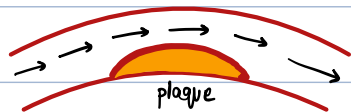


Pathophysiology of Angina:



myocardial cells
↓ O₂ ↑ (ischaemia)

on exertion (physical/mental)

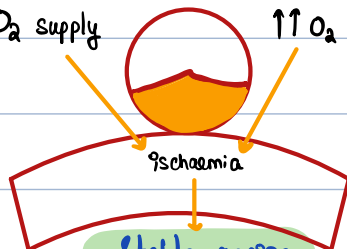
↑ O₂ demand of myocardial cells

Angina

Types:

Stable plaque

↓ O₂ supply ↑↑ O₂ demand



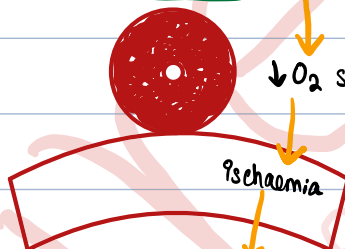
Stable angina

[ischaemic chest pain on exertion]

→ aka classical angina

Vasospasm

↓ O₂ supply

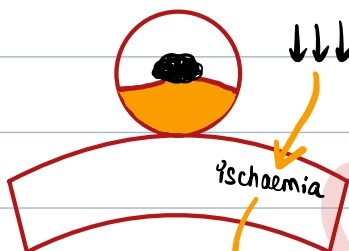


Prinzmetal's / variant /
Vasospastic angina

[ischaemic chest pain that is usually worse early in the morning]

Unstable plaque (rupturing of plaque with clot formation)

↓↓↓ O₂ supply



ischaemia

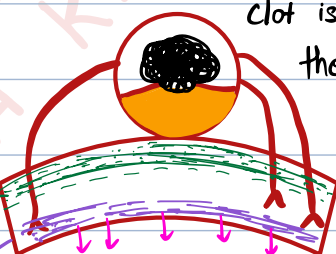
chest pain

[can occur without exertion]

Unstable angina

ischaemia in outer part of myocardial musculature

infarction in inner part



clot is big enough to obstruct the blood flow

ischaemia in outer part of the muscle only

Troponins

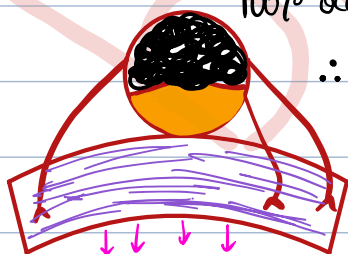
Chest pain

∴ classical ST segment elevation not seen in EKG

Non ST elevation MI (NSTEMI)

100% occlusion by clot

∴ no O₂ supply (↓↓↓↓)



