

HEART FAILURE



- Heart Failure (HF) is a complex progressive disorder in which the heart is unable to pump sufficient blood to meet the needs of the body
- Main symptoms:
 - ▣ Dyspnea
 - ▣ Fatigue
 - ▣ Fluid retention
- HF is caused by inability of the heart to adequately fill with and/or eject blood
- HF is accompanied by abnormal increases in blood volume and interstitial fluid



- Causes of HF:

- ▣ Arteriosclerotic heart disease

- ▣ Myocardial infarction

- ▣ Hypertensive heart disease

- ▣ Valvular heart disease

- ▣ Congenital heart disease

- ▣ Left systolic dysfunction secondary to coronary artery disease is the most common cause of HF

HF


- Physiologic compensatory mechanisms in HF
 - Chronic activation of the sympathetic nervous system and renin angiotensin-aldosterone system is associated with remodeling of cardiac tissue
 - Loss of myocytes, hypertrophy, fibrosis.

Pharmacological treatment of HF

- Goals of HF therapy
 - ▣ Alleviate symptoms
 - ▣ Slow the disease progression
 - ▣ Improve survival
- Drug classes
 1. Inhibitors of renin-angiotensin system
 2. β -Blockers
 3. Diuretics
 4. Direct vasodilators
 5. Inotropic agents
 6. Aldosterone antagonists

Pharmacological treatment of HF

- Individuals might have one or more of the drug classes used for HF depending on the severity of the disease
- Beneficial effects of HF treatment
 - ▣ Reduction of the load on the heart
 - ▣ Decrease in extracellular volume
 - ▣ Improved cardiac contractility
 - ▣ Slowing the rate of cardiac remodeling

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- Non-pharmacological strategies for HF
 - ▣ Reduction in physical activity
 - ▣ Low dietary intake of sodium

 - Drugs that may exacerbate HF
 - ▣ Nonsteroidal anti-inflammatory drugs
 - ▣ Alcohol

 - ▣ Cardioselective calcium channel blockers like verapamil and diltiazem are contraindicated in heart failure because of their negative inotropic effect

Renin-Angiotensin Aldosterone system

- HF activates the renin-angiotensin system by:
 - ▣ Promoting renin release in response to lower renal perfusion pressure caused by the failing heart
 - ▣ Sympathetic stimulation and activation of β receptors in the kidney leading to renin release
- Consequent to renin release, the potent vasoconstrictor angiotensin II is produced
- The resulting stimulation of Aldosterone release causes salt and water retention increasing the preload and afterload that are characteristic of the failing heart

Inhibitors of the renin angiotensin aldosterone system

- Angiotensin converting enzyme inhibitors
- Angiotensin receptors blockers

Angiotensin converting enzyme inhibitors

- Drugs of choice for HF
- Mechanism of action
 - ▣ Block the enzyme that converts angiotensin I to the potent vasoconstrictor angiotensin II
 - ▣ Cause vasodilation
 - ▣ Decrease aldosterone secretion decreasing sodium and water retention

Angiotensin converting enzymes inhibitors



- Captopril
- Enalapril
- Fosinopril
- Ramipril

Angiotensin converting enzyme inhibitors

- Beneficial effects on heart
 - ▣ Reduce vascular resistance and blood pressure
 - ▣ Increase cardiac output

Angiotensin converting enzymes inhibitors

- Adverse effects
 - ▣ Postural hypotension
 - ▣ Renal insufficiency
 - ▣ Hyperkalemia
 - ▣ Persistent dry cough
 - ▣ Angioedema
- Contraindicated in pregnancy

Angiotensin receptor blockers

- Losartan and valsartan
- Competitive antagonists of angiotensin receptor
- Used for HF in patients who can not tolerate angiotensin converting enzyme inhibitors
- Lower blood pressure
- Adverse effects: similar to ACE inhibitors, but do not cause dry cough and angioedema
- Contraindicated in pregnancy

β -blockers

- β -blockers used in HF
 - ▣ Metoprolol (β 1 antagonist)
 - ▣ Bisoprolol (β 1 antagonist)
 - ▣ Carvediol (blocks α and β)
- Block the changes caused by chronic activation of the sympathetic nervous system
- Decrease heart rate and inhibit the release of renin
- Decrease remodeling of cardiac muscle fibers caused by norepinephrine, reduce hypertrophy and cell death
- Beneficial if HF is accompanied by hypertension in the patient

Diuretics


- Thiazide and loop diuretics
- Hydrochlorothiazide, Furosemide
- Relieve pulmonary congestion and peripheral edema
- Decrease plasma volume and venous return to the heart (preload)
- Can decrease afterload by reducing plasma volume, and so reduce blood pressure
- Side effects: (Loop and Thiazide)
 - ▣ Hypotension, hypokalemia, hyperuricemia

Direct acting vasodilators

- Hydralazine, Isosorbide dinitrate, Isosorbide mononitrate
- Cause vasodilation leading to reduced cardiac preload
- Used if patient is intolerant to ACE inhibitors or β -blockers

Inotropic drugs

- Digoxin, increase cardiac muscle contractility by influencing sodium and calcium flow in the cardiac muscle
 - ▣ Inhibits Na/K ATPase pump, which increases intracellular calcium increasing the force of contractility within myocytes
- Dobutamine (β -agonist)
- Enhance cardiac muscle contractility and thus increase cardiac output
- Digoxin has a narrow therapeutic index (shows a small difference between the therapeutic and toxic doses and can be fatal)

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- Digoxin adverse effects
 - ▣ Arrhythmia
 - ▣ Anorexia, nausea, vomiting
 - ▣ CNS effects headache, fatigue, confusion

Aldosterone antagonists

Spironolactone

Eplerenone

- Mechanism of action
 - ▣ Direct antagonist of aldosterone
 - ▣ Prevents salt retention, myocardial hypertrophy
- Used for the most advanced stages of HF
- Adverse effects
 - ▣ Hyperkalemia
 - ▣ GI disturbances (ulcer)
 - ▣ CNS abnormalities (confusion, lethargy)
 - ▣ Endocrine abnormalities

Order of therapy

