

Cardiovascular Disease part II

by Maysam Ali Ameen

II. Drug used in heart failure

Congestive heart failure occurs when **there is an inability of the heart to maintain a cardiac out put sufficient to meet the requirements of the metabolising tissues.**

Heart failure is usually caused by one of the following:

- Ischaemic heart disease,
- Hypertension,
- Heart muscle disorders, and
- Valvular heart disease.

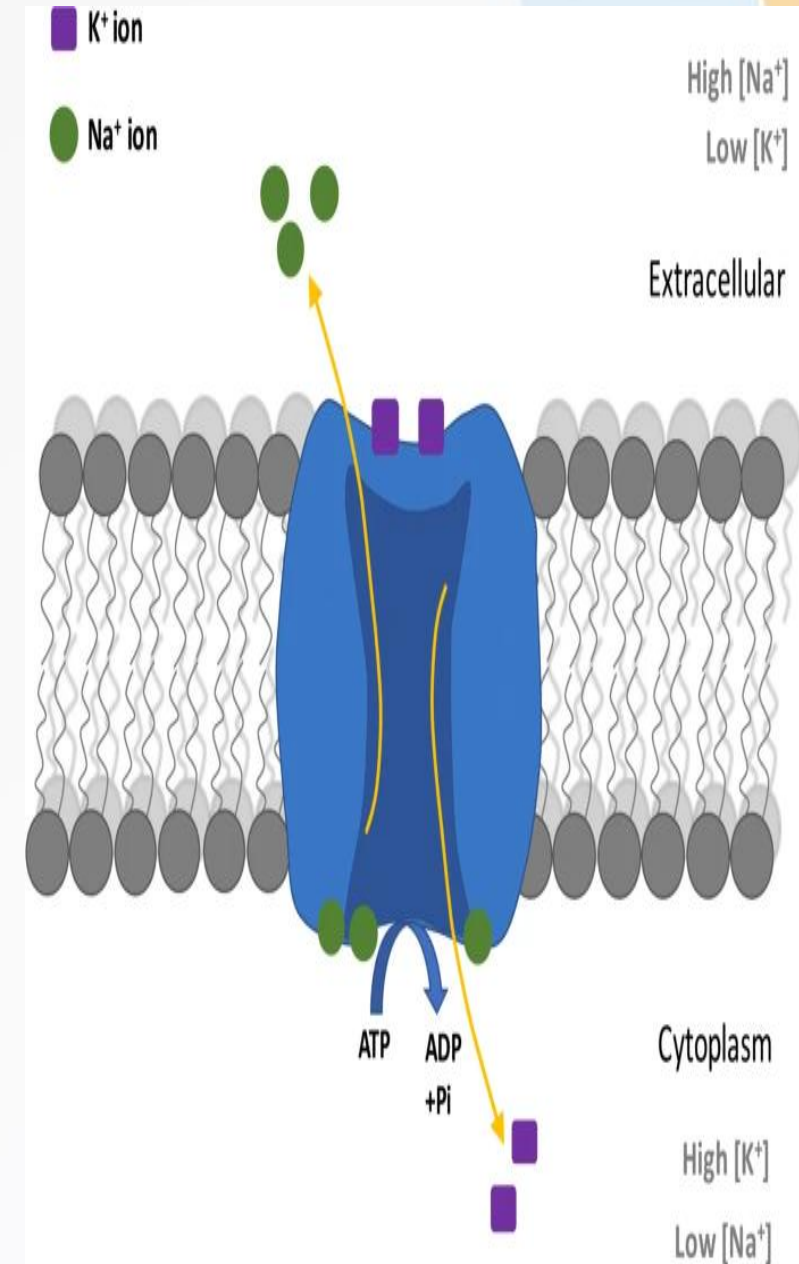
A. Drugs with positive inotropic effect:-

Drugs with positive inotropic effect increase the force of contraction of the heart muscle. These include:

- Cardiac glycosides,
- Bipyridine derivatives,
- Sympathomimetics, and
- Methylxanthines

1\ Cardiac Glycosides

- Composed of steroid compounds that **increase cardiac output** and alter electrical functions.
- Commonly used are digoxin and digitoxin.
- Inotropic action mechanism: **Inhibition of membrane-bound $\text{Na}^+ / \text{K}^+ \text{ATPase}$** , causing increased intracellular sodium movement and accumulation.