→ Complete myocardial infarction

Troponins ↑↑↑

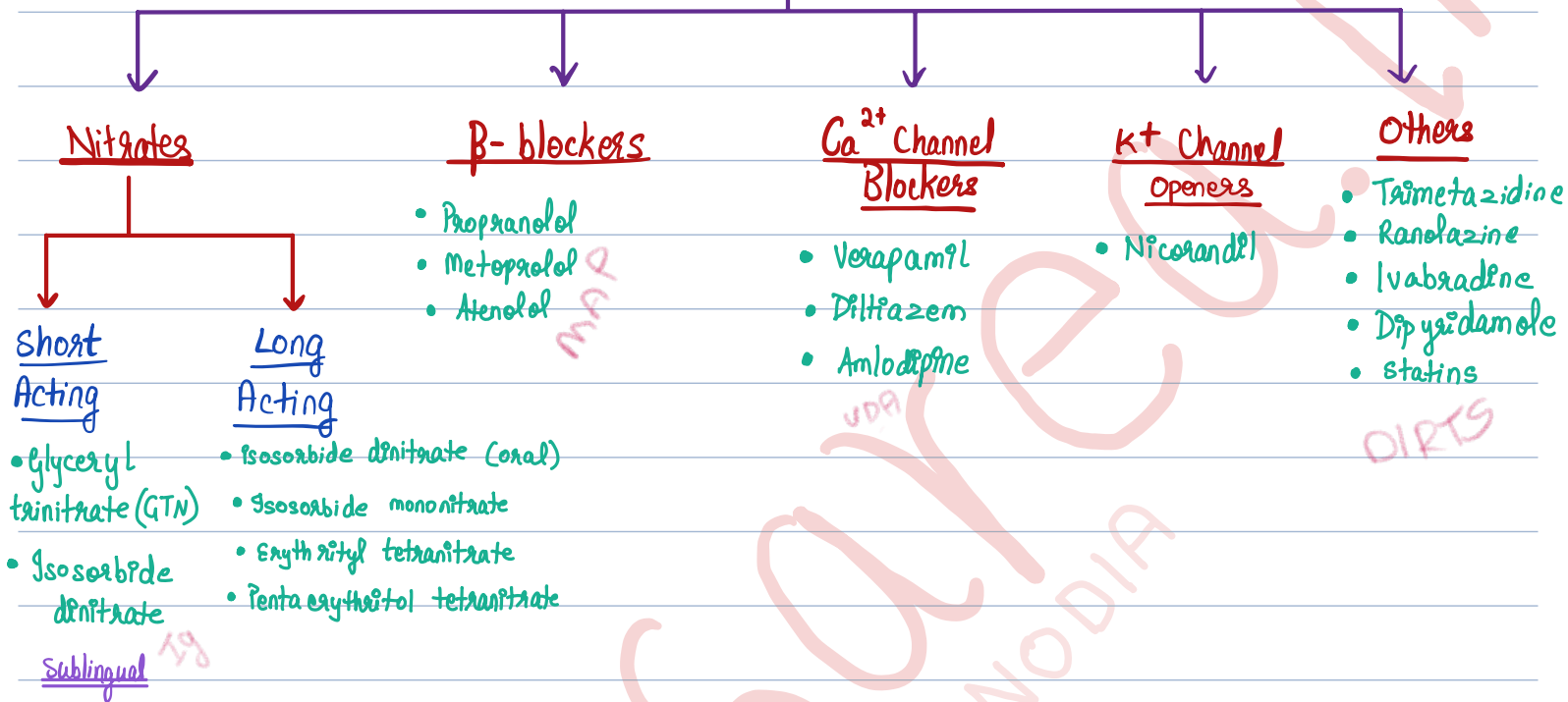
STEMI

- Unstable Angina
- NSTEMI
- STEMI

acute coronary syndrome

↓
ischaemic chest pain at rest (without exertion)

Antianginal Drugs



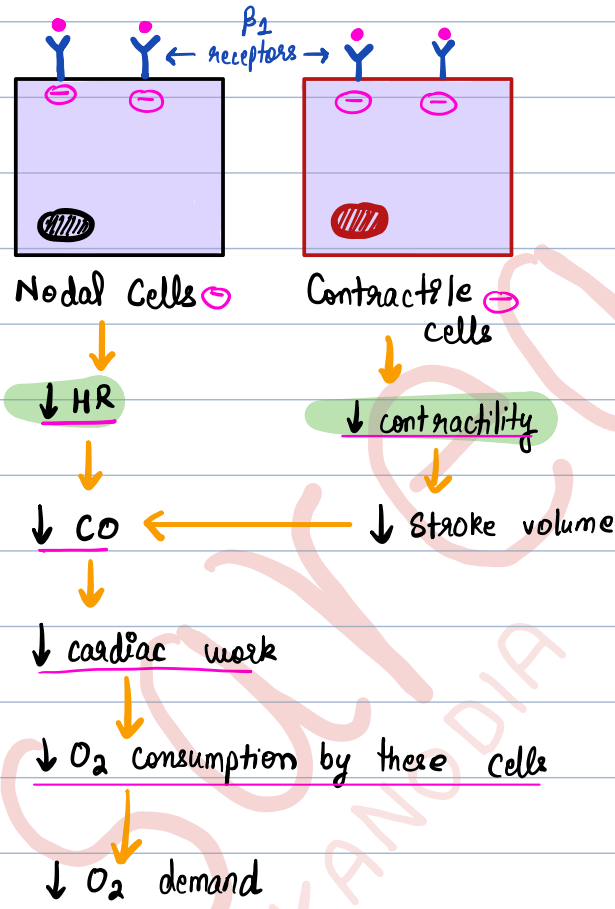
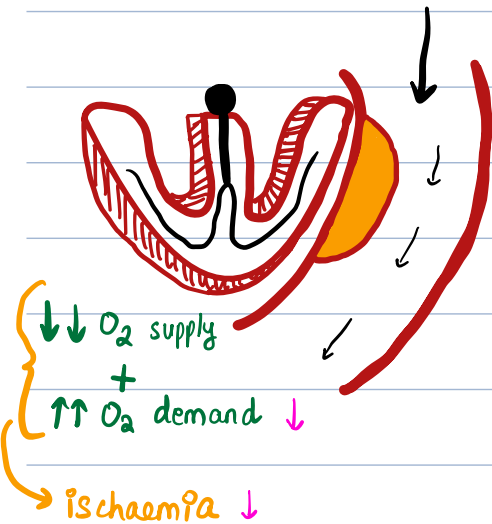
B-blockers:

• = β -blocker

- Metoprolol (β_1)
- Atenolol (β_1)
- Propranolol ($\beta_1 + \beta_2$)

Indications:

- HTN
- Angina
- Arrhythmias
- Heart failure
- MI
- Migraine prophylaxis
- Essential tremors
- Anxiety (particularly performance anxiety)



Adverse effects:

- Bradycardia (due to falling HR)
- Hypotension (due to decreased contractility) $\Rightarrow$ which may lead to shock
- $\therefore$ C/I = decompensated heart failure
- Propranolol ($\beta_1 + \beta_2$) block β_2 receptors in bronchial smooth muscles $\Rightarrow$ bronchospasm C/I = COPD, asthma
- Normally, stimulation of sympathetic system by hypoglycemia causes glucagon release; in case of β -blockers, sympathetic outflow is inhibited $\therefore$ patient develops Hypoglycemia unawareness $\therefore$ C/I in DM.

