

Pharmacology of drugs acting on cardio-vascular system

Introduction to Hemodynamics

Definition

- Hemodynamics refers to the dynamics of blood flow, including how the heart pumps blood, how blood pressure is generated and regulated, and how blood circulates through the vasculature.

Key Terms

- Cardiac Output (CO)** = Heart Rate (HR) × Stroke Volume (SV)
- Stroke Volume (SV):** The amount of blood ejected from the ventricle with each heartbeat.
- Preload:** The degree of ventricular filling (end-diastolic volume) that stretches the cardiac muscle fibers before contraction.
- Afterload:** The resistance to the left ventricle must overcome to pump blood into the systemic circulation.
- Contractility:** The intrinsic ability of cardiac muscle fibers to contract, independent of preload and afterload.
- Ejection Fraction (EF):** The fraction of the end-diastolic volume ejected during systole ($SV \div EDV$).

Regulation of Blood Pressure

1. Baroreceptor Reflex:

- Stretch receptors in the carotid sinus and aortic arch sense changes in blood pressure and modulate sympathetic/parasympathetic outflow.

2. Renin-Angiotensin-Aldosterone System (RAAS):

- Renin (kidneys) → Angiotensin I → Angiotensin II (via ACE in lungs) → Aldosterone (adrenal cortex) → Na^+ and H_2O retention → ↑ Blood volume and pressure.

3. Autonomic Nervous System:

- Sympathetic stimulation increases heart rate, contractility, and vasoconstriction.
- Parasympathetic stimulation (vagus nerve) decreases heart rate.

Electrophysiology of the Heart

Cardiac Conduction System

- Sinoatrial (SA) Node:** The primary pacemaker (60–100 bpm).
- Atrioventricular (AV) Node:** Delays conduction from the atria to the ventricles.

- **Bundle of His → Purkinje Fibers:** Rapid conduction to the ventricles.

Action Potential Phases (Ventricular Myocytes)

- **Phase 0 (Depolarization):** Rapid influx of Na^+ → Sharp upstroke.
- **Phase 1 (Initial Repolarization):** Inactivation of Na^+ channels; K^+ efflux begins.
- **Phase 2 (Plateau):** Balance between Ca^{2+} influx (through L-type Ca^{2+} channels) and K^+ efflux.
- **Phase 3 (Repolarization):** Increased K^+ efflux; Ca^{2+} channels inactivate.
- **Phase 4 (Resting Membrane Potential):** High K^+ permeability through K^+ channels, restoring the resting potential.

Nodal Cells (SA/AV)

- **Spontaneous Depolarization (Pacemaker Potential):** Slower rise, mainly involving Ca^{2+} and reduced K^+ permeability.
- **Autonomic Influences:**
 - **Sympathetic:** Increases the slope of pacemaker potential → Increased heart rate.
 - **Parasympathetic:** Decreases slope → Reduced heart rate.

Drugs Used in Congestive Heart Failure (CHF)

Introduction

- Congestive heart failure is a clinical syndrome where the heart is unable to pump sufficient blood to meet the body's metabolic demands.
- The main goals in pharmacotherapy are to improve hemodynamics, reduce cardiac workload, and prevent disease progression.

Major Classes of Drugs Used in CHF

A. Diuretics

- Used to relieve **congestion** by promoting fluid removal.

Mechanism of Action

- Increase urinary excretion of **sodium and water**
- Reduce **blood volume** → **decreased preload**
- Improve symptoms of edema and pulmonary congestion

Classes

1. Loop Diuretics (e.g., Furosemide)

- Most potent class
- Inhibit **$\text{Na}^+/\text{K}^+/\text{2Cl}^-$ cotransporter** in the thick ascending limb of the loop of Henle

- **Typical dose:** 20–80 mg/day (may go higher depending on severity)

2. Thiazide Diuretics (e.g., Hydrochlorothiazide)

- Act on the **distal convoluted tubule**
- Usually added when loop diuretics alone are insufficient

3. Potassium-Sparing Diuretics / Aldosterone Antagonists (e.g., Spironolactone, Eplerenone)

- Block aldosterone receptors
- Reduce **remodeling and fibrosis** of the heart
- Provide mortality benefit in CHF

Adverse Effects

- **Loop & Thiazide:** Hypokalemia, dehydration, metabolic alkalosis
- **Spironolactone:** Hyperkalemia, gynecomastia

B. ACE Inhibitors and ARBs

- These are **cornerstone therapies** that improve survival.

ACE Inhibitors (e.g., Enalapril, Lisinopril)

Mechanism:

- Inhibit ACE → ↓ Angiotensin II
- → **Afterload reduction** (vasodilation)
- → **Preload reduction** (↓ aldosterone)

Adverse Effects:

- **Dry cough** (due to bradykinin accumulation)
- Hyperkalemia
- Angioedema (rare but serious)

ARBs (e.g., Losartan, Valsartan)

Mechanism:

- Block the **AT₁ receptor** for Angiotensin II
- Similar benefits to ACE inhibitors without causing cough

Contraindications for Both

- Pregnancy
- Existing hyperkalemia
- Severe bilateral renal artery stenosis

C. Beta-Blockers



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