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Supporting Safe Anticoagulation Use in the Community Setting

Practical, evidence-based strategies can help pharmacists improve patient education, promote adherence, and lessen the risk of adverse events.

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ABSTRACT: Effective anticoagulation counseling is a key responsibility in community pharmacy practice, especially given the widespread use of anticoagulants and their narrow therapeutic windows. Practical, evidence-based strategies can help pharmacists improve patient education, support adherence, and reduce the risk of adverse events. Tailoring counseling for vitamin K antagonists versus direct oral

anticoagulants is essential, as it enables pharmacists to emphasize proper dosing, highlight important drug-drug and drug-food interactions, and identify symptoms that require urgent medical attention. In addition, understanding how to manage therapy transitions, such as perioperative management or switching between anticoagulants, further reinforces the pharmacist's critical role in promoting safe and effective anticoagulation therapy in daily practice.

Anticoagulant medications are among the most pre scribed therapies dispensed in community pharmacy practice and arguably the most potentially hazardous. Pharmacists are relied upon to ensure that patients understand how to use these medications safely and effectively. Differences in adherence, diet, comorbidities, and concomitant medications can significantly influence anticoagulation control and bleeding risk, making straightforward counseling essential.[1]

Community pharmacists are uniquely positioned to provide this support. With frequent patient contact, accessibility, and a comprehensive view of medication histories, pharmacists can identify risks, prevent avoidable complications, and empower patients to take an active role in their therapy. Anticoagulation counseling can be complex, requiring knowledge of drug-specific considerations, monitoring needs, transitions of care, and individualized patient factors.

Warfarin

Warfarin was discovered in the early 1900s after a Midwestern farmer lost multiple cows from hemorrhage after eating spoiled clover. Researchers found that coumarin, a naturally occurring chemical in clover, would react with certain mold spores in spoiled clover, forming the hemorrhagic chemical 3,3'-methylenebis(4-hydroxycoumarin). The Wisconsin Alumni Research Foundation assisted researchers in exploring different analogues of this compound and the role it played in hemorrhagic states, hypothesizing that it could be used to prevent blood clots in humans. This led to the compound initially being marketed as a pest-control method under the name warfarin, a compound that showed toxicity in mice and rats but not in human subjects. Subsequently, a water-soluble version better known as warfarin sodium (Coumadin) was approved for human use and marketed in 1954.[2]

Warfarin is a vitamin K antagonist that is used in both the treatment and prevention of thromboembolic events.[3] By blocking the action of vitamin K epoxide reductase (VKOR), it prevents activation of vitamin K and ultimately leads to a decrease in synthesis of vitamin K–dependent clotting factors II, VII, IX, and X and the anticoagulant proteins C and S. Warfarin is the preferred anticoagulant in certain patient situations, including mechanical valve

replacement, moderate-to-severe rheumatic mitral stenosis, or concurrent use with CYP3A4/P-glycoprotein–inducing agents.[4] Warfarin is also available as a generic drug, making it an inexpensive anticoagulant option compared with newer agents. It is known to have a narrow therapeutic index and many food and drug interactions, and it requires frequent monitoring via international normalized ratio (INR), which can lead to highly variable dosing regimens. All of these factors can affect warfarin adherence. These limitations led drug developers to create novel alternatives such as the direct oral anticoagulants (DOACs).

Direct Oral Anticoagulants

DOACs offer multiple clinical advantages over warfarin therapy, contributing to their increased utilization compared with warfarin's decline. There are two classes of DOACs utilized in practice: the factor Xa inhibitors and the direct thrombin inhibitors. Apixaban (Eliquis), edoxaban (Savaysa), and rivaroxaban (Xarelto) inhibit formation of blood clots by selective blockade of factor Xa, which "prevents the conversion of prothrombin into thrombin."[5] On the other hand, dabigatran (Pradaxa) directly inhibits the action of thrombin. DOAC medications have been associated with a lower risk of stroke or bleeding compared with warfarin.[6] Along with their improved safety profile, DOACs offer increased convenience, as they require less monitoring and have fewer dietary and drug interactions compared with warfarin. Nonetheless, disadvantages such as higher cost and a need for consistent adherence, as well as contraindications in certain patient populations, highlight the importance of thorough pharmacist counseling and

individualizing therapy selection as much as possible.

