Summer 2015

Non-Valvular Atrial Fibrillation and Stroke: Novel Oral Anticoagulants versus Vitamin K Antagonists

Kathryn A. Viglietta
Otterbein University, kathryn.viglietta@otterbein.edu

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Kathryn A. Viglietta, RN, BSN
Otterbein University, Westerville, Ohio

Introduction

- Atrial fibrillation (afib) is the most common sustained cardiac arrhythmia and second most common cardiovascular condition in adults in the United States (Zarraga & Kron, 2012).
- 2.2 million affected, increases risk of stroke 4 to 6 times (National Institute of Neurological Disorders and Stroke [NINDS], 2015).
- Vitamin K antagonists (VKAs) have been mainstay of therapy for over 60 years (King, Holley& Moores, 2013).
- Limitations with VKAs such as variability in response, need for frequent lab draws, food and drug interactions which decrease patients adherence and under prescribing by physicians (Halperin & Goyette, 2012).
- Novel oral anticoagulants (NOACs) have been approved by FDA over last 5 years for management of non-valvular afib and stroke prevention.
- Non-valvular afib is afib in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair (Koza, 2014).
- NOACs are direct thrombin inhibitors and Xa inhibitors that intend to improve patient adherence, simplify anticoagulation, and overcome barriers to long term therapy.
- Important to know what population is appropriate, what are bleeding risks, reversal agents, cost, overall benefit to NOACs versus VKAs.

Signs and Symptoms

Atrial fibrillation:

- Obvious for some, asymptomatic in others, difficult to diagnose
- Palpitations, shortness of breath, weakness, exercise intolerance, chest pain, dizziness or fainting, fatigue, and confusion (National Heart. Lung and Blood Institute [NIH], 2014a).

Stroke:

- Major complication of afib is stroke.
- Numbness, tingling in face, arm, or leg, especially on one side of body, weakness, confusion, difficulty speaking or understanding speech, trouble seeing, walking, loss of balance, dizziness, and lack of coordination (NIH, 2014b).

Underlying Pathophysiology

Atrial Fibrillation

Normal conduction of the heart:

- Begins with electrical signal from sinoatrial (SA) node in the right atrium, spreads signal across right and left atria, causing blood filled atria to contract and fill both ventricles (NIH, 2011).
- Electrical signal pauses at atrioventricular (AV) node to allow ventricles to continue filling, then travels down bundle of His to purkinje fibers causing ventricles to contract and force blood out to body and lungs (NIH, 2011).
- Continual process at a consistent and steady rate.

Atrial Fibrillation:

- Cardiac cells have ability to self-stimulate as a protective mechanism in case heart's conduction systems were to fail.
- Multiple atrial cells begin self-stimulating and compete with SA node, eventually taking over causing rapid, irregular beats, and ineffective contractions (Koza, 2014).
- Over self-stimulation of atrial cells due to structural heart defects from heart disease associated with hypertension, coronary artery disease, heart failure, valvular heart disease, and cardiomyopathies, causes increased atrial pressures, atrial dilation, altered wall stress (Koza, 2014).
- Atria quiver and lose atrial kick (effective contraction from atria).
- Blood pooling and stasis occur, commonly in left atrial appendage (LAA), leading to thrombi formation (Koza, 2014).
- Thrombi can become dislodged causing stroke and other systemic thromboembolic.
- Types of afib are paroxysmal (less than 7 days), persistent (greater than 7 days,), long-standing persistent (greater than 12 months), permanent (determined by physician and patient to cease attempts at normal sinus rhythm), and non-valvular (discussed prior) (Koza, 2014).

Stroke

- Blood supply is interrupted or reduced and oxygen and nutrients cannot get to brain tissue, leading to brain cell death.
- Two types are ischemic and hemorrhagic.
- Ischemic stroke include transient ischemic attacks (TIAs) which are temporary blockage that does not leave permanent symptoms (NIH, 2014).
- Ischemic stroke from plaque build up and rupture in arteries, leading to clotting cascade, completely or partially blocking artery (NIH, 2014).
- Embolic stroke is a type of ischemic stroke that is caused either from plaque breaking off of an artery and goes to artery in the brain, or from a blood clot that goes to an artery in the brain (NIH, 2014).
- Hemorrhagic stroke occurs due to increase pressure on the walls of the arteries of the brain.
- High blood pressure, aneurysms, arteriovenous malformations (AVMs) are all causes of hemorrhagic strokes (NIH, 2014).

