Cardiovasculer Disese part II

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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.

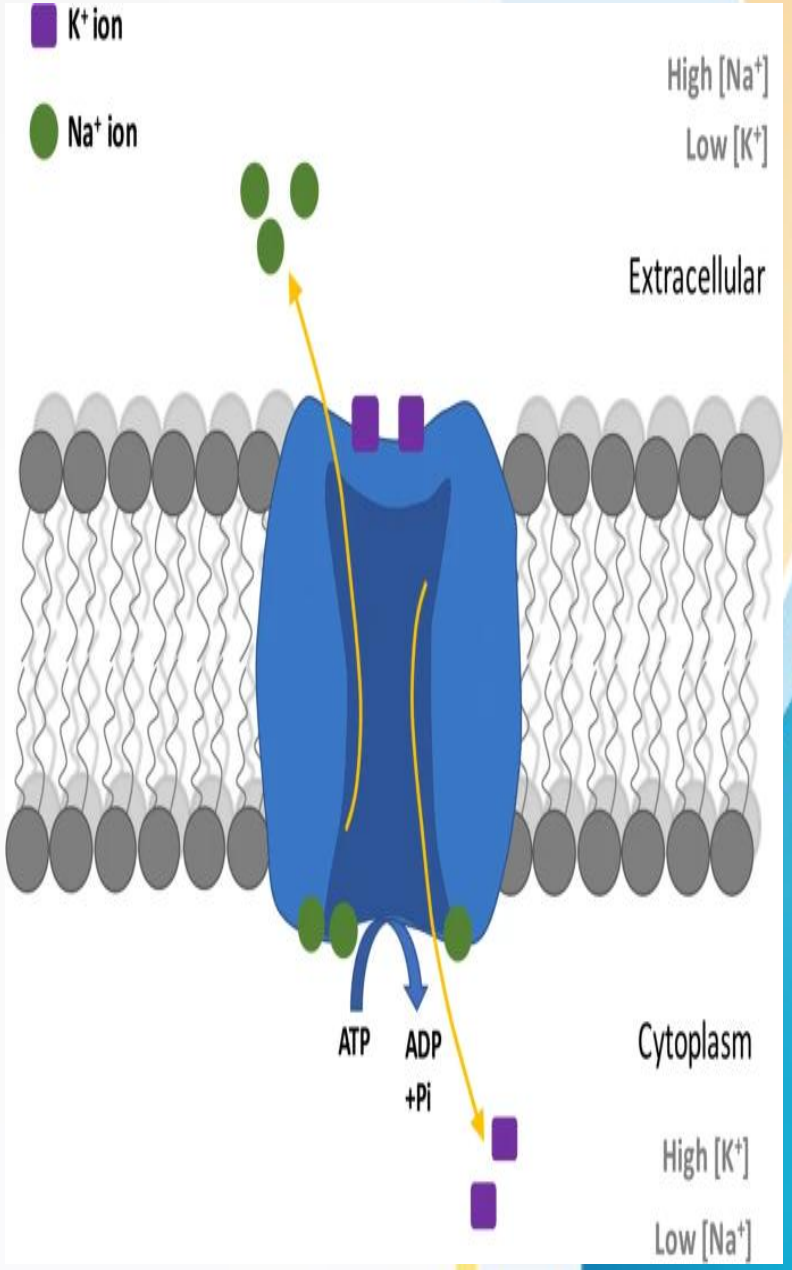
A. Drugs with positive inotropic effect:-

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 Na+ /K+ 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 phophodiesterase, 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 labetolol, atenololmetoprolol, 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 thromboxne A2 without drastically reducing prostacylin 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