CAD = Antiplatelet Drugs = to inhibit platelet function - Normal platelet count is 250K-400K/uL

Created By:
Jasmin Kaur Gill, BSc, PharmD, ACPR Candidate 2025
Ingrid Frank, BSc, PharmD Candidate 2024

Class	Drugs/Dose	MOA	ADME	ADRs/CI
Cyclooxygenase (COX) Inhibitor [NSAID]	**ASA (e.g. Aspirin)** Low dose ASA 81mg/d: used for prevention of heart attacks **Dose:** 75-150mg/day	- Low dose = more effective in inhibiting platelet COX **(irreversible acetylation)** and does not affect COX1 in BV (in EC promote prostacyclin = VD, prevent clumping/activation, reversible in EC b/c has a nucleus) - Irreversible acetylation – once blocked stays for the **lifetime of platelet (7-10 days); platelets have no nucleus** - **Inhibits platelet COX activity by blocking TXA2 formation** - = abolishes ability of platelets to release TXA2 = ↓ overall platelet aggregation - In vascular endothelial cells – also contain COX activated by PGI2 synthesis – but forms prostacyclin → causes VD	- Onset of antiplatelet effect **<60mins** (rapid) - Good efficacy - Inexpensive - Complete inactivation of platelet COX w/ 160mg/daily - Duration: 7-10 days b/c irreversible	- **Prolongs bleeding time** - **GI bleed** [in digestive tract COX1 makes PGs that help protect cells lining stomach against acids/digestive enz) - **Hemorrhage stroke** bleeding within brain (rare) Weakest antiplatelet agent (only blocks one pathway in aggregation**)**
ADP-inhibitors	**Clopidogrel (P)** *1st gen* **Dose:** 300mg LD (need for immed. anti-aggreg. effect) → 75mg OD for LT without food	- **selectively (and irreversibly) ⊣ binding of ADP to its platelet receptor (P_2Y_{12}) ⊣ activation of the GP IIb/IIIa R ⊣ TXA2 generation = ⊣ platelet aggregation** • prevent ↑ Ca+ AND GPIIb/IIIa R from binding = • prevent sustained aggregation	- Prodrug (P) - Esterase covert 85% into inactivate metabolites – only 15% active	- **Drug interactions – CYP3A4, 3A5,2C9** - **Interpatient variability** – resistance (due to genetic polymorphs of CYP450[↓ 30% in active clopidogrel – cant convert prodrug to active metabolite] - **Rash** (back, chest, abd) ~4% - **Major bleeding**
	Prasugrel (P) *1st gen* **Dose:** 60mg LD →10mg OD		- Prodrug (P) – intestinal (esterase) and hepatic (CYP450) – ***require gut and liver*** - 10x more potent > clopidogrel - Rapid action - Can be taken together with **ASA√**	- **Increased risk of bleeding** (higher risk vs Clopidogrel – b/c more efficacious) - **Less sensitive to polymorphisms and drug interactions** (vs Clopidogrel) – CYP 3A4, CYP2B6, CYP2C9
	Ticagrelor *2nd gen* **Dose**: 180mg LD → 90mg **BID**	- Direct and **reversible** P_2Y_{12} antagonists – its changes the conformation of the receptor - **Does not require metabolic activation for its antiplatelet effects (not a prodrug)**	- **More rapid onset** - **Metabolized by CYP 3A4/5** - Can be taken together with **ASA√**	- **CYP 3A4/3A5 interactions** - **↑ dyspnea (SOB)** - **Risk of bleeding ++**
GPIIb/GPIIIa	**Eptifibatide** **Dose:** 180ug/kg IV STAT then continuous infusion 2ug/kg/min until hospital d/c or initiation of CABG up to 72 hrs	- Reversible, small molec, synthetic peptide, resembles RGD sequence of fibrinogen	- MW: 832 Da - RoA: IV - Short T½ :2-4h - Restricted use b/c IV	- **Severe bleeding –** can stop drug and wait for platelet fn to return to normal as drug is cleared
	Tirofiban **Dose:** infusion rate of 0.4 ug/kg/min for 30 min followed by maintenance infusion rate of 0.1 ug/kg/min for at least 48 hrs	- Reversible, small molec, synthetic non-peptide antagonist (inhibitor) of fibrinogen binding to the GPIIb/IIIa receptor (RGD mimetic) **Both:** **MoA:** reversibly blocks GP IIb/IIIa receptors → prevent fibrinogen connecting platelets → doesn't make fibrin = block platelets from aggregating	- Smaller than Eptifibatide - MW: 495Da - RoA: IV - **Rapid onset** - **Short duration (4 hrs)**	- **Severe bleeding**
Organic Nitrate/Nitrates	- **Nitroglycerin (P)** - **Isosorbide dinitrate** - **Isosorbide 5-mononitrate**	- **Used for both tx of acute attacks of angina and for prophylaxis** - **Reduces amount of blood entering into the heart – main effect is VD in veins** - ALL need to convert into **NO via mtALDH2** - **Main effect: *relaxation of smooth muscles of veins*** – affects arteries too but main is in the veins = **↓ preload =↓ EDV = ↓ SV** - Coronary perfusion happens when heart relaxes (at diastole: backflow & closes aorta valve – fluid can only go in 1 direction into coronary BV) - **3 Effects:** **1) Venous VD*main effect =** ↓ preload = ↓ ventricular size, ↓ vent. wall stress (↓ pressure of branches of CBVs and allow flow) **2) Direct coronary VD –** myocardial perfusion **3) Arterial VD – ↓ afterload = ↓ BP** *[b/c VD in arteries = ↓ TPR]*	- **Prodrugs (P)** – require enz processing to form NO - **Poor oral bioavailability** (10-20%) due to first pass liver metab - **Dosage forms: S**L, PO, patch, spray	- **Flushing of face/neck** (due to dilation of arterioles in face/neck) - **Reflex tachycardia** [b/c VD of arteriole = ↓ BP = baroreceptor starts firing = ↑ HR] - Repeated doses can lead to **tolerance** (b/c mtALDH2 gets all used up – need to let it recover – about 8hr drug free intervals) - **Throbbing headache** - **Interactions w/ PDE5 inhibitors** (e.g. sildenafil, tadalafil) **– b/c ↑↑ cGMP**
Direct	- **Sodium Nitroprusside**	- Release NO in circulation - Relax both arteries and veins – b/c both have smooth muscles - Tx of HTN crisis **[v high BP]** - **DIRECT – no need to be converted**	- ***sensitive to light**	- **Cyanide poisoning:** SNP → cyanide → thiocyanate) *add Na thiosulfate into infusion to change into inactive thiocyanate
HCN Channel Blocker	**Ivabradine**	- **Pure heart rate reduction** **Blocks HCN channel in SA node: prevents Na+ from entering into slow Na+ channel (aka HCN channel) by: ↓ slow Na influx into HCN channel →** delayed depolarization → ↓HR → more time for heart to be relaxed (b/c main amount of flow is during diastole)		

Thrombolytic/fibrinolytic tPA = tissue plasminogen activator	**Alteplase (Activase)**	□ **Clot specific – active only at site of clot** □ **tPA only active in presence of fibrin (fibrin specificity) – converts plasminogen into plasmin → fibrin mesh digested** □ ↑ plasmin = greater degradation	Short T ½ = 3-4 mins
	Tenecteplase (TNKASE)		□ Short T ½ = 14-15 mins **Both**: only given in hospital, IV