Antithrombotic Reversal Agents

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KEYWORDS

• Anticoagulate • Antithrombotic reversal agent • Emergency department
• Reversal options • Bleeding • Coagulopathic

KEY POINTS

- The actively bleeding anticoagulated patient presenting to the emergency department requires rapid and simultaneous evaluation and treatment that often also necessitates complex coordination of care with multiple specialists.
- Even with excellent supportive care, the timeliness with which reversal decisions need to be made continues to demand of the emergency practitioner a familiarity with the properties and general characteristics of a variety of antithrombotic agents.
- Reversal options vary and may include vitamin K, FFP, PCC, rFVIIa, platelets, and desmopressin, among others.

INTRODUCTION

The actively bleeding anticoagulated patient presenting to the emergency department (ED) requires rapid and simultaneous evaluation and treatment that often also necessitates complex coordination of care with multiple specialists. In addition to the basics of supportive care, in select patients reversal of an antithrombotic agent needs to be considered. The timeliness with which these decisions often need to be made demands a familiarity with both old and new antithrombotic agents, as well as with the ever-evolving options and approaches to reversal. This review discusses the basics of hemostasis and the specific use of the reversal agents, vitamin K, fresh frozen plasma (FFP), prothrombin complex concentrate (PCC), recombinant Factor VIIa (rFVIIa), protamine sulfate, as well as other agents currently in development. Options for the management of a patient who has received antiplatelet or thrombolytic agents are also discussed.

The basics of bleeding management are fundamental to emergency care. Hemorrhage identification and source control become paramount in the management of an actively bleeding or unstable patient. Although direct pressure may be adequate

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to control most external hemorrhage, it is the coagulopathic and internally bleeding patient that can present an even greater challenge.

Diligent supportive care can be provided as the primary treatment strategy or may serve as a bridge to antithrombotic reversal or intervention (by surgical, endoscopic, or endovascular means) for definitive management. Supportive care includes close monitoring of vital functions, multiple points of large-bore intravenous (IV) access, and maintaining the patient's warmth and comfort. Depending on the source of hemorrhage, supportive care may also include medications targeted to the affected organ system (eg, octreotide for variceal bleeding) or protective strategies to prevent ongoing damage to a critical system (eg, blood pressure control in intracranial hemorrhage). IV fluid replacement and blood product transfusion may be required and should be given aggressively to maintain euvolemia, but with consideration given to the risks and benefits of a volume challenge. It is also important to consider the possible contribution of volume resuscitation toward increasing hemorrhage by increasing circulatory pressure at the site of bleeding. In addition, the allergic and iatrogenic infectious risk that accompanies blood product transfusion needs to be considered.

Generally, antithrombotic reversal is indicated whenever the risks of continued antithrombotic effect outweigh the risks of the reversal. In patients with high-risk bleeding, such as intracranial hemorrhage, active gastrointestinal or genitourinary bleeding, pulmonary hemorrhage, severe trauma, or compartment syndrome, the decision to reverse may be more straightforward; this is also the case in patients that require an emergent invasive procedure. However, the decision is fraught with even more challenges with certain underlying indications for use of antithrombotic agents. For instance, reversal in the case of a patient who is appropriately anticoagulated for the management of a mechanical heart valve poses potentially serious risks to the integrity and function of the valve. As such, the potential risks and benefits of reversal need to be weighed carefully and on a case-by-case basis.

PATHOPHYSIOLOGY

An understanding of the process of hemostasis is essential. There are 3 key components to effective intrinsic hemostasis: platelets, the plasma coagulation cascade, and the endothelium. Primary hemostasis (Fig. 1) results in the formation of a platelet plug at the site of blood vessel injury, which occurs through platelet adhesion via binding to exposed subendothelial von Willebrand factor. Secondary hemostasis stabilizes the initial platelet plug through fibrin deposition. Fibrin cements and stabilizes the platelet plug. Fibrin results from the conversion of soluble fibrinogen to insoluble fibrin via the

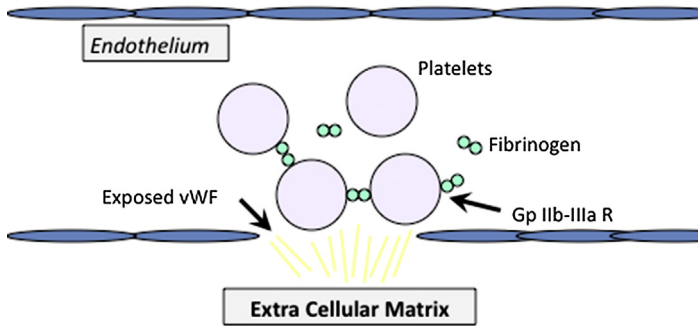

Fig. 1. Primary hemostasis. Platelets organize into a platelet plug at the site of endothelial injury by binding subendothelial von Willebrand factor (vWF) and circulating fibrinogen.