

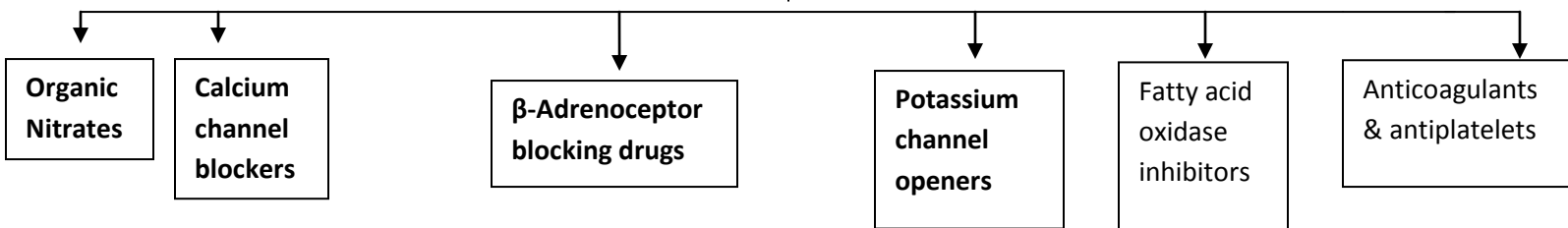
Pharmacology Team

Anti-Angina

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Anti angina






1) Organic nitrates

<p>1- Short acting: (used in acute attack of angina) Start within few minutes and total duration of action 15-30 minutes.</p> <div data-bbox="97 808 246 947"> <p>Clinically only (Acute)</p> </div> <ul style="list-style-type: none"> A) Nitroglycerine (Glyceryl trinitrate) Used as sublingual tablets. B) Isosorbide dinitrate As sublingual spray. 	<p>2- long acting (for prophylactic) Nitroglycerine, Isosorbide dinitrate, Isosorbide mononitrate. Delayed onset of action and long duration of action . Given : Orally, Ointment مرهم, Transdermal patch لصقات, Intravenous .</p>
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Pharmacokinetics

<p> Absorption Well absorbed from all the routes of administration If given orally : first pass hepatic metabolism then apart goes to systemic circulation then a few parts of the drug do it's work Sublingual → to avoid first pass metabolism and rapid rate of absorption .. ans goes to systemic circulation ;)</p>	<p> Metabolism Through first pass hepatic metabolism. Short acting preparations not given orally to avoid first pass metabolism. Nitroglycerine & Isosorbide dinitrate have active metabolites.</p>	<p> Excretion Through the kidney</p>
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Mechanism of action  Nitroglycerine $\xrightarrow{\text{Glutathione S-transferase}}$ Nitric oxide (NO).  NO activates guanylyl cyclase and increase c GMP  Causing smooth muscle relaxation.	Pharmacological actions <u>-Nitrates</u> relax all types of smooth muscles vascular or non vascular . -Potent venodilator (Increased venous capacitance) . -Have no direct effect on cardiac or skeletal muscles. -NO released stimulate guanylyl cyclase in platelets causing increase cGMP that decrease platelet aggregation.	Clinical uses -Treatment of all types of angina. Short acting for acute attacks Long acting for prophylactic. -Treatment of severe heart failure
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Angina of effort Decrease venous return & cardiac work. (causing decrease in myocardial oxygen requirement). Dilate coronary vasculature. Prevent platelet aggregation	Variant angina Relax smooth muscle of epicardial coronary artery and relief coronary spasm.	Unstable angina Decrease myocardial oxygen requirement : Relief coronary spasm. Decrease platelet aggregation
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Adverse effect <div> <div>Due to vasodilator</div> <div>NOT due to vasodilator</div> </div> <div> <div>Postural hypotension (لا يلاحظ الا بتغير وضعيه الجلوس)</div> <div>Tachycardia</div> <div>Salt & water retention</div> <div>Throbbing headache</div> <div>Facial flushing</div> <div>Tolerance</div> <div>Carcinogenicity</div> </div> <p>Tolerance can be limited with nitrates by using nitrate –free interval(10-12 hrs/ day). Patients with nocturnal angina should arrange nitrate – free interval.</p>	Contraindication Increase intracranial pressure.--> لو اعطيه الدواء hemorrhage in the brain Notice: Nitrates can be used safely in Glucoma(increase of intraocular pressure).
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2) Calcium channel blockers

Block calcium entry in myocardium causing :

decrease in myocardium contractility & heart rate

Causing decrease in myocardium oxygen requirement.

Block calcium entry in vascular smooth muscles (arteries & arterioles) leading to vasodilation:

Decrease in peripheral resistance (after load)----- decrease in oxygen requirement.

Relief of coronary spasm.

Classification of calcium channel blockers

Dihydropyridine +Nifedipine → More selective as vasodilator

Verapamil & Diltiazem → More selective as cardiac depressant

Pharmacokinetics	Clinical uses	Adverse effects (MCQ)	Drug interaction
Given <u>orally</u> Verapamil & Diltiazem can be given intravenously Excreted in urine	- In all types of angina but very effective in variant angina . Used mainly as prophylactic therapy -Hypertension → Dihydropyridine (MCQ) -Antiarrhythmic → verapamil & Diltiazem -Peripheral vascular disease	Cardiac arrest, bradycardia (verapamil & diltiazem) Hypotension Reflex tachycardia (nifedipine) Fatigue & headache Ankle edema Constipation (verapamil)	Verapamil or diltiazem with β -blockers causing bradycardia or cardiac arrest

3) β -Adrenoceptor blocking drugs

Not vasodilators (MCQ)

Used in prophylactic treatment of angina through :

Decrease in both heart rate & myocardial contractility that decrease myocardial oxygen requirement at rest & in exercise .

Effective in the prophylactic therapy of all types of angina Except in variant angina.

E.g. Propranolol (non selective) , Metoprolol (cardio selective).

4) Potassium channel openers

Nicorandil

Activation of potassium channels.

Nitric oxide release.

Arterio & venodilator.

Used as prophylactic therapy .

Side effects : Headache, flushing.

5) Anticoagulants & Antiplatelets

 Aspirin & Heparin decreasing the risk in unstable angina .

6) Fatty Acid Oxidase Inhibitors

Oxidation of fatty acids as a source of energy needs more oxygen than oxidation of carbohydrate.

Drugs that shift myocardial metabolism toward use of glucose (fatty acid oxidase inhibitors) have the potential of reducing the oxygen requirement without change hemodynamics , e.g. trimetazidine

Drug treatment of angina

Acute attack : Short acting nitrates .	Prophylactic therapy ; Long –acting nitrates. Calcium channel blockers. β - adrenoceptor blockers. Potassium channel openers. Fatty acid oxidase inhibitors
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Combination therapy (MCQ)

Nitrates and β -adrenoceptor blockers.

Calcium channel blockers(dihydropyridine) and β -adrenoceptor blockers .

Calcium channel blockers and nitrates.

Calcium channel blockers, β -adrenoceptor blockers, nitrates , antiplateles or anticoagulants.

Surgical therapy

Coronary by pass

