

Optimizing Use of Current Anticoagulants

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KEYWORDS

- Warfarin • Administration and dosage • Adverse effects
- Anticoagulants • Drug effects • Drug therapy • Therapeutic use

For decades, vitamin K antagonists (VKAs) like warfarin sodium have served well as the oral anticoagulant drugs of choice for prevention and treatment of thromboembolic disease.¹ Despite excellent clinical efficacy, warfarin remains a difficult treatment to deliver. Because of wide intra- and interindividual variability and the small differential separating beneficial and toxic therapeutic effects, warfarin is classified as a narrow therapeutic index drug. Consequently, frequent assessment of the effect of warfarin on the coagulation system, as measured clinically by the international normalized ratio (INR), is required for the duration of treatment.¹ Frequent INR monitoring and follow-up have potential negative effects on quality of life. The pharmacokinetics and pharmacodynamics of warfarin are altered by several factors, including diet, alcohol use, many medications, and concurrent illnesses.¹ Because of these challenges and fear of bleeding complications, warfarin remains underused despite an increasing number of patients who might benefit from its use.² The many liabilities associated with warfarin therapy have fueled ongoing efforts to develop effective oral anticoagulants that are clinically easier to use.³

New oral anticoagulants (eg, dabigatran and rivaroxaban) have been introduced for selected indications, namely orthopedic thromboprophylaxis, in Canada and Europe and are in different phases of testing for other indications and in preparation for introduction in the United States. There is speculation that the introduction of newer, easier-to-use anticoagulants will eliminate the need for warfarin.⁴ Although the cost of newer agents is yet to be defined in the US market, they will be more expensive than warfarin, which is available as a generic drug. Results of clinical trials comparing new anticoagulants with adjusted-dose warfarin therapy have largely reported similar efficacy and safety,^{5,6} particularly when warfarin therapy is well managed. Patients with stable INR control have been shown to experience significantly fewer anticoagulation therapy-related complications compared with patients with less stable INR

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control.^{7,8} Data from retrospective studies further support the use of INR stability to accurately predict reductions in adverse events.⁹ Therefore, before a tried-and-true therapeutic modality like warfarin with decades of accumulated clinical experience is abandoned in favor of novel newer agents, measures to ensure optimal use of warfarin should be fully explored. In addition, warfarin remains the therapy of choice for patients with mechanical heart valves and for those who experience therapeutic failure on the newer agents. This article examines various approaches to optimize the clinical use of warfarin.

INITIATION OF THERAPY

Selecting appropriate candidates for warfarin therapy is an important first step in achieving optimal anticoagulation. A valid indication for anticoagulation therapy should exist. Although the preceding statement should be intuitive, patients receiving atrial fibrillation with low underlying stroke risk likely receive minimal net benefit from warfarin therapy.¹⁰ Therefore, before initiating therapy, careful weighing of the risk and benefits of warfarin therapy is required.

Before initiating therapy a thorough patient assessment should be performed, including a comprehensive medical, family, medication history (including dietary supplements and over-the-counter drugs); social, lifestyle, and employment profile; and health beliefs and attitudes, level of understanding, health literacy, personal health motivation, and health care resources.¹¹ The risks of warfarin therapy may outweigh benefits in patients with a previous history of medication nonadherence, bleeding risk factors, history of falls, significant alcohol consumption, memory impairment, and lack of adequate support from family members or caregivers. Validated tools exist for conducting formal bleeding risk assessment.^{12,13} Patients and/or their caregivers should be involved in the discussion of the risks and benefits associated with warfarin therapy and should agree with the decision to initiate therapy.¹¹ Some anticoagulation providers require new patients to sign a contract indicating their commitment to adhere to the requirements of warfarin therapy.

PATIENT EDUCATION

When patients are actively involved in, understand, and take responsibility for their care the likelihood of INR stability is improved.¹⁴ Patient education is an essential component in quality management of the anticoagulated patient. Because it is time consuming for clinicians and overwhelming for patients, educating the anticoagulated patient is often neglected.¹⁵ A formalized warfarin education curriculum based on established models may be more likely to improve patient's knowledge level compared with an ad hoc approach.¹⁶ Specific warfarin knowledge-assessment tools have been developed to help assess patients' educational needs.¹⁷ Efforts to educate patients regarding warfarin therapy should continue throughout treatment.

INDUCTION OF THERAPY

Various algorithms aimed at quickly achieving therapeutic INR values during warfarin therapy induction have been developed.^{18–21} The size of the initial warfarin dose is a key differentiation between the various available algorithms. Regardless of the size of the initial warfarin dose, a key component of successful warfarin initiation is a structured initiation process that incorporates frequent INR assessments (at least 2–3 times per week) with subsequent warfarin dose titration.¹

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