Anticoagulation Pharmacology

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Pathophysiology review:

- Platelets serve as the first line of defense against bleeding by forming a temporary plug at the site of injury.
- This initial platelet plug is stabilized and reinforced by fibrin, which is generated through the coagulation cascade.
- Plasmin, an enzyme produced during fibrinolysis, plays a critical role in clot resolution by breaking down fibrin and dissolving the clot.

Anticoagulant / antiplatelet therapy notes:

- All anticoagulants carry an increased risk of bleeding
- Certain anticoagulants may be co-prescribed with a PPI to reduce the risk of GI bleeding
- Most anticoagulants and antiplatelets should be discontinued prior to surgery to minimize bleeding risk
- Patients on anticoagulation therapy should follow bleeding precautions, such as using an electric razor and a soft-bristled toothbrush
- Complementary and alternative medicines (CAMs), including garlic, ginger, ginkgo biloba, and feverfew, can interact with anticoagulants and increase bleeding risk
- Anticoagulants are commonly prescribed for patients with arrhythmias, such as atrial fibrillation, to prevent thromboembolic events
- Assess for bruising, petechiae, hematomas, hematuria, melena, hematemesis, or signs of intracranial bleeding (e.g., headache, confusion, dizziness)
- Evaluate for symptoms of DVT (swelling, redness, pain), PE (dyspnea, chest pain), or stroke (facial droop, weakness, speech changes)

Drug name: Heparin (anticoagulant)

- MOA: Inactivates thrombin and prevents conversion of fibrinogen to fibrin
- Indications: Treatment and prevention of thromboembolic events
 - o Examples include atrial fibrillation, DVT, pulmonary embolism, AMI, and more
- Parenterally only
- SE/AE: Hemorrhage, heparin induced thrombocytopenia (HIT)
- Reversed with protamine sulfate
- Monitored via the lab aPTT
 - o Normal value is 40 seconds. With heparin therapy value should be 60-80 seconds.
- Other labs for monitoring heparin are factor Xa levels and PTT
- Dosage is in units
- Onset is 20-30 minutes

- Does not cross fetal-placenta barrier, generally considered safe in pregnancy
- Also referred to as unfractionated heparin (UFH)
- Monitor for heparin induced thrombocytopenia
- Another drug in this class is Enoxaparin (Lovonox)
 - o Also referred to low molecular weight heparin (LMWH)
 - Onset is several hours

Drug class: Vitamin K antagonist

- Drug:
 - Warfarin (Coumadin)
- MOA: Decreasing production of vitamin K dependent clotting factors (VII, IX, X, and prothrombin)
- Indications: Treatment and prevention of thromboembolic events
 - o Examples include Atrial fibrillation, DVT, pulmonary embolism, AMI, and more
- Onset is around 1-3 days
- Transition from heparin (acute setting) to warfarin (long term) requires overlapping dosing
- Oral anticoagulant
- Monitored via labs PT and INR
 - o Normal INR is 1.1 or below. With therapy the goal would usually be around 2-3
 - Labs are assessed regularly at the start of therapy `
- Contraindicated in pregnancy
- Reversed with vitamin K
- Interacts with many medications
- Nursing education: Patients cannot increase their vitamin K intake and should avoid CoQ-10

Drug class: Direct thrombin inhibitors

- Drugs:
 - Dabigatran (Pradaxa)
- MOA: Direct inhibition of thrombin
- Indications: Treatment of DVT and PE and prevention of clots in patients with atrial fibrillation
- SE/AE: GI upset
- Black Box warning: Abrupt discontinuation carries increased risk of thromboembolic events
- Reversed with idarucizumab (Praxbind)
- Also referred to as direct oral anticoagulants (DOAC)
- Another drug in this class is argatroban that is commonly used in patients that develop HIT
 - Argatroban is IV only

Drug class: Factor Xa inhibitors

- Drug:
 - Rivaroxaban (Xarelto)
 - o Apixaban (Eliquis)
- MOA: Directly inhibits Factor Xa, preventing thrombin generation and clot formation
- Indications: Treatment of DVT and PE and prevention of clots in patients with atrial fibrillation

- Black Box warning: Abrupt discontinuation carries increased of thromboembolic events
- Also referred to as direct oral anticoagulants (DOAC)
- Reversed with factor Xa (Andexanet alfa)
- Generally preferred today over warfarin

Drug name: Aspirin

- MOA: COX inhibition causes suppression of platelet aggregation
- Indications: Prevention of thrombotic events in patients having an AMI, prevention of CVA and ACS, and more
- SE/AE: Increased risk of GI bleeding
- Use as an NSAID discussed separately

Drug class: Glycoprotein IIb/IIIa inhibitors

- Drug:
 - Tirofiban (Aggrastat)
- MOA: Inhibits glycoprotein IIb/IIIa resulting in inhibition of platelet aggregation
- Indications: Prevention of thrombotic events in patients having an AMI
- IV only

Drug class: ADP receptor antagonists

- Drugs:
 - Clopidogrel (Plavix)
 - Ticagrelor (Brilinta)
- MOA: Blocking ADP receptors resulting in reduced platelet aggregation
- Indications: Prevention of thrombotic events in patients having an AMI and risk reduction for patients with a history of MI, CVA, atherosclerosis
- Often given with aspirin
- Rarely can cause thrombotic thrombocytopenic purpura (TTP)

Drug name: Cilostazol

- MOA: Induces reversable platelet aggregation and vasodilation
- Indication: Treatment of intermittent claudication (to improve walking distance)
- Black box warning: Contraindicated in patients with heart failure
- Onset is 2-4 weeks, can be up to 12 weeks
- SE/AE: Headaches, GI issues, infection, rhinitis, dizziness, palpitations

Drug class: Thrombolytics

- Drugs:
 - Alteplase
 - o Reteplase
 - Tenecteplase
- MOA: Activates plasminogen to convert it into plasmin, which breaks down fibrin in clots, initiating fibrinolysis.

- Indications: AMI, CVA, PE
 - o Can also be used to break up clots in a central line
- IV only
- Usually given with a loading dose followed by one hour infusion
- SE/AE: Intracranial hemorrhage (Referred to as conversion in the case of a stroke), hypotension
- Only drugs that can breakdown an existing clot
- Often requires a checklist to assess for high-risk complications and contraindications
 - o i.e. uncontrolled HTN, recent surgery, recent stroke, hx of bleeding stroke
- Avoid extraneous cannulation of arteries or veins when administering thrombolytics
- Reversed with cryoprecipitate (Or sometimes TXA)

Drug class: Hemostatic / antifibrinolytic

- Drug:
 - Tranexamic acid (TXA)
 - o Aminocaproic acid
- MOA: Inhibits fibrinolysis by binding to plasminogen, preventing its activation to plasmin, thereby stabilizing clots and reducing excessive bleeding
- Indications: Bleeding associated with menstruation, trauma, surgery and more
- SE/AE: GI upset, VTE, hypotension

References

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