The Use of Direct Acting Oral Anti-Coagulants in Vulnerable Populations

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Transcripts of audio clips

Case 1

NC is a 68-year-old woman who presents to her primary care office with new onset shortness of breath, fatigue, and palpitations. She is diagnosed with new onset paroxysmal atrial fibrillation.

Medical History: Gout, hypertension, depression, CKD (CrCl 17 mL/min)

Medications: Amlodipine 5 mg daily, allopurinol 100 mg daily, sertraline 25 mg daily, dapagliflozin 10 mg daily

Pause and Reflect: What DOAC should be initiated for stroke prevention in NC?
In this case we have a female with new onset atrial fibrillation and a CHAD 2 VASC score of 3 which warrants anticoagulation. The best-studied anticoagulant with this low of a creatinine clearance is apixaban. Both edoxaban and rivaroxaban can still be utilized in this population, with a creatine clearance down to 15 mL/min, however, patients with a creatinine clearance of less than 30 were excluded from randomized controlled trials, and the data supporting use down to 15 mL/min are solely from PK data. Since there are large, real-world studies using apixaban in ESRD, this is the agent of choice for this scenario. Recall that a dose-adjustment may be required if two of the following three are met: serum creatinine over 1.5, weight less than 60 kg, or age greater than 80.

Case 2

DW is a 48-year-old male (height: 5'10'', weight: 142 kg, BMI: 44.9 kg/m^2) who presents to the emergency department with pain, swelling and redness on his thigh. He recently traveled from the US to Asia and back for work. He is diagnosed with a new proximal DVT.

Medical History: Chronic pain

Medications: Gabapentin 300 mg three times daily

Pause and Reflect: What DOAC should be initiated for treatment of new VTE in DW?
In this case, we're treating a morbidly obese patient for a new, provoked, DVT. Pharmacokinetic, pharmacodynamic, and small case studies suggest poor outcomes utilizing dabigatran in these patients, so this agent should be avoided. Similarly, edoxaban has unfavorable pharmacokinetic and dynamic parameters, suggesting it may not be an ideal agent in this population. Both rivaroxaban and apixaban are endorsed by the International Society of Thrombosis and Hemostasis[1] in this population due to a more favorable pharmacokinetic and dynamic profile and real-world evidence to support their use. Rivaroxaban has significantly more data that's been published in this population, which

generally makes this the optimal agent in obese patients. Rivaroxaban at normal dosing with a 3-week load of 15 mg twice daily followed by 20 mg daily should be initiated.

1. Martin KA, Beyer-Westendorf J, Davidson BL, Huisman MV, Sandset PM, Moll S. Use of direct oral anticoagulants in patients with obesity for treatment and prevention of venous thromboembolism: Updated communication from the ISTH SSC Subcommittee on Control of Anticoagulation. Journal of Thrombosis and Haemostasis 2021.

Case 3

BD is a 91-year-old woman (height: 5'1''; weight: 49 kg; BMI: 19.5 kg/m2) who presents to the emergency department with new onset shortness of breath. She is diagnosed with atrial fibrillation.

Medical History: Hypertension, hyperlipidemia, heart failure with reduced ejection fraction, chronic kidney disease (SCr: 0.8 mg/dL, CrCl 35 mL/min)

Medications: Metoprolol succinate 50 mg daily, atorvastatin 40 mg daily, lisinopril 5 mg daily, spironolactone 12.5 mg daily, dapagliflozin 10 mg daily

Pause and Reflect: Which DOAC would pose the lowest bleed risk for BD?
In this case we're treating an older adult with atrial fibrillation. Both dabigatran with a dose adjustment, or normal dose rivaroxaban can be used in older adults and maintain their effectiveness. However, both of these agents, when compared to warfarin in this population, lose their safety benefit of decreasing intracranial hemorrhage and better options exist. Both apixaban and edoxaban seem to maintain their safety and effectiveness profiles in older adults. It's important to note that in each of these populations, dose adjustments are required for renal function, and in apixaban's case, for age as well. Patients should be closely monitored on these agents and an intervention will be required if a patient's age or renal function changes enough to warrant dose adjustments.

