Pharmacotherapy of Congestive Heart Failure

Drugs providing both symptomatic and survival benefit

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NYHA Functional Classification of Heart Failure

- **Class I :** No limitations of physical activity. **Ordinary physical activity** does not cause undue fatigue, palpitation or dyspnea **(asymptomatic LV dysfunction)**
- **Class II :** Slight limitation of physical activity. **Ordinary physical activity** results in fatigue, palpitation, dyspnea or angina pectoris **(mild CHF)**
- **Class III :** Marked limitation of physical activity. **Less than ordinary activity** leads to symptoms **(moderate CHF)**
- **Class IV** : Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest **(severe CHF)**

Two approaches in pharmacotherapy of CHF

1. **Drugs which provide only symptomatic benefits**: (Overcome low output, overcome congestive symptoms and restore cardiac performance).

E.g. Furosemide, Digoxin, Dobutamine etc.,

2. **Drugs with both symptomatic and survival benefits: (**In addition to above effects, they prevent the disease progression)

E.g. Angiotensin Converting Enzyme Inhibitors (ACEIs), Angiotensin Receptor Blockers (ARBs), Beta-adrenergic receptor blockers and Aldosterone antagonists

Drugs with both symptomatic and survival benefits

1. Angiotensin Converting Enzyme Inhibitors (ACEIs)
2. Angiotensin Receptor Blockers (ARBs)
3. Beta-adrenergic receptor blockers
4. Aldosterone antagonists

Angiotensin Converting Enzyme Inhibitors (ACEIs)

Ramipril, Lisinopril, Enalapril

Why are they explained first?

Pathophysiological role of RAAS in CHF

- Initially contributes to perfusion of major organs by

1. Vasoconstriction (Angiotensin 2)
2. Fluid retention (Angiotensin 2 and aldosterone)

- Angiotensin 2 contributes to symptoms by

1. Vasoconstriction – venous constriction and arteriolar constriction
2. Aldosterone production – retention of sodium and water

Pathophysiological role of RAAS in CHF (continued)

- Angiotensin 2 contributes to progression of disease by

1. Ventricular hypertrophy
2. Ventricular remodelling
3. Myocyte apoptosis
4. Myocyte fibrosis
5. Intercellular matrix changes

Role of ACEIs in CHF (symptomatic benefits)

- Symptomatic benefits or haemodynamic benefits

1. Reduce the load on the heart
2. Improves the stroke volume
3. Renal perfusion improves: diuresis occurs
4. Prevents fluid retention: by reducing aldosterone

Role of ACEIs in CHF (survival benefits)

- Survival benefit ?
- Robust multi-centric trials ---> interfere with progression of Left Ventricular Systolic dysfunction
- Reduce episodes of decompensation, sudden death and MI

Role of ACEIs in CHF (survival benefits continued)

- Retard or reverse

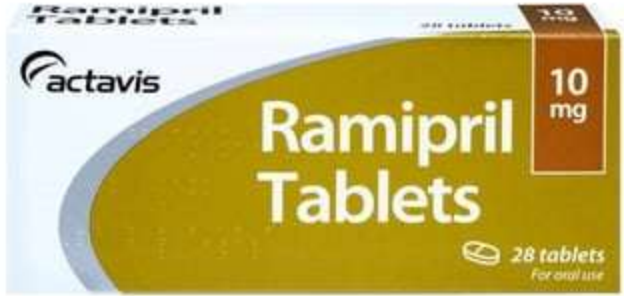
1. Left Ventricular Hypertrophy (LVH)
2. Ventricular remodelling
3. Myocyte apoptosis
4. Myocardial fibrosis
5. Intercellular matrix deposition

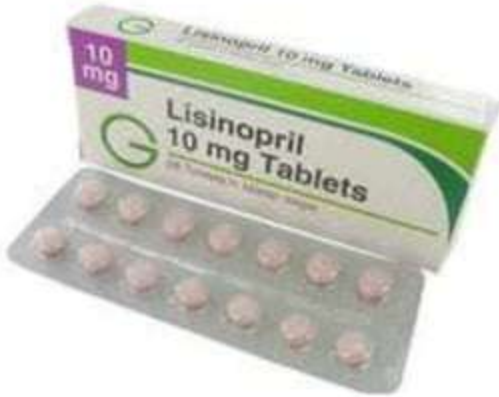
Role of ACEIs in the pharmacotherapy of CHF

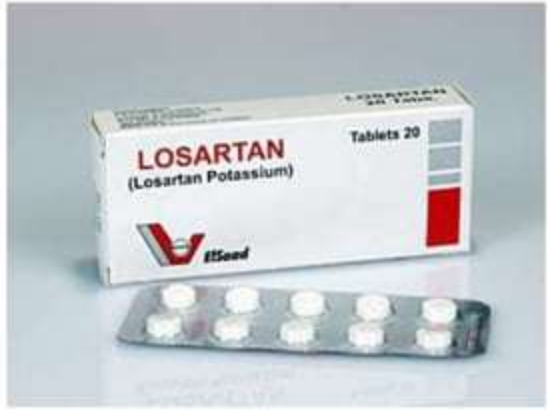
- First line drug in CHF
- Afford both symptomatic and survival benefits
- Can be used for any class of CHF (Class I to IV of NYHA)
- Improve the functional class of CHF

