Drugs used to treat Congestive Heart Failure (CHF)

BY
Ali Alalawi
Drugs used to treat Congestive Heart Failure (CHF)

- Angiotensin Converting Enzyme Inhibitors.
- Angiotensin II Receptor Antagonists.
- Opening of potassium channels e.g. Hydralazine.
- Release of nitric oxide e.g. Nitroprusside
- B- blockers e.g. Carvedilol.
- Organic nitrates.
- Positive Inotropic Agents.
  - Beta Receptor Agonists e.g. Dopamine.
  - Phosphodiesterase inhibitors e.g. Milrinone
  - Na+,K+-ATPase Inhibitors e.g. digoxin.
Angiotensin Converting Enzyme Inhibitors

Example for this group:

- Benazepril - Metabolized to benazeprilat
- Captopril
- Enalapril - Metabolized to enalaprilat
- Fosinopril - Metabolized to fosinoprilat
- Lisinopril
- Moexipril - Metabolized to moexiprilat
- Quinapril - Metabolized to quinaprilat
- Ramipril - Metabolized to ramiprilat
- Trandolapril - Metabolized to tandolaprilat
- Perindopril - metabolized to perindoprilat
Mecahnism of action:

- **Angiotensinogen**
- **Angiotensin (in active)**
- **Angiotensin II (active)**
- **AT receptor**
- **Aldosterone**
- **Output of sympathetic nervous system**
- **Vasodilation of vascular smooth muscle**
- **Retention of sodium and water**
- **Level of bradykinin**

**Improved cardiac function**
**Angiotensin Converting Enzyme Inhibitors**

- ACE-inhibitors are first line medications in the treatment of heart failure. Numerous clinical trials have shown that these drugs decrease the risk of death, improve outcomes and decrease symptoms of patients with heart failure.

- ACE-inhibitors have been shown to be effective in reducing morbidity and mortality in patients following myocardial infarction.

- ACE-inhibitors are also drugs of first choice in the treatment of hypertension and are especially useful in patients with co-existing heart failure or post MI.
Side effects of ACE inhibitors

- Angioedema
- Hypotension
- Renal insufficiency
- Rash
- Cough
ANGIOTENSIN II RECEPTOR ANTAGONISTS

Example for this group:
- *Losartan*.
- *Valosartan*.
- *Irbesartan*. 
Mecahnis of action:

- Angiotensinogen
- Renin
- Angiotensin Conversion Enzyme
- Angiotensin (in active)
- Angioitesin II (active)
- Output of sympathetic nervous system
- Vasodilation of vascular smooth muscle
- Retension of sodium and water
- Level of bradykinin

Decrease blood pressure
ANGIOTENSIN II RECEPTOR ANTAGONISTS

- AT\(_1\) receptors antagonists are first line agents in the treatment of heart failure. Clinical trials have shown that these drugs decrease the risk, improve outcomes and decrease symptoms of patients with heart failure.

- Similarly, AT\(_1\) receptors antagonists are alternatives to ACE-inhibitors in reducing morbidity and mortality in patients following myocardial infarction.

- AT\(_1\) receptors antagonists are also first line agents in the treatment of hypertension.

- There is no evidence that AT\(_1\) receptors antagonists are superior to ACE-inhibitors. Therefore, the drugs should be considered as alternative choices in treating cardiovascular disease.
Side effects of Angiotensin II Receptors Antagonists

- Fewer side effects have been reported with AT₁ receptors antagonists.
- They less likely cause cough or angioedema.
HYDRALAZINE

- Opening of potassium channels

- An arterial selective vasodilator that works by activation of guanylate cyclase to increase the levels of smooth muscle cGMP.

- The predominant activity is to decrease peripheral vascular resistance.

- In heart failure this decreases the afterload leading to an increase in cardiac output.

- However, when used alone sympathetic reflexes can be activated as a result of the decrease in peripheral vascular resistance resulting in a reflex acceleration of heart rate.
Hydralazine:

- The use of hydralazine has decreased due to the introduction of safer more effective agents such as ACE inhibitors and AT₁ receptor antagonists.

- However, a very recent report has show that a combination of a nitrate and hydralazine had significant benefit when given to African Americans.

- Hydralazine is also used to treat hypertension. However, it is not a drug of first choice nor can it be used as monotherapy due to the reflex tachycardia and increase in fluid retention seen when the drug is used alone.
Side effects of Hydralazine:

- Lupus-like symptoms

- Typical arterial vasodilator side effects, headache, tachycardia. The tachycardia can be blocked by co-administration of beta blockers

- Water and salt retention occur as a result in the fall of blood pressure. This problem can be alleviated by diuretics
Nitroprusside

- A balanced vasodilator that produces its effects by activating guanylate cyclase increasing the smooth muscle levels of cGMP.

- These actions result in a decrease in preload and afterload that ultimately increases cardiac output and decreases pulmonary congestion.

- It is unstable in solution and has an ultra short duration of action.

- The very short duration of action also makes nitroprusside useful in treating hypertensive emergencies.

- Nitroprusside must be reconstituted prior to use and given via infusion.

- It is also light sensitive and solutions must be protected from light.
SODIUM NITROPRUSSIDE

• Nitroprusside is a very potent vasodilator.

• It is used in the acute management of congestive heart failure and hypertensive emergencies.
Side Effects of Sodium Nitroprusside

- Hypotension

- Nitroprusside is metabolized to cyanide and thiocyanate. The body can buffer some of this cyanide with thiosulfate, cysteine or cystine. However, large blood concentrations or prolonged infusions of nitroprusside can overwhelm the ability to buffer the cyanide and increase the risk of cyanide poisoning.
β Blockers:

- Has been traditionally contraindicated in patients with CHF
- Now they are the mainstay in treatment on CHF & may be the only medication that shows substantial improvement in LV function
- In addition to improved LV function, multiple studies show improved survival
- The only contraindication is severe decompensated CHF
Questions