Pharmacologic Therapies in Anticoagulation

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KEYWORDS

• Anticoagulation • Venous thromboembolism • Atrial fibrillation • Warfarin
• Direct oral anticoagulants • Heparin

KEY POINTS

- Anticoagulants are beneficial for prevention and treatment of venous thromboembolism and stroke prevention in atrial fibrillation.
- Approach to antithrombotic therapy varies according to indication, patient's bleeding risk, presence of comorbidities, cost, and patient's preference.
- The development of new target-specific oral agents is changing the landscape of anticoagulation therapy; data are evolving on indications, drug interactions, and relative efficacy and risks versus vitamin K antagonists and other anticoagulants.
- Understanding the pharmacology of different anticoagulants is required to adequately treat patients while minimizing risk of serious complications.

INTRODUCTION

Venous thromboembolism (VTE), a common condition affecting hospitalized and ambulatory patients, is associated with significant morbidity, mortality, and health care costs.[1] The etiology of VTE is usually multifactorial, resulting from risk factors that either predisposes to venous stasis, vascular wall injury, and/or hypercoagulability (eg, thrombophilia, pregnancy, cancer).

Normal hemostasis is achieved through a complex interplay between vascular endothelium, platelets, coagulation factors, and natural anticoagulants.[2] The anticoagulant drugs act by inhibiting, directly or indirectly, specific coagulation factors to prevent thrombus formation (**Fig. 1**). Different classes of anticoagulants have been approved for prevention and treatment of thromboembolic events, including deep venous thrombosis (DVT), pulmonary embolism (PE), stroke prevention in patients with atrial fibrillation (AF), or thrombus formation in patients with mechanical heart valves.

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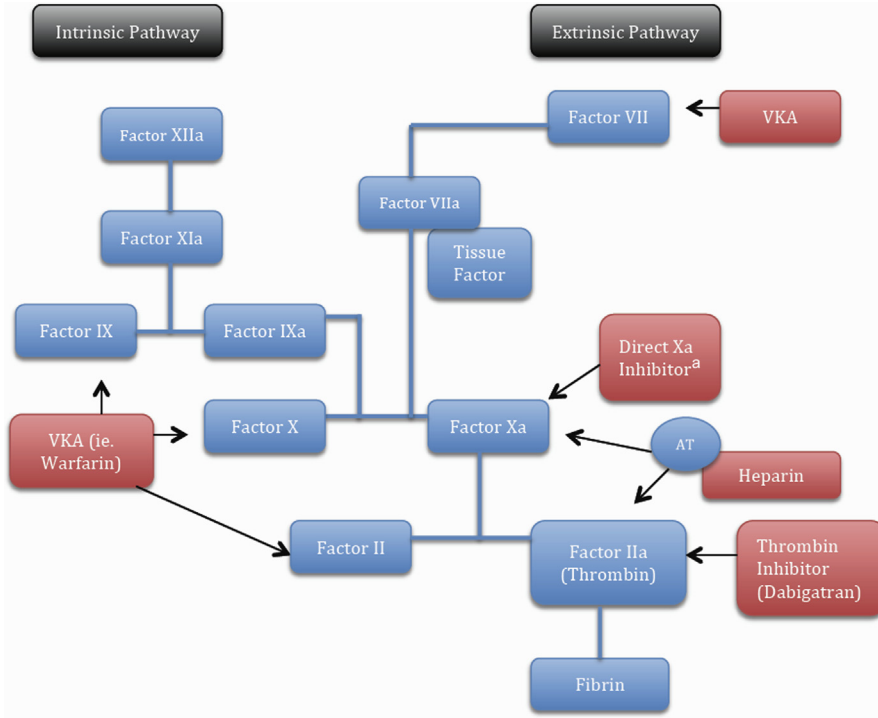

Fig. 1. Coagulation cascade and therapeutic targets of the anticoagulant drugs. [a] Rivaroxaban, apixaban, edoxaban. AT, antithrombin; VKA, vitamin K antagonist.

The vitamin K antagonists (VKA), such as warfarin, have been the standard of care for more than 50 years in long-term oral anticoagulation therapy for most of the indications above. Parenteral anticoagulants, such as unfractionated heparin (UFH) and low molecular weight heparin (LMWH), also have an important and established role in the anticoagulation treatment in both inpatient and outpatient settings.[1] However, these medications have several limitations. The VKAs have a narrow therapeutic index, wide interpatient and intrapatient variability due to genetic mutations as well as multiple food and drug interactions, thus requiring frequent monitoring to enhance its efficacy and safety.[3] The LMWHs have more predictable pharmacokinetics but the need for parenteral application and high cost are limitations.

In the hopes to overcome these issues, researchers have worked for many years on the development of safe oral drugs that would provide same or superior benefits as the VKAs without the need for frequent monitoring. These drugs were initially referred as "new" oral anticoagulants (NOACs), but as time passes preference has been to call them "direct" oral anticoagulants (DOACs) or target-specific oral anticoagulants (TSOAC), which more accurately reflects their mechanism of action.[4] In 2010, the US Food and Drug Administration (FDA) approved the direct thrombin inhibitor dabigatran for the prevention of thromboembolic complications in patients with AF. In the following years, 3 direct factor Xa inhibitors (rivaroxaban, apixaban, and edoxaban) were approved for treatment of AF and venous thromboembolism. Since then, other DOAC drugs are in development and/or pending approval process by the FDA.