Drugs in Heart Failure

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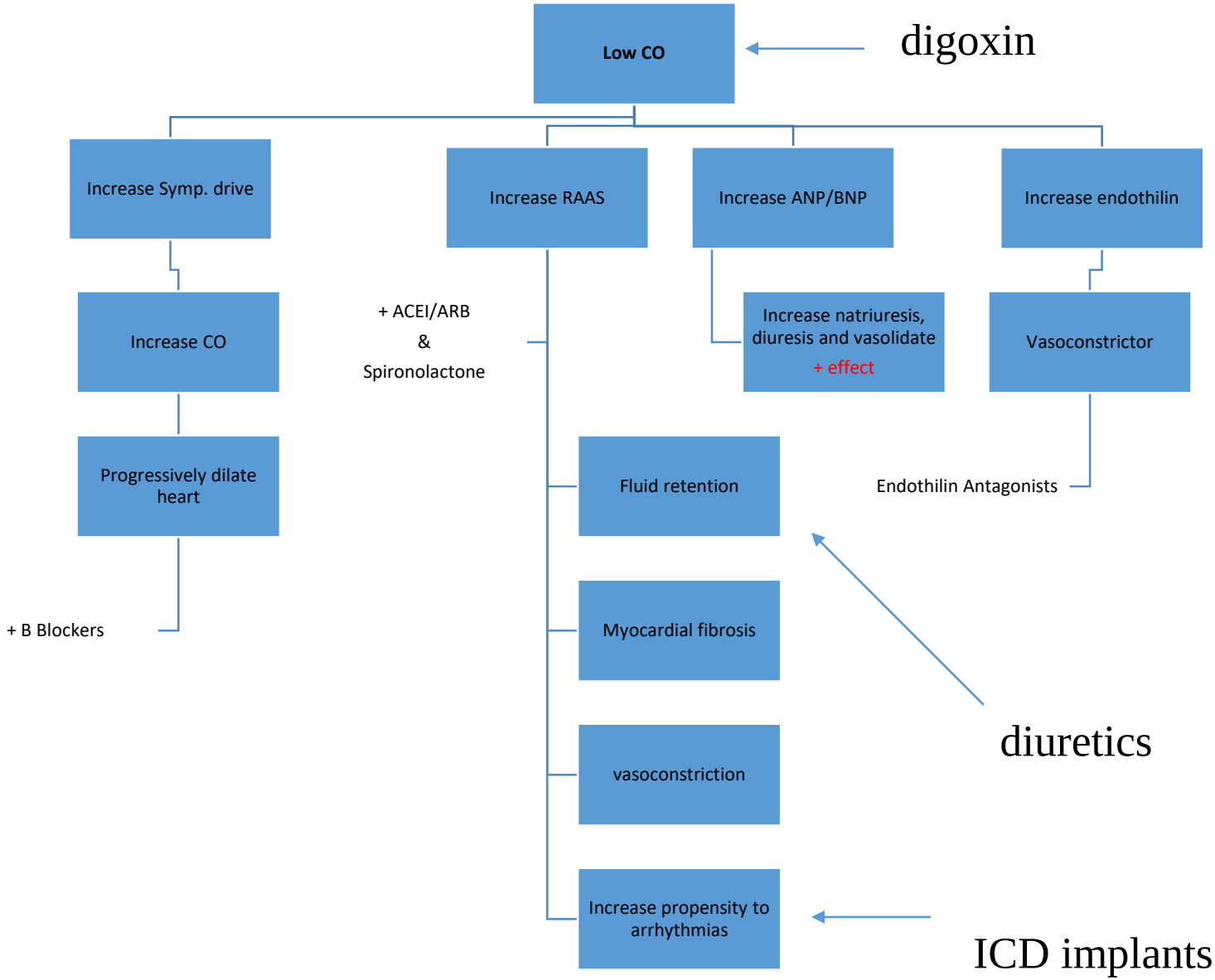
Objectives

- Introduction
- Pathophysiology of HF
- Different drugs used in HF
- Principles of drug usage

What is HF?

- Cardiac output fails to maintain adequate blood supply to other organs to meet their demands
- Classification;
  - Backward failure –
    - JVP elevated
    - Peripheral oedema
    - Hepatomegaly
  - Forward failure –
    - Lethargy, SOB on exertion
    - Features of poor organ failure
      - Renal failure
  - Acute / chronic HF

Pathophysiology of HF



Pathophysiology of HF and drugs

- Initially compensatory (physiological) but later pathological

- Drugs are used for –
  - To improve morbidity (symptomatic benefit)
    - Symptoms of forward failure

      Fatigue, exertional dyspnea
    - Symptoms of backward failure

      SOB due to pulmonary oedema, generalized oedema
  - To improve mortality (survival benefit)

What drugs?