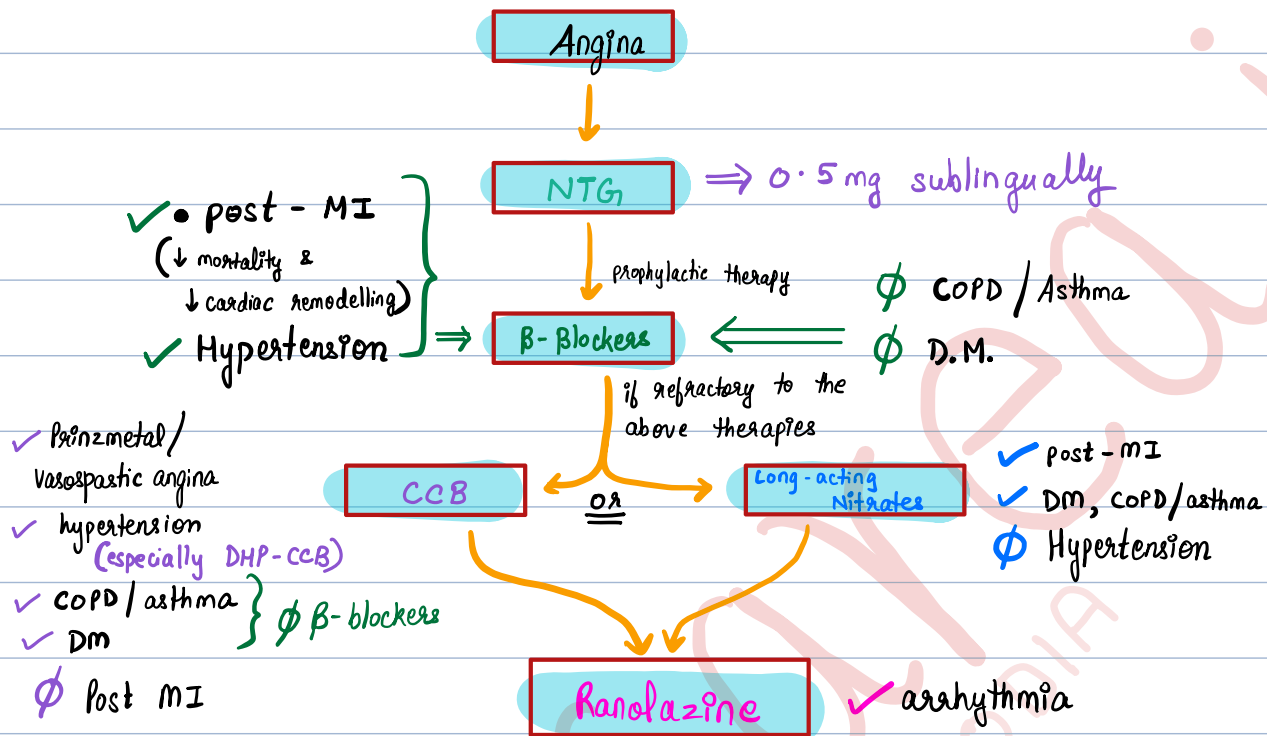
C/I: • Asthma / COPD • Heart Block / Bradycardia • PVD

• Pregnancy

TREATMENT ALGORITHM: (IN ANGINA)

(ϕ = caution)

($\checkmark$ = preferred indication)



⇒ preferred indication ⇒ Prinzmetal's / Vasospastic Angina

Ca²⁺ Channel Blockers: (CCBs)

Non-DHP CCBs

DHP-CCBs

(DHP = dihydropyridine)

