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

- 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 (β1 antagonist)
  - Bisoprolol (β1 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 contractiliy 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)

- 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