Medicines and Transfusions

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* Platelet function
* Drugs affecting Coagulation;
  * Anti-platelet drugs
  * Anticoagulants
    * Oral anticoagulants
    * Parenteral anticoagulants
* Drugs affecting Haemoglobin levels
Platelet Function

**Figure 1: Normal Platelet Function and Antiplatelet Agents**

- Aspirin inhibits cyclooxygenase, thereby decreasing prostaglandin synthesis.
- Clopidogrel and ticlopidine block ADP receptors on platelets.
- Thromboxane A2 (TXA2) potentiates the release of cytoplasmic granules.
- Inactive platelets.
- Activated platelets.
- Aspirin inhibits cyclooxygenase and TXA2.
- Binding of TXA2 to ADP receptors causes platelet activation and change of platelet shape.
- GP Ib/IIa receptor now has increased affinity for fibrinogen which cross-links platelets. The result is a platelet aggregate.
- GP Ib/IIa antagonists prevent fibrinogen binding to activated platelets.
Involved in haemostasis and formation of blood clots

Present along the surface of the blood vessel wall, which is lined by endothelial cells. The endothelium prevents anything from sticking to it.

When there is an injury or cut, and the endothelial layer is broken, the tough fibres that surround a blood vessel are exposed to the liquid flowing blood.

Platelets that react first to injury
The tough fibres surrounding the vessel wall, attract platelets like a magnet, and the platelets then clump onto these fibres, providing the initial seal to prevent bleeding and the leak of red blood cells and plasma through the vessel injury.

- Lifespan of 5-9 days
- Thrombocytopenia (low platelets) $\rightarrow$ bleeding
- Thrombocytosis (↑ platelets) $\rightarrow$ clotting
Anti-platelet Drugs

* Aspirin - induces irreversible inactivation of COX-1, which lasts the lifetime of platelet
* Dipyridamole - inhibits the uptake of adenosine into erythrocytes, platelets and endothelial cells
* Clopidogrel - prodrug, of which its metabolite is an inhibitor of platelet aggregation
* Prasugrel - irreversible inhibitor of platelet activation and aggregation
* Ticagrelor - selective adenosine diphosphate (ADP) receptor antagonist acting on the P2Y₁₂ ADP-receptor that can prevent ADP-mediated platelet activation and aggregation
Anti-platelet Drugs

Reported side effects on blood:
- Thrombocytopenia (low platelet count)
- Aplastic anaemia—when body stops making new red blood cells
- Thrombotic thrombocytopenic purpura (TTP)—the development of tiny blood clots
- Neutropenia—low white blood cell count
- Agranulocytosis
<table>
<thead>
<tr>
<th></th>
<th>Aspirin</th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
<th>Ticagrelor</th>
<th>Dipyridamole</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mode of Action</strong></td>
<td>COX-1 inhibitor</td>
<td>P2Y12 inhibitor</td>
<td>P2Y12 inhibitor</td>
<td>P2Y12 inhibitor</td>
<td>Phosphodiesterase inhibitor</td>
</tr>
<tr>
<td><strong>Onset of action after loading dose</strong></td>
<td>Minutes</td>
<td>1 hour</td>
<td>2 hours</td>
<td>2 hours</td>
<td>Slow</td>
</tr>
<tr>
<td><strong>Half-life</strong></td>
<td>0.5 hour</td>
<td>6 hours</td>
<td>7 hours</td>
<td>7-9 hours</td>
<td>15 hours</td>
</tr>
<tr>
<td><strong>Bleeding risk</strong></td>
<td>+</td>
<td>+++</td>
<td>++++</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Time to normal platelet function after stopping</strong></td>
<td>5-7 days</td>
<td>5-7 days</td>
<td>5-7 days</td>
<td>3-5 days</td>
<td>24 hours</td>
</tr>
<tr>
<td><strong>Elective surgery</strong></td>
<td>Stop 7 days before</td>
<td>Stop 7 days before</td>
<td>Stop 7 days before</td>
<td>Stop 7 days before</td>
<td>Stop 24 hours before surgery</td>
</tr>
<tr>
<td><strong>Reported side effects on blood results</strong></td>
<td>N/A</td>
<td>Leucopenia, Thrombocytopenia, Agranulocytosis</td>
<td>Anaemia, Thrombocytopenia</td>
<td>N/A</td>
<td>Thrombocytopenia</td>
</tr>
</tbody>
</table>
Bleeding Risks