Non-DHP CCBs: • Verapamil • Diltiazem

Normally, if Ca²⁺ channels are open & Ca²⁺ enters the cell

↓

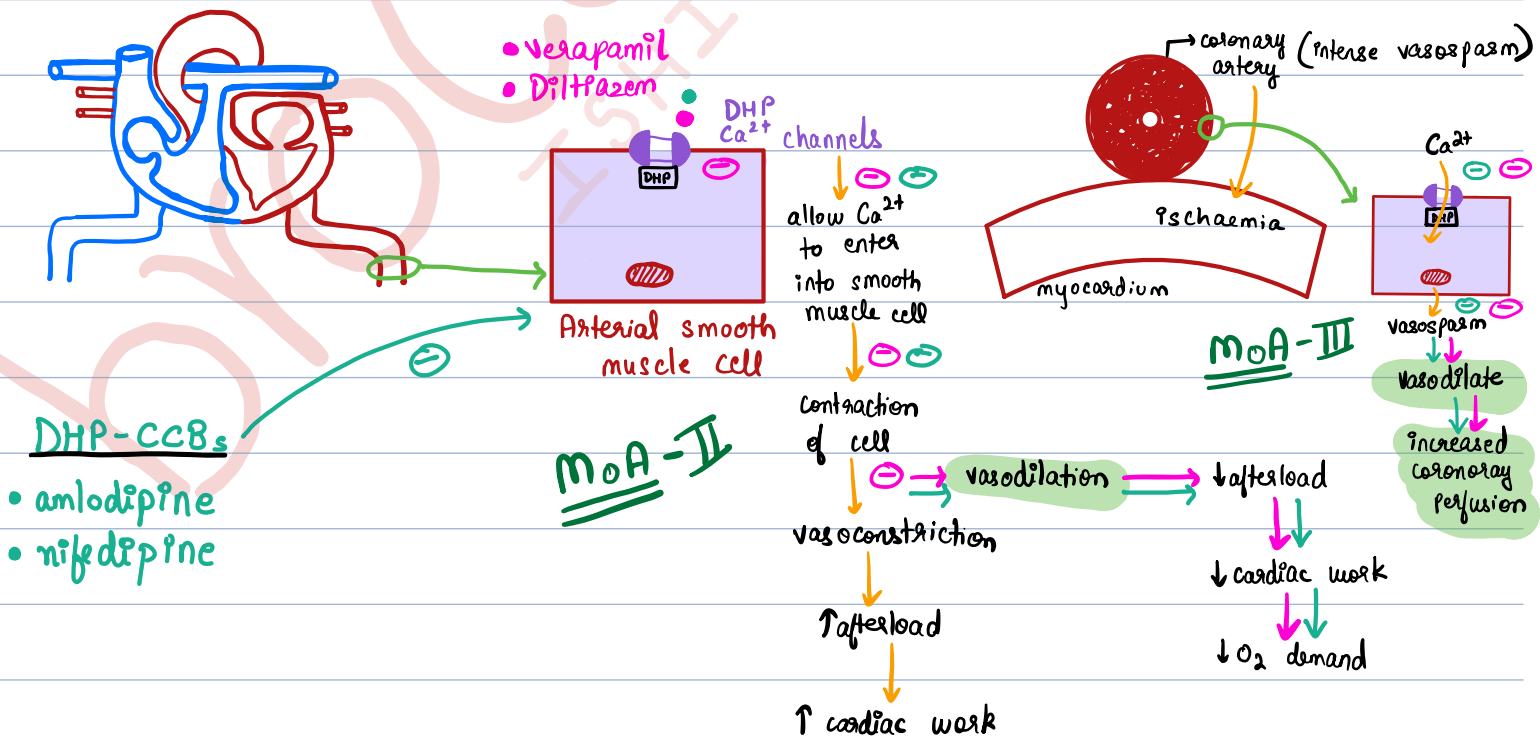
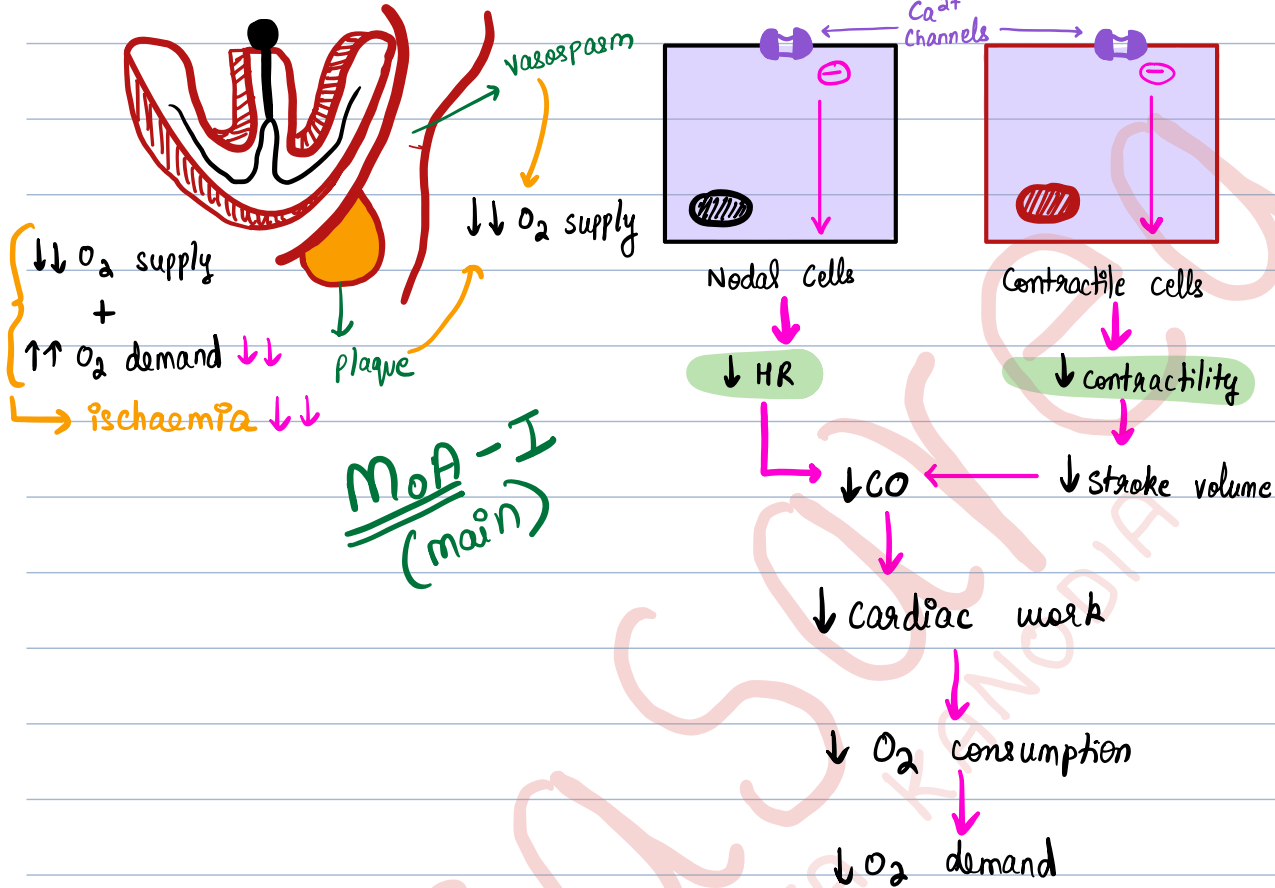
increase action potential

