UAB Clinical Practice Guideline for the Treatment of Blunt Traumatic Brain Injured Patients on Anticoagulants and/or Antiplatelets

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I. General Considerations:
   a. Consider discontining the antiplatelet/anticoagulant medications
      i. Evaluate the risk-benefit for high-risk patients, such as those with mechanical heart valves.
      ii. Evaluate the risk-benefit for high-risk patients, such as those with recent stents
   b. **Reversal should primarily be guided by major intracranial bleeding and/or clinical examination rather than solely relying on patient history or laboratory testing.**
      i. Need attending approval to treat those patients who would otherwise meet BIG1/2 size criteria outside of their antiplatelet/anticoagulation
      ii. Need attending approval to treat those patients who have a stable repeat head CT
   c. It is recommended to avoid reversal in cases of cerebral venous thrombosis.
   d. Assess the risk-benefit ratio for reversal in patients with concurrent symptomatic or life-threatening thrombosis, ischemia, heparin-induced thrombocytopenia (HIT), or disseminated intravascular coagulation (DIC).
   e. FFP reversal of INR can take up to 30 hours making it an ineffective treatment of early hematoma expansion. It requires high volumes and can worsen fluid balance in patients with heart failure resulting in pulmonary edema as well as transfusion reactions. Thusly, rapid administration time, low volume infusion, leukocyte-free product, minimal risk for transfusion-related lung injury, and safety in heart failure make 4F-PCCs favorable over FFP.

II. Vitamin K Antagonists (VKA): *Warfarin*
   a. Administer Vitamin K to ensure durable reversal
      i. Initial dose 10mg IV
      ii. If INR >1.4 in 24 hr, redose 10mg IV
   b. Prothrombin Complex Concentrate (PCC)
      i. Initial dose INR based:
         1. INR 2-<4: 25units/kg (max dose 2500units)
         2. INR 4-6: 35 units/kg (max dose 3500 units)
         3. INR >6: 50 units/kg (max dose 5000 units)
      ii. If PCC required urgently (prior to INR value obtained) utilize fixed dose PCC of 2000 units
      iii. Repeat INR no sooner than 30-60 minutes

iv. Consider repeat dosing cautiously due to increased thrombotic risk. If a repeat dose is needed, would consider lower dose.
    1. If patient has received PCC dosing at outside facility, obtain INR and reassess need for additional dosing.

c. Fresh Frozen Plasma 10-15ml/kg if PCC not available

III. Direct Oral Anticoagulants (DOAC): *Apixaban, Rivaroxaban, Dabigatran*

a. PCC (if intracranial hemorrhage occurred within 3–5 terminal half-lives of drug exposure or in the context of liver failure)
    i. 25-50units/kg

b. Prefer PCC over Andexxa because of lower risk of adverse thrombotic events. Need verbal confirmation between Trauma and Neurosurgery attending if Andexxa to be administered.

IV. Direct Thrombin Inhibitors (DTI): *Dabigatran, Argatroban, Bivalirudin*

a. For Dabigatran reversal:
    i. Administer Idarucizumab (if within a period of 3–5 half-lives and there is no evidence of renal failure or there is renal insufficiency leading to continued drug exposure beyond the normal 3–5 half-lives)
        1. Dose: 5g IV (divided in two doses)
    ii. If Idarucizumab is unavailable, use PCC:
        1. Dose: 50 units/kg.

b. For other DTIs, short half life makes reversal likely unecessary. However, if within a period of 3–5 half-lives and there is no evidence of renal failure or there is renal insufficiency leading to continued drug exposure beyond the normal 3–5 half-lives use PCC.

c. Hemodialysis may be considered.

d. Recommend against fresh frozen plasma (FFP).

V. Heparins

a. Unfractionated Heparin (UH) [full-dose]
    i. Protamine sulfate
    ii. Dose 1mg/100u heparin in previous 2-3 hrs with maximum single dose of 50mg
    iii. If aPTT remains elevated, repeat dosing at 0.5mg/100u heparin

b. LMWH (full-dose)
    i. Enoxaparin
        1. Protamine

a. Enoxaparin administered within 8 hours = 1mg/1mg enoxaparin up to maximum single dose of 50mg
b. Enoxaparin administered within 8-12 hours = 0.5mg/1mg enoxaparin
c. After 3-5 half-lives protamine not needed

2. Consider rFVIIA (90ug/kg IV) if protamine is contraindicated.
3. Recommend against FFP, PCC

VI. Antiplatelet: Clopidogrel, Ticagrelor, Prasugrel, ASA

a. Indications for obtaining platelet mapping: All patients with an intracranial hemorrhage should have platelet mapping ordered in addition to basic coagulation studies, TEG and Anti-Xa testing.
b. Interpretation of Platelet Mapping and Treatment: ADP or AA inhibition of >60% is indicative of antiplatelet function.
    i. Reversal should be primarily guided by major intracranial bleeding and/or examination rather than solely relying on patient history or laboratory testing
        1. Need attending approval to treat those patients who would otherwise meet BIG1/2 size criteria outside of their antiplatelet
        2. Need attending approval to treat patients who have a stable repeat head CT
    ii. No reversal (i.e. platelet transfusion) is indicated for patients with laboratory-documented platelet function within normal limits even if they report a history of being on antiplatelets (up to 45% of patients on antiplatelet medications will be 'non-responders')
    iii. For patients with ADP or AA inhibition >60% and meet BIG3 size criteria, transfuse 1u platelets and repeat platelet mapping should be performed 1 hour after transfusion.
        1. Transfuse up to total of 2u platelets as needed in effort to correct platelet mapping
        2. Consider Desmopressin (DDAVP) 0.4ug/kg in addition to platelets

VII. References:

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