Dosing and Adherence

Dosing of warfarin is unique and should be individualized to each patient. Factors including age, nutritional status, comorbidities, concomitant medications, and current diet should be considered when determining an appropriate starting dose. Genetic alterations in the VKOR complex subunit 1 (VKORC1) enzyme or a variant in CYP2C9 may also alter how warfarin doses should be initiated and maintained. When available, pharmacogenetic test results can also be used to inform dosing.[7]

For healthy people with no major comorbidities or other altering factors, warfarin is often initiated at a dosage of 5 to 10 mg once daily. For older adults, those with comorbidities such as liver disease or heart failure, or those who are at an increased risk for bleeding, an initial daily dosage of 2.5 mg should be considered.[7] The initial dosage is then titrated to maintain a target INR range. For most indications, targeting an INR goal of 2 to 3 is appropriate. Mechanical mitral valve replacement should be targeted to an INR goal of 2.5 to 3.5.[7]

Patients should be instructed to take their daily dose at the same time in the evening. This can allow for same-day dose adjustments based on their INR status that day.[8] Because each regimen is unique, patients may be required to take multiple tablet strengths to achieve

their recommended dose. Warfarin tablets come in nine different strengths, each with their own unique identifying color. Patients should be aware of the color of the tablet that correlates with their appropriate dose each day. For patients who are intolerant to any dyes, the white 10-mg tablet can be used.

The DOACs have a more standardized dosing schedule compared with warfarin, but each DOAC has its own unique considerations to keep in mind. For example, when using apixaban for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), a patient is to take 10 mg by mouth twice daily for 7 days, followed by a decrease to 5 mg twice daily thereafter.[9] Rivaroxaban has a slightly longer initial duration of therapy for treatment of DVT and PE. This standard dosing includes 15 mg twice daily with food for 21 days, followed by 20 mg daily with food thereafter. Administration with food is important with rivaroxaban in doses of 15 or 20 mg as it helps to increase absorption and bioavailability.[10] Because these medications have shorter half-lives compared with warfarin, it is very important to counsel patients to take the dose at the same time each day and emphasize the importance of not missing a dose to maintain adequate anticoagulation.

Monitoring

Using warfarin requires extensive monitoring, not only initially but throughout the continuation of therapy.

Upon starting warfarin, patients should have their INR checked every few days, if not daily. This is because the full antithrombotic effects of warfarin are not seen for approximately 5 days owing to the varying half-lives of the coagulation cascade proteins. A weekly INR should be monitored for at least the first month of therapy. From there, a patient can be assessed for compliance and other factors such as diet changes and status of comorbidities, and if stable, frequency of INR monitoring can be extended. Upon a dosage change, an INR should be checked within 1 to 2 weeks. Once a patient is stabilized on a consistent dosage, monitoring can be extended to every 4 to 12 weeks.[11]

DOACs do not require routine laboratory monitoring. Certain assays such as activated partial thromboplastin time, thrombin time, and prothrombin time can be used if needed for compliance purposes.[12] Factor Xa levels and plasma drug concentrations can also be measured, but there is no currently established role for these tests to be routinely used in clinical practice. A complete blood count and comprehensive metabolic panel before initiating a DOAC should be performed to ensure proper renal and liver function. These tests should be routinely done at follow-up visits.[13]

Bleeding Risk

Both warfarin and DOACs increase the risk for bleeding. Patients should be educated on the difference between minor bleeding and major bleeding, as well as when to manage at home versus seeking immediate medical attention. Some examples of less serious bleeding, or “nuisance” bleeding, include easier bruising, having a cut bleed for a bit

longer than normal, and the occasional nosebleed, as well as bleeding gums after brushing teeth. Counseling points to help prevent or treat these instances of less serious bleeding include applying pressure to the bleeding area, brushing teeth more softly, and using extra caution with sharp objects such as kitchen knives or shaving razors.[8,14]

On the other hand, major or more serious bleeding can occur in patients taking anticoagulants and may include blood in the urine or stool, coughing or vomiting up blood, or bleeding from a cut that will not stop after appropriate pressure is applied. A fall or trauma in which a patient hits his or her head is also cause for concern in patients taking an anticoagulant owing to the risk for intracranial hemorrhage. When these happen, patients need to seek immediate medical attention, as reversal agents may be required to stop the bleeding.[8]

Drug, Diet, and Lifestyle Interactions

Warfarin is notorious for its multiple drug and diet interactions. Some important classes of medications that interact with warfarin include antibiotics, antifungals, and antivirals.[5] The mechanism by which certain antibiotics interact with warfarin is twofold. First, antibiotics affect the normal gut microbiome, which is a rich source of vitamin K, potentially increasing the anticoagulant effects of warfarin.[5] On the other hand, antibiotics that inhibit the CYP2C9 enzyme, such as sulfamethoxazole/trimethoprim or metronidazole, can also alter the

metabolism of warfarin, ultimately increasing the risk for bleeding.[5] If a patient must be on an antibiotic course during their treatment with warfarin, it is important either to find an alternative that does not interfere with the metabolism of warfarin or to monitor the INR more closely and make dosage adjustments, if needed.

