D.PHARM • SECOND YEAR

Pharmacology

CHAPTER 5

Drugs Acting on the Cardiovascular System



ENGLISH CHAPTER NOTES

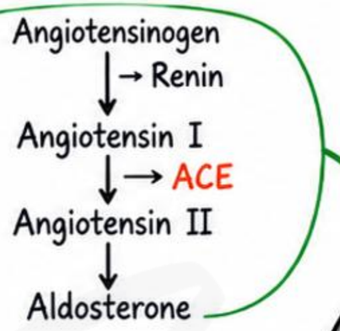
DIPLOMA IN PHARMACY

ANTIHYPERTENSIVE DRUGS: CLASSIFICATION

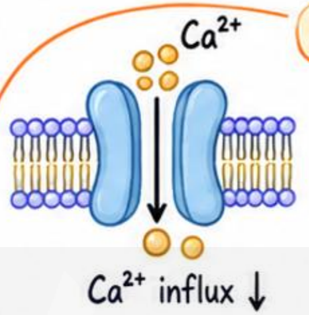
Antihypertensive drugs lower elevated arterial blood pressure and help prevent stroke, myocardial infarction, renal failure and heart failure.

A. RAAS-BLOCKING DRUGS

- ACE inhibitors: enalapril, lisinopril
- ARBs: losartan, telmisartan
- direct renin inhibitor: aliskiren
- aldosterone antagonists: spironolactone, eplerenone



B. CALCIUM CHANNEL BLOCKERS, CCBs

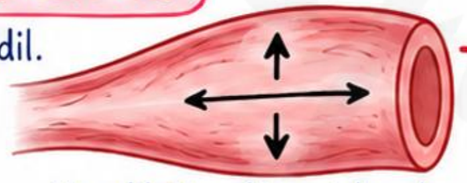


- dihydropyridines: amlodipine, nifedipine — mainly vascular
- non-dihydropyridines: verapamil, diltiazem — cardiac plus vascular



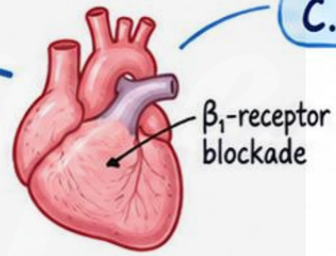
F. DIRECT VASODILATORS

Hydralazine, minoxidil.



Vasodilation (↓ peripheral vascular resistance)

C. BETA-ADRENERGIC BLOCKERS



↓ Heart rate and cardiac output

- non-selective: propranolol
- β_1-selective: atenolol, metoprolol
- with α-blocking action: labetalol, carvedilol

D. DIURETICS

- thiazide or thiazide-like: hydrochlorothiazide, chlorthalidone
- loop: furosemide — useful with edema, advanced CKD or resistant hypertension
- potassium-sparing: amiloride, spironolactone



Kidney

↑ Na^+ and water excretion (diuresis)

E. CENTRALLY ACTING DRUGS



α_2-agonists: clonidine, methyldopa.

MEMORY LINE

Control BP by reducing volume, cardiac output, vascular resistance or RAAS activity.

ANTIHYPERTENSIVE ACTIONS AND DOSE EXAMPLES

ACE inhibitors or ARBs:
↓ angiotensin II action → vasodilation + ↓ aldosterone → less Na^+ and water retention

CCBs:
block L-type Ca^{2+} channels → arterial vasodilation; verapamil and diltiazem also ↓ heart rate and contractility

direct vasodilators:
relax arterial smooth muscle → ↓ systemic vascular resistance

BP = cardiac output × systemic vascular resistance

beta-blockers:
↓ heart rate + ↓ contractility + ↓ renin release → ↓ cardiac output

diuretics:
initial ↓ plasma volume; long-term ↓ peripheral resistance

central α_2-agonists:
↓ sympathetic outflow from the CNS

DOSE EXAMPLES

1. **amlodipine:** 5–10 mg once daily
2. **losartan:** 50–100 mg/day oral
3. **enalapril:** 5–20 mg/day oral
4. **metoprolol:** 25–100 mg twice daily oral
5. **hydrochlorothiazide:** 12.5–25 mg/day oral
6. **clonidine:** 0.1–0.3 mg twice daily oral

PRACTICAL RULE: Start with patient-specific therapy, reassess BP, renal function and electrolytes, then titrate. Combination therapy is often needed because different classes act at different control points.