↓

increase heart rate & contractility

↓

increase cardiac output



Adverse Effects:

- **Bradycardia** (due to ↓ in HR)
- **Heart Failure** (due to ↓ in contractility)
- **DHP-CCBs**: ↓ systemic vascular resistance → ↓ BP → **reflex tachycardia**
- **DHP-CCBs**: ↑ risk of mortality in patients with H/O CAD/MI.
↑ urination difficulty in elderly males
- Constipation
- Headache
- Ankle edema

Ca²⁺ Channel BlockersPhenyl alkylamine

- Verapamil

Benzothiazepine

- Diltiazem

Dihydropyridines

- Nifedipine
- Amlodipine
- Lacidipine
- Benidipine
- Nimodipine
- Felodipine
- Nitrendipine
- Lercanidipine
- Nicardipine

C/I: • Heart Block/Bradycardia ⇒ CCBs further ↓ HR

- Acute MI ⇒ CCBs -vely effect heart functions
- Severe hypotension
- Congestive heart failure ⇒ Non-DHPs ∅
- Hepatic impairment ⇒ dosing to be adjusted
- Pregnancy & Breastfeeding

CHAPS

Uses: • Angina pectoris (classical & variant)

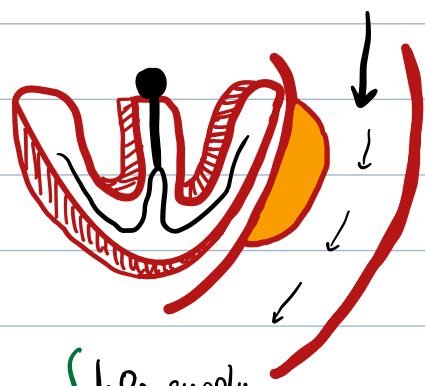
- Hypertension
- Cardiac arrhythmias
- Hypertrophic cardiomyopathy
- in premature labor
- Reducing severity of Raynaud's episodes

CHAIR

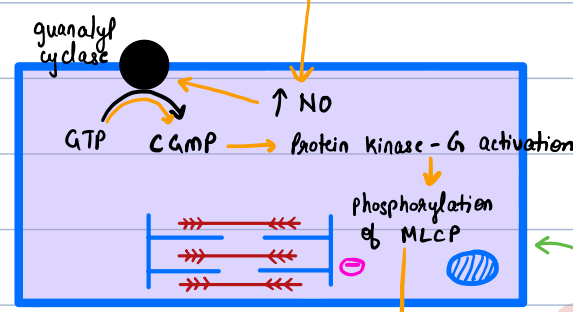
Drug	Preparations	Dose & Route
Verapamil	CALAPTIN 40, 80 mg tabs ; 120, 240 mg SR tabs, 5 mg/2ml inj. VASOPTEN 40, 80, 120 mg tab.	→ 40-160 mg TDS oral → 5mg by slow i.v. infusion
Diltiazem	DILZEM 30, 60 mg tabs; 90mg SR tab.; 25 mg/5ml inj. ANGIZEM 30, 60, 90, 120, 180 mg tab. DILTIME 30, 60 mg tab ; 90, 120 mg SR tab.	→ 30-60 mg TDS - QID oral
Nifedipine	CALCIGARD, DEPIN, NIFELAT 5, 10 mg cap. ; also 10mg, 20mg S.R. tab. ADALAT RETARD 10, 20mg SR tab.	→ 5-20 mg BD - TDS oral
Amlodipine	AMLOPRES, AMCARD, AMLOPIN, MYODURA 2.5, 5, 10 mg tabs.	→ 5-10 mg OD
Felodipine	FELOGARD, PLENDIL, RENDIL 2.5, 5, 10 mg ER tab.	→ 5-10 mg OD (max = 10mg BD)
Nitrendipine	NITREPIN, CARDIF 10, 20 mg tabs	→ 5-20 mg OD
Lacidipine	LACIVAS, SINOPIL 2, 4 mg tabs.	→ 4mg OD (increase to 6mg OD if required)
Clevidipine	CILACAR, CILAGARD 5, 10mg tabs	→ 5 - 20 mg OD.
Nimodipine	VASOTOP, NIMODIP, NIMOTIDE 30 mg tab ; 10mg/50 ml inj.	→ 30-60 mg 4-6 hourly for 3 weeks following subarachnoid haemorrhage
Nicardipine	NICARDIPINE 25mg/10 ml inj. 5-15 mg/hour i.v. infusion	→ 20-40 mg TDS or 30-60 mg BD as ER tab.
Lercanidipine	LEREZ, LERKA 10, 20 mg tabs.	→ 10-20 mg OD
Benidipine	CARITEC 4, 8 mg tab.	→ 4-8 mg OD

no direct action on heart.
Nitrates: → venodilation (of large veins)
 → improves perfusion of myocardium