Because warfarin prevents production of vitamin K–dependent clotting factors, foods that are rich in vitamin K can pose a risk for interaction. Patients do not need to stop eating these foods completely, but they should be counseled to maintain a consistent intake of vitamin K–containing foods, as significant changes may alter their anticoagulant response to warfarin. Common vitamin K–containing foods include leafy greens such as spinach, kale, broccoli, lettuce, and Brussels sprouts, among others.[8]

A drug interaction that occurs with both warfarin and DOACs includes nonsteroidal anti-inflammatory drugs (NSAIDs). This is a risk with both COX-2-selective NSAIDs as well as nonselective NSAIDs.[5] If a patient on anticoagulation needs an OTC method for pain relief, emphasize nonpharmacologic options such as heat/ice or recommend an alternative pain reliever such as acetaminophen or topical agents, which minimize systemic absorption.

Rivaroxaban and apixaban are both metabolized by CYP3A4 and are substrates of P-glycoprotein.[5] It is important to screen the medication list for coadministration of any CYP3A4 or P-glycoprotein inducers or inhibitors and to tell patients to always discuss the starting or stopping of any new medications, herbal supplements, or OTC products with their healthcare provider.

Common inhibitors of CYP3A4, such as clarithromycin, ketoconazole, and ritonavir, can lead to increased concentrations of DOACs in the blood, increasing risk for bleeding. Conversely, CYP3A4 inducers such as rifampin, carbamazepine, phenytoin, and St. John's wort can lead to decreased concentrations of DOACs, causing a reduction in effectiveness and increased risk for thromboembolic events. Educating patients about these interactions can help to prevent significant changes in response to anticoagulation therapy.

Missed Doses

The approach to handling missed doses varies between warfarin and DOACs owing to their differing pharmacokinetic profiles and half-lives. Because the anticoagulant effects of warfarin last beyond 24 hours, it is not as important for patients to immediately take a dose after they forget. If they miss their dose on a certain day, they should try to take it as soon as possible on that same day.[7] Patients should be educated not to double their dose on a day following a missed dose to make up for the missed dose. It is also important for patients to make their provider aware of the missed dose, as it could potentially alter INR results at an upcoming visit.

Depending on the DOAC, rules for missed doses may be similar. For apixaban, if patients miss their regularly scheduled dose, they should take it as soon as they remember that same day, followed by

resuming the normal twice-daily administration.[9]

Management of a missed dose of rivaroxaban depends on the dose. For patients who take rivaroxaban 2.5 mg twice daily, a single dose should be taken at the next scheduled time. If a patient is taking 15 mg twice daily, a dose should be taken immediately to ensure that the 30-mg-per-day threshold is reached. In this situation, two 15-mg tablets may be taken at once. Lastly, for patients who take 10 mg, 15 mg, or 20 mg once daily, a single dose should be taken immediately but should not be doubled up within the same day.[10]

Perioperative Management

Management of anticoagulant therapy in relation to surgery and other procedures requires a careful balance between minimizing bleeding risk and preventing clotting events. When indicated, warfarin should be stopped 5 days before a scheduled procedure and reinitiated 24 hours following the procedure or when hemostasis is achieved. The use of bridging with a low- molecular-weight heparin, such as enoxaparin, is a decision made by the provider managing the patient's anticoagulation.[15] **TABLE 1** depicts clinical situations in which bridging would be recommended.

Table 1 Indications for Bridging Anticoagulation During Warfarin Therapy Interruptions

Level of Risk	Mechanical Heart Valve	Atrial Fibrillation	Venous Thromboembolism
High risk of thrombosis (e.g., >10% annual risk of arterial thromboembolism or >10% monthly risk of vs. thromboembolism)	Any mechanical mitral valves Tilting-disc or caged ball aortic valve Stroke or TIA in past 3 months	CHA2DS2VASc ≥7 Stroke or TIA within past 3 months Rheumatic valvular heart disease	VTE in past 3 months Severe thrombophilia (e.g., protein C or S deficiency, antithrombin deficiency, antiphospholipid syndrome) Multiple thrombophilias Active cancer associated with high risk of VTE

CHA2DS2VASc: congestive heart failure, hypertension, age 75 years or older, diabetes mellitus, prior stroke or transient ischemic attack (TIA), vascular disease history, age 65 years or older, female sex; VTE: venous thromboembolism.
Source: Reference 15.