Significance of Pathophysiology

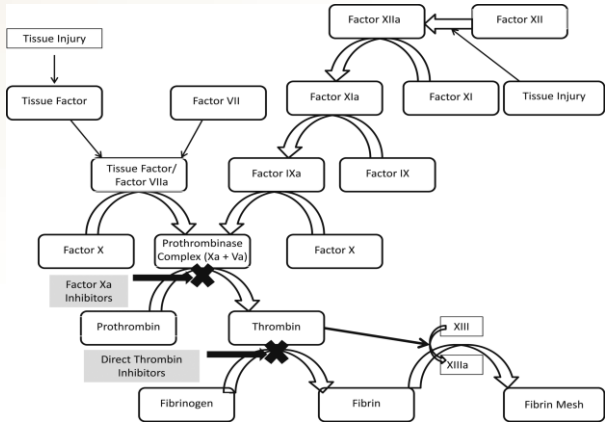
- Important to know the pathophysiology of afib and stroke to understand why anticoagulation is needed.
- Non-valvular afib independently increases the risk of embolic stroke five fold (Deedwania & Huang, 2011).
- Risk of ischemic stroke and systemic embolism increases 4-5% per year without thromboprophylaxis (Halperin & Goyette, 2012).
- Specifically for non-valvular afib, two categories of anticoagulants can be used, VKAs, and NOACs.
- In relation to clot formation from the pathophysiology of afib and stroke, health care provider should understand how each medication works in the coagulation cascade.

VKAs

- VKAs such as warfarin, interrupt the conversion of vitamin K, which then inhibits the formation of vitamin K-dependent clotting factors in the coagulation cascade (Ogbonna & Jeffery , 2013).
- Coagulation factors II, VII, IX, and X are vitamin K-dependent proteins in the coagulation cascade.
- Interruption of the clotting factors prevents conversion of VII, IX, and X to factor Xa, and factor II ((prothrombin) to factor IIa (thrombin).

NOACs

- Most studied are factor Xa inhibitors, rivaroxaban and apixaban, and direct thrombin inhibitor, dabigatran.
- Factor Xa and cofactor Va form prothrombinase complex that activates prothrombin to thrombin, which is a major part of clotting process (King, Holley &Moores, 2013).
- Thrombin converts fibrinogen to fibrin, as well as other factors that lead to further strengthening of the clot.
- Thrombin has three sites it can be bound. Heparin requires binding to all three sites to inactivate thrombin, therefore bound thrombin is not effected by heparin (King, Holley & Moores, 2013).
- Direct thrombin inhibitors bind directly to thrombin, and inhibit both soluble and clot bound thrombin, and factor Xa inhibitors can act on both free and clot-bound factor Xa (King, Holley & Moores).
- Have ability to improve accuracy of treatment for afib and stroke.



The coagulation cascade and basic mechanisms of action of NOACs (King, Holley & Moores, 2013).

Implications in Nursing

- Non-valvular afib increases in prevalence with age and often requires the use of oral anticoagulants to prevent ischemic stroke (Halperin & Goyette, 2012).
- Will likely see many patients with non-valvular afib and stroke and need evidence based knowledge to decide between VKAs and NOACs.
- CHA2DS2-VASc is newest index to determine risk for stroke with afib.
- The higher the individuals score, the higher the chance of thromboembolic events (Zarraga & Kron, 2013).

Direct Thrombin Inhibitor-Dabigatran

- Dabigatran study showed 32% less likely to have ischemic stroke, systemic embolism, hemorrhagic stroke and acute myocardial infarction, no relation between dabigatran and harm outcomes except for gastrointestinal (GI) bleeding (Lauffenburger, Farley, Gehi, Rhoney, Brookhart, & Fang, 2015).
- Study used a large database of participants in real world practice, 2 years after dabigatran became available.
- Precaution and dose adjustment for renal impairment and elderly at increased risk for GI tract bleeding (Adam, McDuffie, Ortel, & Williams, 2012).
- Stopped more often than other NOACs due to adverse side effects in GI system (Adam et al., 2012).

Factor Xa inhibitors (rivaroxaban and apixaban)

- Rivaroxaban found to be non-inferior to VKA warfarin for prevention of stroke or systemic embolism but was found to have less intracranial and fatal bleeding (Ogbonna & Jeffery, 2013).
- Apixaban found to be superior to VKA warfarin in prevention of stroke or systemic embolism as well as lower rates of bleeding complications (Ogbonna & Jeffery, 2013).

Endoxaban

- Newest direct factor Xa inhibitor being studied for non-valvular afib and stroke prevention.
- Found to be non-inferior to VKA warfarin in reducing the rate of stroke and systemic embolism, with a lower incidence of bleeding complications and cardiovascular deaths (Acharya & Deedwania, 2015).

Conclusion

- NOACs more viable option for long-term anticoagulation due to more predictable results, fewer drug interactions, and equal or better mortality and vascular outcomes in comparison to VKA warfarin (Adam et al, 2012).
- Fixed, consistent dose, no lab draws, little food and drug interaction increase chance of adherence by patient.
- Cost and reversal agent remains an issue yet to be completely fixed and studied.
- NOACs are on the way to becoming the new mainstay of treatment of non-valvular afib and stroke.

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