MLCP = myosin light-chain phosphatase

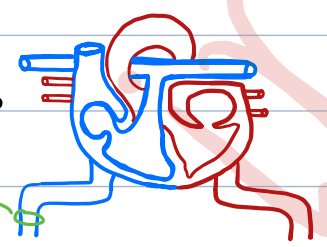


↓ O₂ supply
 ↑ O₂ demand
 → ischaemia



venous smooth muscle cell

inhibits contraction of smooth muscle in a vein



venodilation

↓ preload

↓ stroke volume

↓ CO

↓ cardiac work

↓ O₂ demand

↓ BP during positional changes

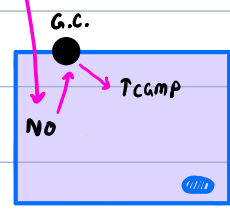
orthostatic hypotension

Patients already on phosphodiesterase-5 inhibitors (which also work to ↑ cGMP)
 → profound venodilation
 → ↓ preload
 → ↓ CO
 → ↓ BP

R.V. MI
 → ↓ preload
 → ↓ CO
 → ↓ BP

headache
 weakness
 flushing
 syncope

Nitrates



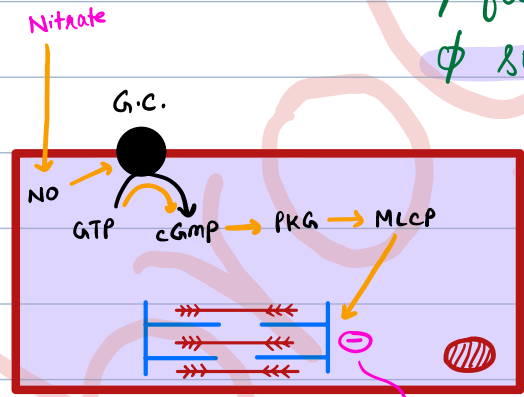
With continuous usage of nitrates, guanylyl cyclase (G.C.) starts getting desensitized

↓ efficacy of drug

to improve sensitivity

nitrate-free interval (10-12 hours)

Tolerance on prolonged use



coronary arterial smooth muscle cell

↓ coronary artery smooth muscle cell contraction

coronary vasodilation

improved perfusion to myocardium

Monday disease - caused by industrial exposure to nitrates at work. Individuals develop tolerance for the vasodilator action during the week & lose tolerance over the weekend. On re-exposure on Monday, drastic vasodilation produces a fast heart rate, dizziness, headache.

NitratesShort Acting

- glyceryl trinitrate (GTN)
 - Isosorbide dinitrate
- Sublingual
or transdermal patch

Long Acting

- Isosorbide dinitrate (oral)
- Isosorbide mononitrate
- Erythritol tetranitrate
- Pentaerythritol tetranitrate

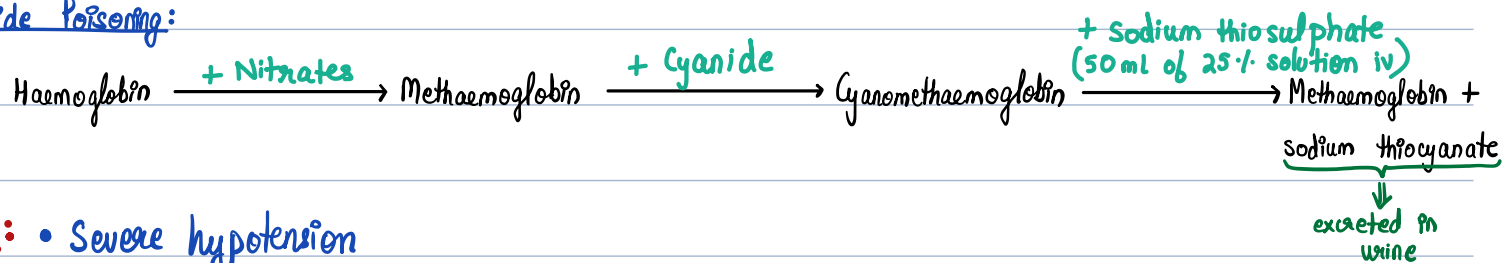
Drug	Preparations	Dose & Route
GTN (Nitroglycerine)	ANGISED 0.5 mg tab. NITROLINGUAL, GTN SPRAY 0.4 mg/spray ANGISPAN-TR 2.5, 6.5 mg SR cap. NITROCONTIN, CORODIL 2.6, 6.4 mg tabs. NITRODERM - TTS 5, 10 mg patch MYOVIN, MILLISROL, NITROJECT 5 mg/ml inj.	→ 0.5 mg sublingual → 0.4-0.8 mg s.l. spray → 5-15 mg SR oral → One patch for 14-16 hr/day → 5-20 µg/min i.v.
Isosorbide dinitrate	SORBITRATE 5, 10 mg tab ISORDIL 5 mg sublingual, 10 mg oral tabs. DITRATE 5, 10 mg tab; 20, 40 mg SR tab.	→ 5 mg sublingual → 10-20 mg oral → 10-40 mg SR oral
Isosorbide - 5 - mononitrate	MONOTRATE 10, 20, 40 mg tab; 25, 50 mg SR tabs 5-MONO, MONOSORBITRATE 10, 20, 40 mg tab.	→ 10-40 mg oral → 10-40 mg SR oral
Erythritol - tetranitrate	CARDILATE 5, 15 mg tab	→ 15-60 mg oral
Pentaerythritol - tetranitrate	PERITRATE 10 mg tab PERITRATE-SR 80 mg SR tab.	→ 10-40 mg oral → 80 mg SR oral.

