ANTICOAGULANTS: THE GUIDE TO REVERSAL

Definition of Bleeding:
Minor bleeding – Any clinically overt sign of hemorrhage (including imaging) that is associated with a <5 g/dl decrease in the hemoglobin concentration or < 15% decrease in the hematocrit felt by the clinician to be related to anticoagulation
Major bleeding – Intracranial hemorrhage or a ≥5 g/dl decrease in the hemoglobin concentration or a ≥15% absolute decrease in the hematocrit resulting in hemodynamic compromise or compression of a vital structure and felt by the clinician to be related to anticoagulation

ANTIPLATELET AGENTS

Aspirin
Minor – desmopressin 0.3 mcg/kg x 1
Major - platelet transfusion – consider one pheresis unit (RCT showed worsened outcomes in ICH)

Clopidogrel (Plavix®)
Minor – desmopressin 0.3 mcg/kg x 1
Major - platelet transfusion – consider two units if life or brain threatening bleeding

Prasugrel (Effient®)
Minor – desmopressin 0.3 mcg/kg x 1
Major - platelet transfusion – consider two units if life or brain threatening bleeding

Ticagrelor (Brilinta®)
Minor – desmopressin 0.3 mcg/kg x 1
Major - platelet transfusion – consider two units if life or brain threatening bleeding

Sustained Release Aspirin/Dipyridamole (Aggrenox®)
Minor – desmopressin 0.3 mcg/kg x 1
Major - platelet transfusion

Abciximab (Reopro®)
Major - platelet transfusion

Eptifibatide (Integrilin®)
Minor – desmopressin 0.3 mcg/kg x 1
Major Bleeding Reversal: platelet transfusions plus infusion of 10 units of cryoprecipitate

Tirofiban (Aggrastat®)
Minor – desmopressin 0.3 mcg/kg x 1
Major bleeding Reversal: platelet transfusions plus infusion of 10 units of cryoprecipitate

HEPARIN AND HEPARIN LIKE AGENTS

Standard Heparin

Time since last heparin dose	**Dose of Protamine**
< 30 minutes	1 unit/100 units of heparin
30-60 minutes	0.5 - 0.75 units/100 units of heparin
60-120 minutes	0.375 - 0.5 units/100 units of heparin
> 120 minutes	0.25 - 0.375 units/100 units of heparin

Infusion rate should not exceed 5 mg/min. Maximum dose is 50 mg per dose

Low Molecular Weight Heparin
Reversal of Life Threatening Bleeding: Protamine (works just as well with LMWH as heparin) - if with-in 4 hours of dose: 1 mg of protamine for each 1 mg of enoxaparin or 100 units of dalteparin and tinzaparin. Repeat one-half dose of protamine in 4 hours. If 4-8 hours after dose: give 0.5 mg for each 1 mg of enoxaparin or 100 units of dalteparin and tinzaparin.

Fondaparinux (Arixtra®)
Major Bleeding Reversal - Protamine ineffective – Kcentra (4-factor PCC) 50 units/kg may be of use

Dabigatran (Pradaxa®)
Reverse if patient shows signs of intracranial hemorrhage
1. Idarucizumab 5 grams (two 2.5g vials)

Xa Inhibitors

Apixaban (Eliquis) ®
Reverse if patient shows signs of life threatening bleeding
1. Kcentra (4 factor PCC) 50 units/kg
2. Andexanet (dosing below)

Edoxaban (Savaysa®)
Reverse if patient shows signs of life threatening bleeding
1. Kcentra (4 factor PCC) 50 units/kg

Rivaroxaban (Xarelto®)
Reverse if patient shows signs of life threatening bleeding and has an INR > 1.5
1. Kcentra (4 factor PCC) 50 units/kg
2. Andexanet (dosing below)

Use of Andexanet for Xa inhibitor bleeding (not for pre-procedure use due to short duration of effect)
Two Doses:
- Low Dose: 400mg bolus then 4mg/min for 120 minutes
- High Dose: 800mg bolus then 8 mg/min for 120 minutes

Dosing
- Low dose: Apixiban 5mg or less dose or rivaroxaban 10mg or less dose; Apixaban and rivaroxaban any dose over 8 hours after taking
- High dose: Apixaban over 5 mg dose within last 8 hours, Rivaroxaban over 10mg dose within last 8 hours

THROMBOLYTIC THERAPY

Reversal: Immediate infusions of equivalent of 6-8 units of platelets (or one platelet pheresis product), 2 units of plasma, and 10 units of cryoprecipitate. No value in infusing anti-fibrinolytic agents

WARFARIN

Not Bleeding: Goal is INR in 2-3 range

INR	Action
3- 4.5	Hold dose until INR decreased
4.5-10	1.25 mg Vitamin K PO
> 10	2.5 - 5 mg Vitamin K PO

Should see INR back in therapeutic range in 24-48 hours

Bleeding: Goal is INR under 2

INR	Action
2-4.5	2.5 mg Vitamin K ± FFP (15 ml/kg)
4.5-10	5 mg Vitamin K ± FFP (15 ml/kg)
>10	5-10 mg Vitamin K ±FFP (15 ml/kg)

FFP: Fresh Frozen Plasma

Warfarin Life or Brain Threatening Bleeding:

4-factor PCC (Kcentra)
If INR 2-4: 25 units/kg (not to exceed 2500 units)
If INR 4-6: 35 units/kg (not to exceed 3500 units)
If INR > 6: 50 units/kg (not to exceed 5000 units)

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