effect of FFP will start in 10 minutes but it may take a few hours to show reversal of INR and up to 9 hours before the complete reversal of INR.[9]

Prothrombin complex concentrate PCC is a pharmacologic product made up of clotting factors II, IX, and X. Different processing techniques enable the production of