Uses of Nitrates: - Angina - Acute Coronary Syndrome

- MI - CHF & acute LVF

- Biliary colic - Oesophageal spasm - Cyanide poisoning

Cyanide Poisoning:



C/I: • Severe hypotension

- Use of PDE-5 inhibitors $\Rightarrow$ concomitant use of nitrates & PDE5 inhibitors can result in severe drop in BP
- Increased ICP $\Rightarrow$ nitrates further $\uparrow$ ICP
- Cardiogenic shock
- Severe anemia $\Rightarrow$ nitrates worsen the symptoms of anemia by dilating blood vessels & increasing blood flow, potentially leading to strain on the heart.

PG - S²UIC side

• Glaucoma $\Rightarrow$ nitrates $\uparrow$ IOP

• Pregnancy & Breastfeeding

D: Dependence
S: Skin rashes
T: Throbbing, Tolerance
O: Orthostatic
R: R V MI
M: Methemoglobinemia

Indications:

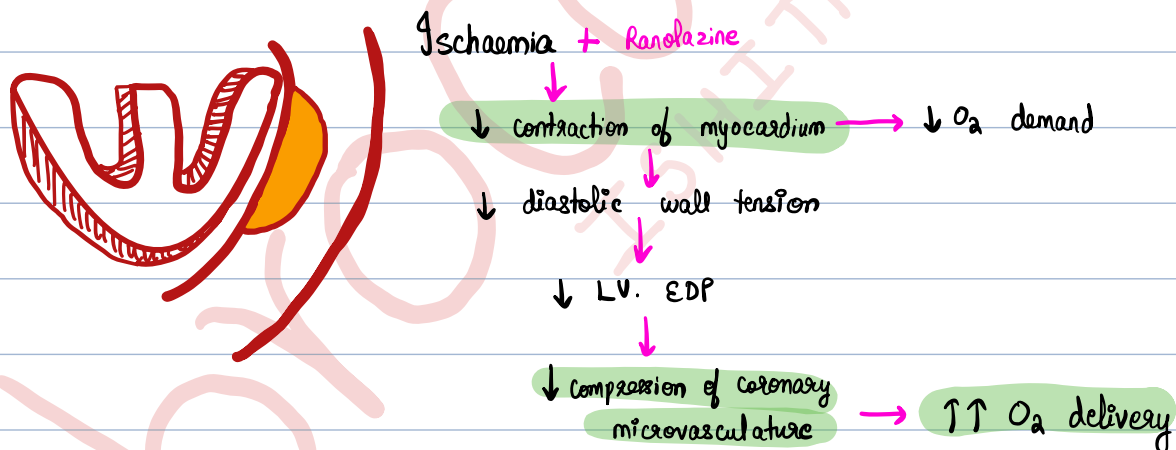
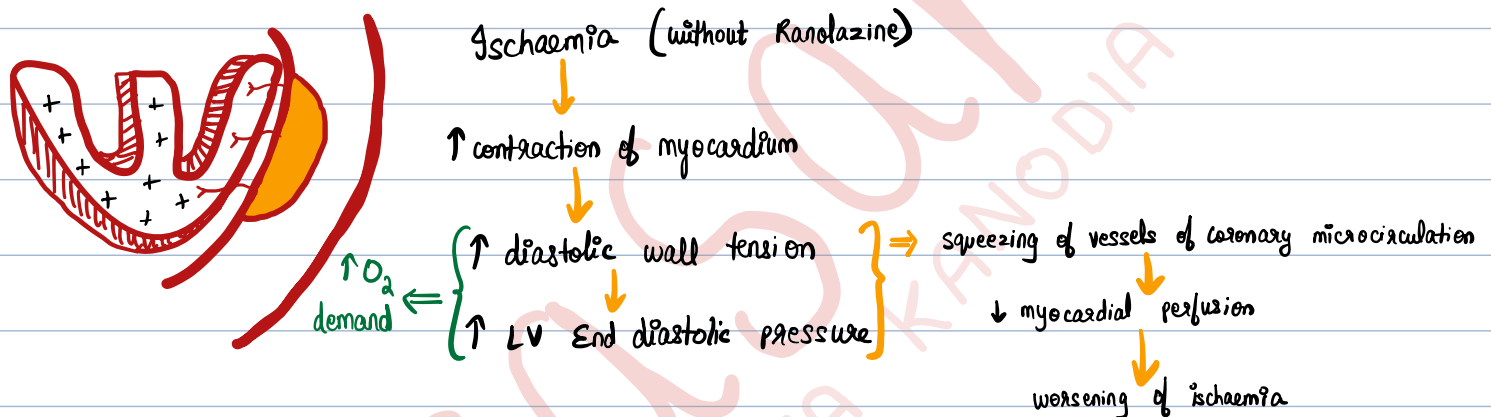
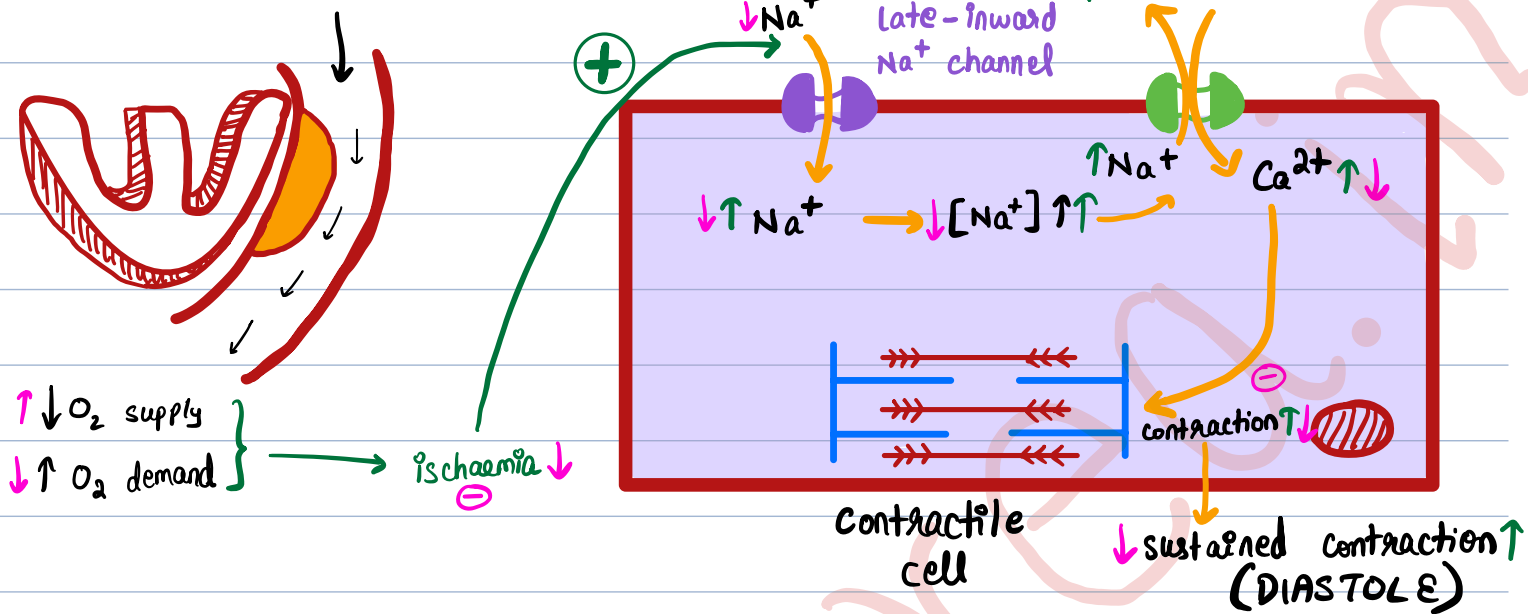
- Acute Angina $\Rightarrow$ nitrates provide quick relief by rapidly dilating coronary arteries & improving myocardial perfusion
- Chronic stable angina • Cyanide poisoning • Oesophageal spasm • Biliary colic
- Prinzmetal's angina $\Rightarrow$ nitrates relax the smooth muscles in the coronary vessels & improve perfusion to the affected area
- Heart failure $\Rightarrow$ nitrates improve exercise tolerance & alleviate symptoms by dilating blood vessels, reducing cardiac work & improving myocardial perfusion
- Pulmonary hypertension $\Rightarrow$ nitrates dilate the pulmonary blood vessels, thus $\downarrow$ pressure & improve perfusion through lungs.