Case 4

KR is a 37-year-old individual with colorectal cancer status-post resection. They present to their oncologist complaining of new shortness of breath. After further work-up KR is determined to have a new pulmonary embolism.

Medical History: colorectal cancer (active), hypothyroidism

Medications: Oxaliplatin 85 mg/m2 every two weeks, levothyroxine 25 mcg once daily

Pause and Reflect: Which DOAC would be most optimal to treat KR's new PE?
In this case, we're treating a patient with active cancer which will dictate our choice of anticoagulant. Dabigatran has minimal data in cancer-induced VTE and it should, thus, be avoided. Rivaroxaban appears to remain effective in patients with cancer, but does increase the risk of GI bleeding which

may be of particular concern in this patient with a GI malignancy. For this reason, alternatives are preferred. Both apixaban and edoxaban appear to be safe and effective in patients with cancer to treat cancer-associated VTE. It's important to note the narrow range of renal function that edoxaban has been approved for and, therefore, many younger patients with good renal function will not qualify and patients with ESRD may not qualify. For these reasons, it may be most practical to use apixaban in these patients to avoid potential drug change as their renal function changes.

Case 5

MT is a 58-year-old woman who has a FVL hypercoagulable state. She presents to her primary care clinician with new onset swelling and redness in her calf and thigh. MT is frustrated because they have developed VTEs on warfarin in the past and wonder if there are any alternatives.

Medical History: Factor V Leiden, multiple VTEs

Medications: Warfarin (INR goal 2-3, 2.7 today)

Pause and Reflect: Is a DOAC a reasonable alternative for MT? If so, which DOAC would you suggest? In this case, we're treating a patient with a genetic mutation, Factor V Leiden, making the patient hypercoagulable. This is a gain-of-function mutation and gain-of-function mutations are lower risk for VTE events than loss-of-function mutations. For this reason, if the patient desired, it may be reasonable to try a DOAC as an alternative agent. Most data as an alternative exist with rivaroxaban, so this would generally be the alternative of choice. This decision should be shared with the patient and provider being sure to explain the minimal data for use in this population.

Audio: What is the pharmacist's role in designing anticoagulation regimens for transitions between anticoagulants and for use in combinations with other interacting medications?

The pharmacist has a unique perspective and in-depth knowledge of the individual characteristics of each oral anticoagulant. This gives them the ability to understand the scenario as a whole and select an agent that would be the most safe and effective for a given patient. This may take into consideration other medications that increase a patient's bleeding risk, such as antiplatelet agents or NSAIDS. This can also help the pharmacist determine appropriate transitions between anticoagulants if a patient needs to be admitted to the hospital for a surgery or a procedure. Additionally, the pharmacist can communicate the limitations and the lack of in-depth evidence and have a high-level conversation with providers about the risks and benefits of different treatment options in patients in vulnerable populations such as end stage renal disease, obesity, cancer, and genetic mutations. The pharmacist also has the ability to lead a shared decision-making conversation. They can communicate with the patient and lead these team-based conversations with the health care provider to help explain the risks and benefits of different treatment options in a way that the patient can understand, allowing the patient to make the ultimate choice of what's best for them. Lastly, the pharmacist can monitor patients over time as

individual characteristics change, such as renal function, age, etc. and this may warrant a change in therapy as the patient progresses throughout their treatment.

Audio: What is the pharmacist's role in formulating patient education interventions for high-risk patients?

The pharmacist can help formulate patient education interventions for high-risk patients by using patient-friendly language to discuss the risks and benefits of DOACS. As the pharmacist should already have a baseline understanding of how to counsel a patient with a DOAC, it's still important to utilize that information, but integrate the patient-specific information that may make a DOAC particularly beneficial or particularly risky based on those patient-specific factors. Using language so that the patient can understand and comprehend this information is important and the pharmacist has the ability to do this based on the skills they have developed throughout their training.