

High-Yield Summary – Clinical Pharmacology of Angina

Definition

Angina pectoris = chest pain due to transient myocardial ischemia caused by an imbalance between oxygen supply and oxygen demand.

Types of Angina

1. Stable (Effort) angina – worse with exertion.
2. Variant (Prinzmetal) – coronary artery spasm.
3. Unstable angina – plaque rupture + thrombosis.

Non-Pharmacological Measures

- Weight reduction
- Stop smoking
- Exercise



Pharmacological Treatment

Pharmacological Treatment (3 x 3)

A) Anti-Anginal Drugs

1 Organic Nitrates

Mechanism:
 $NO \uparrow \rightarrow cGMP \uparrow \rightarrow$ Venodilation $\uparrow \uparrow \rightarrow$ ↓ preload \rightarrow ↓ myocardial O_2 demand
 • Coronary vasodilation.

Clinical Uses:

- All types of angina
- Heart failure
- Cyanide poisoning (methemoglobin formation)
- Congestive heart failure: ↓ ↓ preload and relieve pulmonary congestion

Important Notes:

- SL nitroglycerin: rapid onset
- Tolerance \rightarrow requires 8–12 h nitrate-free interval
- **Contraindicated with sildenafil (PDE-5 inhibitors) \rightarrow fatal hypotension**

Adverse Effects: headache, flushing, hypotension, reflex tachycardia.

Handwritten notes: ↑ NO, hyper sensitivity reaction, ↓ ability β-blockers or verapamil (Ca-blockers), cGMP ↑↑, Not with phosphodiesterase inhibitors (sildenafil) due to fatal hypotension and tachycardia.

2 Calcium Channel Blockers (CCBs)

DHPs (amlodipine, nifedipine)

- Strong arteriolar vasodilation \rightarrow ↓ afterload
- May cause reflex tachycardia (especially nifedipine)

Non-DHPs (verapamil, diltiazem)

- ↓ HR (negative chronotropy)
- ↓ contractility (negative inotropy)
- ↓ AV conduction (negative dromotropy)

Do NOT combine with β-blockers \rightarrow severe cardiac depression

Contraindicated in: heart block, severe heart failure.

Uses:

- All angina types
- Arrhythmias (verapamil/diltiazem)
- Hypertension
- Subarachnoid hemorrhage (nimodipine)

Ankle edema (due to ↑ capillary permeability- treated or avoided by elastic stocks)

3 β-Blockers

Mechanism:
 ↓ HR \rightarrow ↑ diastolic perfusion
 ↓ contractility & BP \rightarrow ↓ myocardial O_2 demand

Uses:

- Stable angina
- Unstable angina
- Post-MI protection

Not used in variant angina (worsens vasospasm)

Avoid in asthma, severe bradycardia, PVD.

Adverse Effects: bradycardia, heart block, fatigue, ↑ risk of type 2 DM.

Other Anti-Anginal Drugs

Trimetazidine: improves cellular metabolism, reduces lactate and Ca^{2+} overload.

Ranolazine: blocks late Na^+ current; does not affect HR or BP.

Ivabradine: inhibits If current \rightarrow ↓ heart rate without affecting contractility.

- ✓ Anti-Ischemic & Cytoprotective
- ✓ Improves cell respiration \rightarrow ↓ ↓ lactate production \rightarrow ↓ ↓ intracellular acidosis
- ✓ ↓ ↓ Intracellular Ca^{2+} overload
- ✓ ↓ ↓ Free radical production

- ✓ Prevents abnormal sustained opening of the late Na^+ channels (due to deficiency of ATP)
- ✓ Ranolazine increases ATP synthesis
- ✓ Does not affect heart rate or blood pressure
- ✓ Adverse effects: constipation, nausea, dizziness, headache

- Mechanism of action:**
- Ivabradine inhibits the cardiac pacemaker If current that controls the spontaneous diastolic depolarization in SAN and regulates heart rate.
- Pharmacological actions:**
- Ivabradine produces dose-dependent reduction in heart rate.
- Therapeutic Use:**
- Stable angina pectoris in adults with normal sinus rhythm.

Drug Combinations

✓ **Good combinations:**

- Nitrate + β-blocker
- Nitrate + Verapamil

✗ **Bad combinations:**

- Nitrate + Nifedipine \rightarrow severe hypotension
- β-blocker + Verapamil \rightarrow severe cardiac inhibition
- Two drugs from same class

B) Adjuvant / Supportive Drugs

- Anti-platelets:**
- Aspirin (75–150 mg)
 - Clopidogrel
- \rightarrow Prevents progression to unstable angina.

Statins:

Used even if lipid levels are normal.
 \rightarrow Stabilize plaques, ↑ NO, antioxidant effects.

Control of risk factors:

HTN, DM, hyperlipidemia.

Management of Acute Angina

Acute attack

- SL nitroglycerin every 5 min x up to 3 doses
- If no relief \rightarrow possible MI

Before exertion

- Take nitrate 5 minutes before exercise

Avoid	Useful	Condition
✗ β-blockers	Nitrates + CCBs	Variant angina
✗ β-blockers	Nitrates + CCBs	Asthma / PVD / Diabe
✗ β-blockers, Verapamil	Nitrates + Nifedipine	Heart block + Angina
✗ High-dose β-blockers, Verapamil	Nitrates + Nifedipine	Heart failure + Angina



Hypertension

Peripheral vascular disease

→ L type Ca⁺⁺ channels

• Dihydropyridines (DHPs): VD > cardiac depression:

✓ Long-acting: **amlodipine**

✓ Intermediate-acting: **nifedipine**, felodipine

✓ Short-acting: isradipine & nimodipine

✓ VD > cardiac depression: **arteries** > veins: ↓ ↓ TPR → ↓ ↓ afterload and ↓ cardiac work
✓ Weak venodilator → ↓ ↓ VR → ↓ ↓ preload → ↓ ↓ O2 consumption

✓ Hypotension → reflex sympathetic activation → tachycardia → short diastolic filling time (minimal with amlodipine)

Cerebral spasm due to subarachnoid hemorrhage

Cardiac arrhythmia

Migraine headache prophylaxis

• Non-DHPs: verapamil & diltiazem: cardiac depression > VD

Constipation

Liver impairment

Hypertrophic obstructive cardiomyopathy with subaortic stenosis

not use more than 1g.

Heart: (verapamil & diltiazem)

✓ Negative inotropic → heart failure
✓ Negative chronotropic → bradycardia
✓ Negative dromotropic → heart block

✓ Negative chronotropic effect
✓ Negative inotropic effect (contraindicated in heart failure)
✓ Negative dromotropic effect (contraindicated in heart block)
✓ **NOT** combined with β-blockers or digitalis.
✓ Automaticity → ↓ Ectopic Focus Formation → Class IV Anti-Arrhythmic

Therapeutic uses of CCBs:

Adverse effects of CCBs:



إلى طلاب وطالبات الطب :

« كل كرسي من كرسي كلية الطب هو بمثابة أحد سدود الواجب الكفائي المفروض على الأمة ... أنت على تفرع عظيم فأحسنه القيام على تفرع »