Anti-platelet Therapy

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Background

- Platelets play a central role in the pathophysiology of arterial thrombosis
- Following plaque disruption, erosion or rupture there are several steps involved in the formation of a platelet-rich thrombus
  - Platelet adhesion
  - Platelet activation
  - Platelet aggregation
Antiplatelet Therapy

• Aspirin
• P2Y12 Inhibitors
  – Ticlopidine (Ticlid)
  – Clopidogrel (Plavix)
  – Prasugrel (Effient)
  – Ticagrelor (Brilinta)
Effient, Ticagrelor

Clopidogrel

Dipyridamole

Prostacyclin

ADP

Collagen

Thrombin

Thromboxane A₂

GP IIb/IIIa

Ilb/IIIa antagonists

Aspirin

Activation

Thromboxane A₂

COX
Biotransformation and Mode of Action of Clopidogrel, Prasugrel, and Ticagrelor.

Aspirin

• Inhibits the platelet cyclooxygenase-1 enzyme by irreversible acetylation of the amino acid serine
• This prevents the conversion of arachidonic acid to prostaglandin H2, which in normal platelets is converted to thromboxane A2
• Thromboxane A2 promotes platelet activation through binding with the thromboxane A2 receptor on the platelet surface
Aspirin

- 2012 meta-analysis of 9 studies
- 20% relative risk reduction of non-fatal MI
- No significant change in non-fatal CVA
- 12% relative risk reduction in cancer incidence
- 54% increased relative risk of non-fatal extracranial bleeding
- Dosing 75-100 mg daily

F S Spencer MD, G Guyatt MD. Aspirin in the primary prevention of cardiovascular disease and cancer. UpToDate 2014
Peri-operative Aspirin

• POISE-2
  – Increased bleeding
  – No improvement in CV or mortality

• Patient characteristics

• Who should be on aspirin in the peri-operative period?

P2Y12 inhibitors

- Inhibit platelet activation and aggregation through the binding of its active metabolite to the P2Y12 class of ADP receptors on platelets.
- Irreversible vs. reversible
P2Y12 Inhibitors

• Ticlopidine
  – Mostly a historical drug now
  – Significant bone marrow toxicity
  – ANC, CBC, Platelet count, peripheral smear at baseline and q 2 weeks x 3 months
P2Y12 Inhibitors

• Clopidogrel (Plavix)
  – Well studied and a large amount of clinical experience
  – Generic
  – Metabolism issues
  – Stop 5 days prior to elective surgery
Plavix Trials

• Established clopidogrel as the gold standard in PCI and MI.
  – CURE/PCI CURE
  – COMMIT
  – CAPRIE
  – CHARISMA
P2Y12 Inhibitors

• Prasugrel (Effient)
  – Clinical trial=TRITON TIMI 38
  – Very Potent
  – Stop prior to elective surgery (7 days)
  – CAUTION
    • **Contraindication** - Prior TIA or CVA
    • Reduce dose if
      – Weight < 60 Kg
      – Age >75 years
P2Y12 Inhibitors

- Ticagrelor (Brilinta)
  - Clinical trial=PLATO
  - Very Potent
  - Reversible
    - Due to potency still need to stop 5 days prior to elective surgery
  - Aspirin dose must not be > 100 mg daily
  - Twice daily dosing
  - Side effects
Adenosine  

Ticagrelor
Indications

• PCI
  – Bare metal stent
    • 4-6 weeks
  – Drug eluting stent
    • 1 year?
  – Angioplasty
    • 2 weeks
  – Brachytherapy
    • At least 6 months, ideally 1 year
Triple Therapy

• 45% annual risk of bleeding
• WOEST trial
  – Class IIb recommendation
• Danish group looked at 12165 pts
  – Retrospective data

Wilde, W et al. Triple Therapy for Atrial Fibrillation and Percutaneous Coronary intervention. JACC. Vol 64. No 12 2014
Case Study

76 female underwent PCI. What P2Y12 inhibitor do you choose?

Do you need to know more?