For patients who are taking DOACs, interruption of regularly scheduled dosing for perioperative management depends on the bleeding risk associated with the procedure. For procedures with very minimal bleeding risk, the DOAC may be continued. For procedures with low/moderate-to-high bleeding risk, the DOAC is typically held for 24 to 48 hours, respectively, depending on the agent. The DOAC should be held the day of the procedure and then resumed when hemostasis is achieved in 24 to 48 hours for low/moderate and high bleeding risk procedures, respectively.[16]

Switching Between Warfarin and DOACs

Switching between warfarin and DOACs is a common clinical situation that requires close monitoring and patient education to prevent any lapses in therapy. When converting from warfarin to a DOAC, it is recommended to discontinue current warfarin therapy and initiate DOAC therapy once the INR reaches a certain threshold. If transitioning from warfarin to rivaroxaban, patients should wait to start new therapy until their INR is less than 3.[9] When transitioning from warfarin to apixaban, warfarin should be held and apixaban initiated when the INR is less than 2.[9]

In the clinical situation wherein a patient needs to be transitioned to warfarin after being on DOAC therapy, two different approaches could be utilized. Owing to the longer onset of action of warfarin, the DOAC should be initiated concomitantly to offer appropriate protection.[12] The INR should be checked between 3 and 5 days of therapy, right before dosing the DOAC, because DOACs can potentially elevate INR values.[12] Once INR is stabilized, the DOAC can be discontinued. The other approach entails discontinuing the DOAC altogether and starting both warfarin and a parenteral anticoagulant upon when the next scheduled DOAC dose would have been. The parenteral anticoagulant can be discontinued once the INR reaches the patient's specified goal range.[9,10]

Reversal Agents

Reversal of anticoagulation is an important consideration when managing patients on warfarin or DOAC therapy, especially in the setting of life-threatening bleeding or need for urgent procedures. Several commercially available products to reverse the effects of warfarin and DOACs are available.

Reversing the effects of warfarin is well established through the use of vitamin K. Both elevated INR and symptoms of major bleeding need to be taken into account when considering if administration of vitamin K is appropriate. If the INR is above the therapeutic target but is less than 4.5 with no signs or symptoms of major bleeding, the dose of warfarin should either be decreased or held completely. Similarly, if the INR is between 4.5 and 10 and the patient is not experiencing any signs or symptoms of major bleeding, the dose of warfarin could be held or

lowered. For an INR greater than 10, oral vitamin K at a dose of 2.5 to 5 mg should be administered, even if there are no signs of major bleeding present. To treat warfarin-associated major bleeding, administration of prothrombin complex concentrate (PCC; Kcentra) is suggested in addition to 5 to 10 mg of vitamin K given IV.[17]

PCC can aid in the management of DOAC-associated bleeding or when rapid reversal of a DOAC is needed, as well. Idarucizumab (Praxbind) is a monoclonal antibody that has high affinity for the DOAC dabigatran, causing rapid anticoagulation reversal.[18] Andexanet alfa (Andexxa), recombinant factor Xa used to reverse the effects of anticoagulation by the factor Xa inhibitors rivaroxaban and apixaban, was withdrawn from the market in December 2025.[19]

Strategies to Enhance Patient Counseling

Practicing effective patient counseling is imperative to safe use of anticoagulant therapy. Because these medications can carry certain risks such as increased bleeding or drug/diet interactions, pharmacists play a key role in ensuring that patients understand and can safely use their therapy. Some strategies that pharmacists can employ to enhance overall anticoagulant counseling include tips to improve medication adherence, individualizing education, and promoting overall safety associated with warfarin or DOAC usage.

Regardless of anticoagulant, individualizing education and utilizing periodic reinforcement through follow-up calls or anticoagulation clinic visits can help to optimize adherence and overall safety. Using reminders for medication use, such as pill boxes and alarms, can improve adherence. By standardizing counseling practices and encouraging active patient engagement, pharmacists can significantly improve outcomes and reduce overall complications.

Conclusion

Patient counseling is a critical role of the pharmacist to ensure that patients can use anticoagulant therapy safely and confidently. Understanding the unique considerations for each anticoagulant, helping patients understand their therapy, guiding them through therapy transitions, and recognizing when to seek medical attention are all essential elements of the counseling experience. Through proactive communication, patient engagement, and collaboration with other healthcare professionals, community pharmacists are well positioned to make a positive impact on patient safety and contribute to successful outcomes.

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