ANTIHYPERTENSIVE USES AND SAFETY

MAIN INDICATIONS

Antihypertensive uses

1. Primary
   - primary or essential hypertension
2. Secondary
   - secondary hypertension, for example renal disease
3. Hypertensive emergency
   - hypertensive emergency: monitored IV treatment such as labetalol or nitroprusside, with controlled BP reduction
4. Heart failure / post-MI
   - heart failure or after myocardial infarction: selected ACE inhibitors and beta-blockers
5. CKD with proteinuria
   - CKD with albuminuria or proteinuria: ACE inhibitor or ARB when suitable



EMERGENCY NOTE

Very high BP with chest pain, neurological deficit, pulmonary edema or organ injury needs urgent hospital assessment.

MAJOR CAUTIONS OR CONTRAINDICATIONS

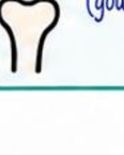
- **ACE inhibitors**: pregnancy, bilateral renal-artery stenosis, previous ACE-inhibitor angioedema; monitor creatinine and K^+
- **ARBs**: avoid in pregnancy; monitor renal function and K^+
- **beta-blockers**: bradycardia, AV block; non-selective agents can worsen asthma
- **verapamil or diltiazem**: AV block, marked bradycardia and HFrEF
- **thiazides**: gout, hyponatraemia and hypokalaemia risk
- **spironolactone**: hyperkalaemia and renal impairment risk

IMPORTANT ADVERSE EFFECTS

- **ACE inhibitors**: dry cough, hyperkalaemia, angioedema
- **amlodipine**: ankle edema, flushing, headache
- **hydralazine**: reflex tachycardia and lupus-like syndrome
- **minoxidil**: edema, tachycardia and hypertrichosis

DO NOT STOP CLONIDINE ABRUPTLY

Sudden withdrawal may cause severe rebound hypertension. Taper under supervision.



SAFETY BY ORGAN SYSTEM



Pregnancy (ACE inhibitors, ARBs) — Avoid



Kidneys (monitor creatinine and K^+) — Use with caution



Heart (bradycardia, AV block, HFrEF) — Use with caution



Respiratory (non-selective beta-blockers) — Use with caution



Metabolic (gout, electrolytes) — Use with caution

ANTI-ANGINAL DRUGS: CLASSIFICATION

Anti-anginal drugs prevent or relieve angina pectoris caused by myocardial ischemia. They work by reducing myocardial O_2 demand, improving coronary O_2 supply, or both.

A. NITRATES

- short acting: nitroglycerin, sublingual
- long acting: isosorbide dinitrate, isosorbide mononitrate

B. BETA-ADRENERGIC BLOCKERS

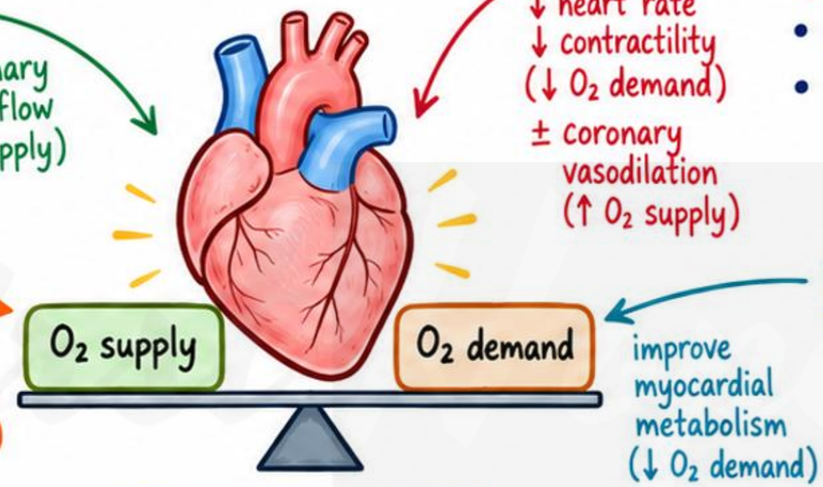
Atenolol, metoprolol, propranolol.

C. CALCIUM CHANNEL BLOCKERS, CCBs

- dihydropyridines: amlodipine, nifedipine
- non-DHPs: verapamil, diltiazem

D. OTHER ANTI-ANGINAL AGENTS

- late Na^+-current inhibitor: ranolazine
- metabolic modulator: trimetazidine
- nitrate plus K_{ATP}-channel opener: nicorandil



O_2 BALANCE

O_2 demand rises with heart rate, contractility and wall tension. Therapy aims to lower demand or improve coronary blood flow.

CLINICAL PATTERNS

1. **stable exertional angina:** beta-blocker, CCB, nitrate or another suitable anti-anginal.
2. **acute coronary syndrome or unstable angina:** anti-anginal relief is only one part; urgent antiplatelet, anticoagulant and reperfusion assessment may be needed.
3. **vasospastic or Prinzmetal angina:** CCBs and nitrates are preferred.

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