FT² - DROPS

Adverse Effects: • Throbbing headache • Flushing • Sweating • Palpitation
• Rashes • Orthostatic hypotension • Dependence • Tolerance

→ improves exercise tolerance

Ranolazine:



Adverse Effects:

- $\uparrow \uparrow \uparrow$ risk of drug interactions
- it prolongs QT-interval $\Rightarrow \uparrow$ torsades de pointes

C/I:

- **Liver impairment:** Ranolazine is primarily metabolized by the liver ∴ make dose adjustments
- **Use of strong CYP3A inhibitors or inducers:** Ranolazine is metabolized by CYP3A enzyme
 - CYP3A inhibitors ⇒ **Clarithromycin, Ketoconazole**
 - CYP3A inducers ⇒ **rifampicin, phenytoen**
- **QT prolongation & Arrhythmias**
- **Severe renal impairment**
- **Pregnancy & breastfeeding**

Indications:

- **Chronic Stable angina**
- **Angina prophylaxis**
- **Combination therapy** - with other anti-anginals when monotherapy is insufficient.
- **CAD**

K⁺ Channel Openers: Nicorandil $\Rightarrow$ 2nd line antianginal drugs

- dilates coronary vessels & improves blood flow to the myocardium
- has cardioprotective effect
- no tolerance
- Adverse effects: - headache, hypotension, palpitation, flushing, nausea, vomiting
 - large painful aphthous ulcers in the mouth

Dose: 5-20 mg BD

NIKORAN 5, 10 mg tabs; 2 mg/vial, 48 mg/vial inj.

KORANDIL 5, 10 mg tabs.

Indications:

- Chronic Stable Angina
- Prinzmetal's angina

C/I: • Severe hypotension

- Hypovolemia
- Cardiogenic shock
- Severe renal &/or hepatic impairment
- Concomitant use of PDE5 inhibitors
- Pregnancy & breastfeeding
- Obstructive hypertrophic cardiomyopathy