Pharma

lec (1)

- Reduce clotting
  - → anti platelets (prophylactic) | (facilitate clotting → helps)
  - → anticoagulant (→
  - → Thrombolytic (stop clotting)

P2Y12 receptor (upregulation)

ADP + TXA2 → activation of platelest → fibrinogen → fibrin → clotting
↳ from cell membranes

(3A+2B) rec glycoprotein

or Phosphodiesterase inhibitor → ↑cAMP → ↓Ca^{+2}

or vWB stoping

Antiplatelet (given to prevent)

→ (not enough)

1) Aspirin (irreversible to cox) → increase leukotriens → bronchospasm

contra with (children/ peptic ulcers/ asthma)

don't use 1 drug for anticoagulation

2) Ticlopidine clopidogrel (anti ADP) P2Y12

- Ticlopidine (first one) (TPP → TPP: vWB protease inhibition → more vWB
  - not used ↳ leukopenia

* Purple → arteriole blokade
* adamts XIII

- clopidogrel (neutropenia / less TPP ↳ 4/1000000)

↳ prodrug (needs to be activated by (CYP2C19) → intermediate metabolizer / OR → poor metabolizer / OR → ultra rapid metabolizer

contra with liver failure

No.

Date

external: For emergencies we give → cangrelor
or → clopidogrel
or → prasugrel

3 cangrelor (for emergencies) · 25 min (t 1/2)
- IV
- MI
- not give boluses

4 Prasugrel → given for patients with stent for long time
- bleeding / hypo hyper tension / bradycardia

5 Ticagrelor → (dyspnoea) / bleeding / Twice daily
- The only reversible drug

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(3) Abciximab / eptifibatide / tirofiban (2b/3A inhibition

- abciximab ~~is~~ can be take instead of (cangrelor) for emergencies
irreversible

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(4) Dipyridamole / cilostazol (↑cAMP) → weak anti platelets

- Dipyridamole → inhibit PhosPhodiesterase → ↓cAMP → inhibit platelet
- vasodilator / given only with another drugs (warfarin / aspirin)

2 cilostazol → intermittent claudication

Lec ⑨ → inhibit Thrombin (you dissolve the clot on the long term (days — years))

Anticoagulant → given as a therapy after clot injury
└ narrow (TI)

extrinsic (from Tissues) — intrinsic (from Platelets) — Common Pathway

hyperkalemia

① Heparin (large/pentasaccharide) (30 min $t_{1/2}$) (heterogeneous) → from animals → allergy / immunogenic
└ binds to (AT III) → breaks factor (X) and (II) with high efficacy
- needs to be monitored through (aPTT) → (coagulation time)
└ control aPTT → 24-36 sec
aPTT ratio → Patient aPTT / control → should be (2-2.5)
- also, platelets should be (counted) → HIT (index ③ and ⑤)
└ it can bind to (PTF 4) → haptan → (immunogenic) → IgG → Platelet activation → coagulation → cause Thrombocytopenia

- Fondaparinux to treat (HIT)
└ (injectible)

(*) heparin antidote is Protamine sulfate

No.

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② low molecular weight heparin (LMWH) → only Factor (X) inhibitor

heparin but without full glucoseamine

short

- (Enoxaparin/ dalteparin/ tenzeparin/ ardeparin) both the same → all with same efficacy

bind to (AT III) → ~~high efficacy for (X)~~ low efficacy

→ high binding for (X) / low binding for Factor (II)

- no monitoring needed / no aPTT / twice daily
- ↓ risk of Thrombocytopenia due to low ~~heparin~~ heparin effect

③ oral anticoagulant (dabigatran/ rivaroxaban/ warfarin)

- dabigatran/ rivaroxaban → excreted in urine → do not give with kidney failure
- warfarin → metabolized by (CYP2C9)

warfarin → ~~stops~~ inhibits vit K epoxide reductase therefore vit K synthesis

↳ (vit K work as antidote)

- INR (PT) → same concept with (aPTT) → Patient / control = (2-3)

(can cause deep venous thrombosis) because it inhibits both protein C and Thrombin but (protein C) is faster inhibited due to ($\downarrow t_{1/2}$)

- Purple toe syndrome

contraindicated in Pregnancy → Drug X

it needs to be (bridged) in the first (60h) → to prevent Thrombosis

- it interacts with (Protein bound drugs / CYP 2C9 def).

Lec (3)

① Dabigatran (Thrombin inhibitor) (factor II) (aPTT monitored) (like heparin)

no bridging // no thrombosis / bleeding

interaction: P-glycoprotein inducers and inhibitors

side effects: ① GI upset and bleeding (due to acids) (tartaric)
② esophagitis

(bleeding treated with (PPI / H_2 antagonist)) (Antidote: Idarucizumab)

contra with → bleeding
→ Prosthetic heart valves

② (rivaroxaban / apixaban) → Warfarin alternative / factor (X) inhibitor

↓

→ riva: CYP 3A4 / P-glycoProtein metabolized

→ apixaban: hematoma / paralysis with spinal anesthesia

contra heart valves

antidote: Andexanet

Thrombolytics (to dissolve a thrombus)

Streptokinase / urokinase / t-PA (alteplase) → more specific

- we target plasminogen in clot not circulating ones
- fibrinogen will be degraded

- t-PA → endogenous → (fibrinolysis) cause

- given with antiplatelet or anticoagulant
  ↳ when Thrombi is dissolved → it induces more fibrin