- **Decreased transmembrane exchange of sodium and calcium** leads to increased intracellular calcium acting on contractile proteins.
- All glycosides have **similar pharmacodynamic** properties but **differ in pharmacokinetic properties**. Digitoxin is more lipid soluble and has longer half-life.

Therapeutic uses of cardiac glycosides include:

- Congestive heart failure
 - Atrial fibrillation,
 - Atrial flutter, and
 - Paroxysmal atrial tachycardia.

2\ Bipyridine Derivatives :

- Possess **positive inotropic** and **vasodilator** effects.
- Mechanism of action: **Inhibition of phosphodiesterase, inactivating cyclic AMP.**
- Increase in cAMP.
- Used in heart failure resistant to cardiac glycosides and vasodilators.

3\ Beta-Adrenergic Stimulants :

ex. dopamen and doputamin

- Increase myocardial contractility, increasing cardiac output.
- Positive chronotropic effect minimizes benefits, especially in ischaemic heart disease patients.
- Dobutamine's positive inotropic effect is greater than heart rate, reserved for acute failure or failure refractory to other oral agents.

B. Drugs without positive inotropic effect. These include:

- Diuretics, e.g. hydrochlorothiazide, furosemide
- Vasodilators, e.g. hydralazine, sodium nitroprusside
- Angiotensin converting enzyme inhibitors e.g. captopril, enalapril

Pharmacotherapy of Angina pectoris

- Angina pectoris develops as a result of **an imbalance between the oxygen supply and the oxygen demand of the myocardium.**
- It is a symptom of myocardial ischemia.
- When the increase in coronary blood flow is unable to match the increased oxygen demand, angina develops.
- It has become apparent that spasm of the coronary arteries is important in the production of angin

1\ Organic Nitrates: A Potent Vasodilator

- Used in therapy of angina pectoris for over 100 years.
- Mediates effects through **direct** relaxant action on smooth muscles.
- Mimics vasodilator action of endothelium derived relaxing factor (EDRF), **nitric oxide**.
- Action begins **after 2-3 minutes** when chewed or held under tongue.
- Action duration varies for different nitrates and pharmaceutical preparations.

- Adverse effects include flushing, weakness, dizziness, tachycardia, palpitation, vertigo, sweating, syncope localized burning, and contact dermatitis.
- Therapeutic uses include prophylaxis and treatment of angina pectoris, post myocardial infarction, coronary insufficiency, and acute LVF.

2\ Adrenergic Blocking Agents

- **Exercise** and emotional excitement cause angina by **increasing** heart rate, blood pressure, and myocardial contractility.
- Beta receptor blocking agents **prevent angina by blocking these effects.**
- Common agents include labetalol, atenolol, metoprolol, propranolol **LAMP**.
- Adverse effects include lethargy, fatigue, rash, cold hands and feet, nausea, breathlessness, nightmares, and bronchospasm.
- Other therapeutic uses include hypertension, cardiac arrhythmias, post myocardial infarction, and pheochromocytoma.

3\Calcium Channel Blockers

- Interference with calcium entry into myocardial and vascular smooth muscle.
- Decreases intracellular calcium availability.
- Therapeutic uses include hypertension, acute coronary insufficiency, tachycardia.
- Adverse effects include flushing, nausea/vomiting, headache, ankle swelling, dizziness, constipation.

4. Miscellaneous drugs, e.g. Acetylsalicylic acid

Acetylsalicylic acid (aspirin) at low doses given **intermittently decreases the synthesis of thromboxane A₂ without drastically reducing prostacyclin synthesis**. Thus, at the doses of 75 mg per day it can produce antiplatelet activity and reduce the risk of myocardial infarction in anginal patients.

THANK YOU

A decorative graphic on the right side of the slide, consisting of several overlapping, curved shapes in shades of light blue, yellow, and dark blue, creating a modern, abstract design.