- To improve mortality (survival benefit)
  - **A**CEI
  - ARB
  - **B**eta blockers
  - **Spironolactone** (Aldosterone antagonists)
  - Nitrate + hydralazine
- To improve morbidity (symptomatic benefit)
  - Loop **D**iuretics
  - **D**igoxin
  - Nitrates

❖A, B, D,D,S

ACEI and ARB .....

- Both symptomatic benefit and survival benefit
- Inhibit RAAS

Beta blockers

- Mechanism of action:
  - ➢ Blunting of activated sympathetic nervous system
    - Negative inotropic and chronotropic action
    - Vasoconstriction
  - ➢ Reduce risk of sudden death(via antiarrhythmic effect)

- Clinical uses:

  Not suitable for **unstable** heart failure
  - ➢ Chronic stable heart failure
  - ➢ Asymptomatic heart failure

- Gives survival benefit.

Loop diuretics

Frusemide, Bumetanide

Inhibits Na resorption in the thick Ascending limb of loop of Henle

Increase Na+ and water loss

Reduce preload

venodilataion

reduce preload

Loop diuretics…

- Well absorbed via gut

Exception; oedematous gut

- Onset of action – Oral : 1 hour

  IV : 5-10 mins

- Modes of administration :oral / iv (slow) / iv infusion
- Usual maintenance dose : 40-80mg daily (up to 2g)
- Indication: Symptomatic benefit only, no survival benefit

Loop diuretics ....

Adverse affects

- Hypokalemia, hyponatraemia
- Hypotension
- Transient deafness and tinnitus (with rapid IV & large doses)
- Hyperuricaemia and gout
- Temporary increase in serum cholesterol and TG
- Rashes and photosensitivity - rare

Digoxin

- Cardiac glycoside
- Natural substance from Fox glove plant
- Oleander (Kaneru) also has this
- Increase myocardial contractility

- **Indication:**
  - only in Symptomatic chronic heart failure
  - Supra-ventricular tachyarrhythmias

Digoxin – Mode of action

1. Binds and inhibit Na+ K+ATPase pump intra

⬇

Accumulation of Na+ ions intracellularly

⬇

increase intracellular Ca++ (by NA/Ca pump)

⬇

Inotropic effect

2. Electrical effect on cardiac conduction system
   - Direct effect – reduce refractory time in cardiac cycle
   - Indirect effect – Increase vagal activity and slow AV conduction

Digoxin Pharmacokinetics

- well absorbed orally
- Therefore use IV only in emergencies
- t1/2 long : 36hours
- renal excretion (unchanged), CI in advanced renal failure
- Narrow therapeutic index
- Na/K ATPase pump sensitivity is high in the following situations, hence those patients may be more sensitive to digoxin,
    - Hypokalaemia
    - Hypercalcaemia
    - hypothyroidism

Digoxin contraindications

- Complete heart block
- Second degree AV block
- Supraventricular arrhythmias caused by wolf-Parkinson-white syndrome
- Ventricular tachycardia or fibrillation
- LV outflow tract obstruction

Digoxin adverse effects

- Usually associated with excessive dosage
  - GI disturbance - Nausea, anorexia, diarrhea (earliest symp of toxicity)
  - Disturbance of colour vision eg: xanthopsia
  - Ventricular ectopics (ventricular bigeminy)

- **Any symptom of toxicity →**
  - should do digoxin level, SE and renal function
  - Antidote: IV digoxin binding antibody

- **Toxicity Mx :**
  - Stop digoxin
  - Correct electrolytes
  - Manage arrhythmias accordingly
  - Digoxin AB

Aldosterone antagonists
Spironolactone

* Competitive blocking of aldosterone receptor

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Inhibit Na reabsorption in DCT

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Reduce Na and water retention

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Reduce preload

* Conserves K+ and Mg++ → anti-arrhythmic

Spironolactone cont.

- **Clinical uses :**
  - Symptomatic chronic heart failure

    - symptomatic and survival benefits

    - Add on therapy in patients with **persisting symptoms in spite of optimal treatment** with diuretic, ACEI and beta blocker

    - Target dose 25mg daily
  - Cirrhosis (high doses up to 400mg)

Spironolactone cont.

Adverse effects

- Hyperkalemia
- Gynaecomastia, impotence
- Hypernatremia

Contraindications

- Hyperkalemia
- Hyponatremia
- Renal failure

Nitrates

Veno-dilatation / vaso-dilatation

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Reduce venous return

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Reduce preload

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Relief from congestive features

Nitrates in HF

- Main clinical use is in acute LVF – GTN
- In chronic heart failure - Nitrates + hydralazine
  symptomatic and survival benefit (VHeFT)

HF management summary