- **On Aspirin**
  - Surgical bleeding $\uparrow$ 2.5-20%
  - No increase in surgical mortality or morbidity
  - Post-op intracerebral haematoma $\uparrow$ in neurosurgery

- **On dual therapy**
  - Surgical bleeding $\uparrow$ 30%
  - No increase in surgical mortality or morbidity
  - Except intracranial surgery
Anti-coagulants

* Oral Anticoagulants;
  1. Coumarins: Warfarin, acenocoumarol, phenindione
  2. Dabigatran
  3. Rivaroxaban
  4. Apixaban

* Parenteral Anticoagulants;
  a. Heparins – unfractionated and low molecular weight
  b. Fondaparinux
  c. Argatroban
1. Coumarins eg. warfarin
   * Antagonise effect of vitamin k
   * Block clotting factors II, VII, IX & X
   * Half-life of approx. 40 hours
   * Increases patients’ INR reading
   * Increases Prothrombin Time
   * Shouldn’t affect APTT (but reports of prolonged APTT)
   * Shouldn’t affect platelets
2. Dabigatran - direct thrombin inhibitor
* Increases APTT
* Don’t use INR tests to measure dabigatran levels – unreliable
* Half-life approx. 11 hours
* Side effects; anaemia (common), thrombocytopenia (uncommon), low Hb (uncommon)
3. Rivaroxaban - direct factor Xa inhibitor
   * Prolongs Prothrombin Time especially when patient is bleeding
   * Increases APTT
   * Does not affect platelets
   * Half-life = 5-9 hours (longer in elderly)
   * Side Effects; Anaemia (common), Thrombocythemia (uncommon)
4. Apixaban - direct factor Xa inhibitor
   * Prolongs Prothrombin Time especially when patient is bleeding
   * Increases APTT
   * Does not affect platelets
   * Half-life = 12 hours
   * Side Effects; Anaemia (common), Thrombocythemia (uncommon)
a. Heparins;
   i) Unfractionated heparin – dose adjusted according to APTT levels
      * Very short half-life
      * Side effects; Thrombocytopenia (HIT)
   ii) Low molecular weight heparin – dose depending on weight of patient
      * Longer half-life than UFH
      * Side effects; Thrombocytopenia (HIT)
b. Fondparinux;
* Synthetic & selective inhibitor of activated Factor Xa
* Interrupts blood coagulation cascade and inhibits thrombin formation and thrombus development
* Does not inactivate thrombin (activated Factor II)
* Has no effects on platelets
* Used in patients with history of HIT or patients who refuse LMWH on religious grounds
* Half-life; 17 hours in young and 21 hours in elderly
* Side Effects; Bleeding (common), anaemia (common)
c. Argatroban;

- Direct thrombin inhibitor
- Used for treatment of patients with heparin-induced thrombocytopenia (HIT)
- Dose adjusted according to APTT ratio
- Very short half-life
- Side Effects; Anaemia (common), coagulopathy (uncommon), leukopenia (uncommon)
Warfarin Reversal with vitamin K

- **BCSH Guidelines;**
  - Major bleeding
    - Rapid reversal with PCC
    - + IV vitamin K
  - Non-Major bleeding
    - IV vitamin K (1-3mg)
    - Dose reduction
  - INR > 8 & no bleeding
    - Oral vitamin K (1-5mg)
Warfarin Reversal with vitamin k

- **Oral vitamin k;**
  - Works within 24 hours
  - Use IM preparation but give ORALLY
  - Can mix in orange juice

- **IV vitamin k;**
  - Works within 6-8 hours
  - NOT S/C as absorption erratic
  - NOT IM as risk of haematoma

- **Doses**
  - If you plan to restart anticoagulation at some point – never use more than 5mg!
  - 2mg is usual dose
Drugs affecting Haemoglobin Levels

* Aspirin & NSAIDs
* Dapsone
* Cephlasporins (eg. Cefalexin)
* Sulfasalazine
* Levofloxacin
* Nitrofurantoin
* Proton Pump Inhibitors (eg. Lansoprazole)
* Anabolic steroids
Platelet function

Drugs affecting Coagulation;
  - Anti-platelet drugs
  - Anticoagulants
    - Oral anticoagulants
    - Parenteral anticoagulants
    - Reversal of anticoagulants using vitamin K

Drugs affecting Haemoglobin levels