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Antiplatelet and anticoagulation medications and the surgical patient

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Abstract

BACKGROUND: Acute coronary syndrome affects more than 750,000 Americans per year, and antiplatelet agents are the cornerstones of treatment. Atrial fibrillation affects 2.4 million patients in the United States, and venous thromboembolism occurs in 1 to 2 per 1,000 adults per year. Anticoagulants are commonly prescribed to affected patients. Surgeons are commonly called upon to care for patients taking medications that affect normal coagulation. It is important that the surgical community has a fundamental understanding of these agents' pharmacology, which may impact patients' clinical course.

METHODS: A review of recent literature on pharmacologic agents that affect coagulation was performed.

RESULTS: A number of medications that alter normal coagulation were reviewed in this article including their pharmacologic properties and reversal strategies.

CONCLUSIONS: There are a variety of medications that affect a patient's coagulation ability, including many newer agents on the market. This review provides surgeons with the knowledge needed to assist in caring for individuals receiving these drugs.

Medications that alter normal coagulation are commonly prescribed for a variety of conditions.[1] These medications present a challenge for a surgeon when called on for a patient receiving these agents who sustains an illness or injury or requires an invasive procedure. There have been many advances with new drugs during recent years, particularly the novel oral anticoagulants (NOACs). The surgeon needs to be aware of these drugs along with their basic pharmacology, including half-lives and reversal strategies.

The surgeon must determine whether to continue or discontinue the drug(s) along with timing the resumption of the medication(s) when discontinued. Although many have attempted to create algorithms for this situation, it must be based on the drug's pharmacologic profile along with an individualized care strategy for each patient. This care strategy should include risk stratification of both the patient-specific risk of thrombosis and the procedure-specific risk of bleeding.[2] Often this strategy includes a preoperative discussion with the patient's provider or discipline who prescribes the agent(s) and possibly anesthesiology. Some of these agents present difficulties when neuraxial anesthesia is being considered (Table 1).[3]

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Table 1 Neuraxial anesthesia considerations[3]

Agent	Timing of discontinuation for neuraxial anesthesia
Ticlopidine	14 d before procedure
Clopidogrel	7 d before procedure
GP IIb/IIIa inhibitors	8–48 h before procedure
Warfarin	Normal INR before procedure, INR <1.5 for catheter removal
UFH subcutaneously	Twice daily dose total <10,000 units/d no need to discontinue
	More than twice daily or >10,000 units/d no safety established
UFH intravenously	Heparinize 1 h after neuraxial procedure, remove catheter 2–4 h after last dose
LMWH	Therapeutic dose 24 h, prophylactic dose 10–12 h before procedure
	Catheter removal 10–12 h after last dose, after removal dose withheld for at least 2 h
Fondaparinux	Avoid indwelling catheters
Rivaroxaban	Catheter removal >18 h after last dose, resume >6 h after catheter removal, hold for >24 h if traumatic puncture[22]
DTIs	Insufficient information, suggest avoiding neuraxial procedures

DTIs = direct thrombin inhibitors; LMWH = low-molecular-weight heparin; UFH = unfractionated heparin.

Risk assessment

Risk assessment begins with a thorough history of each patient including the type and dose of the coagulation-affected drug, personal characteristics of the patient (age, comorbidities, weight, and concomitant medications), and length of time in which the agent(s) had been prescribed (particularly in the setting of a coronary stent, heart valve replacement, and venous thromboembolism). Current appropriate laboratory values are important to obtain. When using anticoagulant medication for prophylaxis of venous thromboembolism (VTE), it is important to review the individual's risk factors for an event. Additionally, the risk of hemorrhage from the proposed procedure or the disease entity the patient may face needs to be taken into consideration before continuing, discontinuing, or resuming medications that alter coagulation.[2–6]

Antiplatelet Agents

Aspirin is one of the oldest agents that affect the coagulation cascade. The pharmacologic effect on platelets is through irreversible acetylation and the inhibition of platelet cyclooxygenase-1, a critical enzyme involved in the production of thromboxane A2. The release of thromboxane A2 stimulates the recruitment and activation of further platelets and increases platelet aggregation.[7]

Ticlopidine (Ticlid; Roche, San Francisco, CA) and clopidogrel (Plavix; Bristol-Meyers Squibb, New York, NY) belong to a class of thienopyridines, drugs that block $P2Y_{12}$, a receptor on platelets for adenosine diphosphate (ADP). These drugs irreversibly inhibit ADP-induced platelet aggregation.[7] Because clopidogrel is a prodrug that must be metabolized by hepatic conversion, its effectiveness on platelet inhibition correlates with the metabolic activity of several cytochrome P450 enzymes. Thus, there is a variable degree of antiplatelet activity based on the individual patient. This variability launched the search for more reliable drugs.[8]

Two newer ADP receptor antagonists used in acute coronary syndrome have been developed. Prasugrel (Effient; Eli Lilly, Indianapolis, IN), an irreversible inhibitor, and ticagrelor (Brilinta; AstraZeneca, Wilmington, DE), a reversible inhibitor, have a faster onset of action and stronger, more reliable antiplatelet activity than clopidogrel. They are more potent $P2Y_{12}$ receptor inhibitors; however, with their benefits of increased potency come risks.[8]

When compared with clopidogrel, prasugrel had increased bleeding events including vascular access site and coronary artery bypass graft (CABG)-related bleeding. CABG bleeding complications were 4-fold higher than those treated with clopidogrel. Also, major bleeding events were higher (ie, 2.4% compared with 1.8% in patients receiving clopidogrel). The bleeding risk was higher in patients greater than 75 years and less than 60 kg. There was a reduction in cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke in patients receiving prasugrel.[9] The dose for prasugrel is 10 mg/d and 5 mg/d if patients are less than 60 kg. The loading dose, if indicated, is 60 mg.[10]

Ticagrelor showed a decreased rate of myocardial infarction, stroke, and cardiovascular death. There was not a dramatic increase in all major bleeding events in the ticagrelor patients when compared with clopidogrel (ie, 11.6% vs 11.2%, respectively). However, there was a statistical increase in intracranial bleeding and non–CABG-related bleeding. There is no need for dose reduction in renally impaired patients.[11] The dose for ticagrelor is 90 mg/d with a loading dose of 180 mg. It is not recommended for patients with severe hepatic impairment, and it must be used with caution in patients with moderate hepatic impairment.[12]

Both agents show an overall increased risk of bleeding compared with clopidogrel, and the bleeding risk increases with the duration of therapy. In the pivotal studies of these drugs, one of the most common etiologies of bleeding was gastrointestinal. Thus, the liberal use of gastrointestinal acid suppression should be considered.[8]

Dipyridamole (Persantine; Boehringer-Ingelheim, Ridgefield, CT) is a weak antiplatelet agent. It inhibits