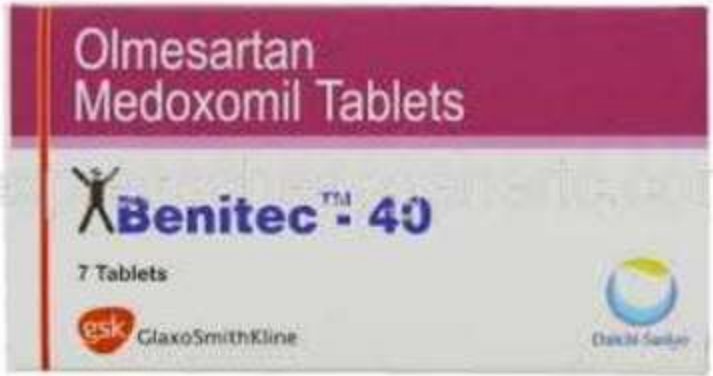
Role of ACEIs in the pharmacotherapy of CHF (continued)

- Can be used in any grade of CHF (asymptomatic, mild, moderate and severe)
- Only class beneficial in asymptomatic heart failure
- Start with a low dose
- Titrate to the maximal tolerated dose


Ramipril Tablets
actavis
10 mg
Ramipril Tablets
28 tablets
For oral use


10
mg
Lisinopril
10 mg Tablets


LOSARTAN
(Losartan Potassium)
Tablets 20
ElSaad


Olmesartan
Medoxomil Tablets
Benitec™ - 40
7 Tablets
GlaxoSmithKline

Beta-adrenergic receptor blockers

Why second?

Bisoprolol, Carvedilol, Metoprolol, Nebivolol

Pathophysiological role of sympathetic overactivity in CHF

- Initially aids in maintaining perfusion

- Later contributes to progression of disease by

1. Enhancing ventricular stress
2. Myocyte apoptosis
3. Ventricular remodelling

Can also cause dangerous arrhythmias

Role of Beta blockers in CHF: Hemodynamic benefits of Beta blockers

- Initially reduce cardiac contractility
- Ejection fraction (EF) increases in a couple of months
- EF improves with gradual increase in the dose
- Hemodynamic benefits remain consistent

Role of Beta blockers in CHF : Disease modifying actions (Survival benefits)

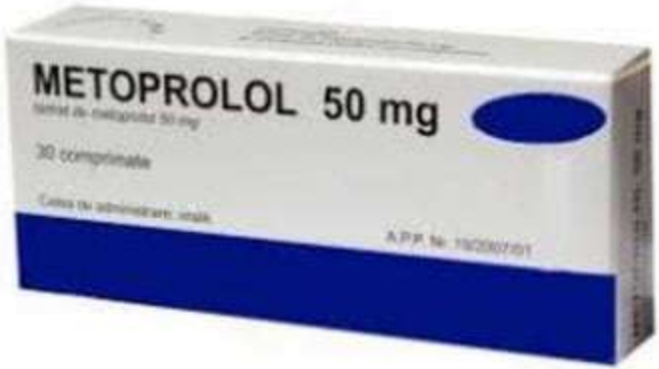
- Antagonize harmful sympathetic over activity on heart

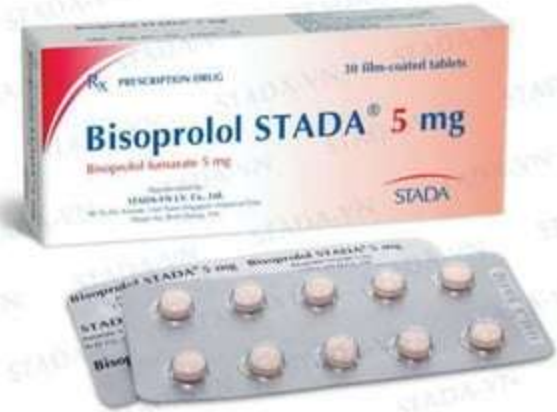
- Prevent

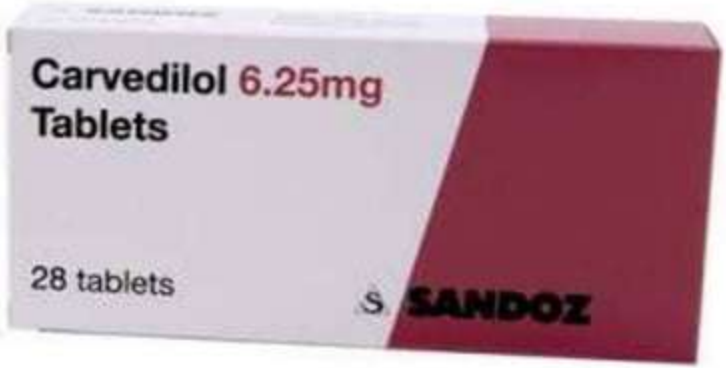
1. Ventricular stress enhancing effect of catecholamines
2. Myocyte apoptosis
3. Ventricular remodelling
4. Arrhythmias

Role of Beta blockers in pharmacotherapy of CHF

- Indicated as add-on to ACEIs in mild to moderate CHF
- Not indicated in asymptomatic CHF
- Contraindicated in symptomatic/decompensated CHF
- Start with low dose
- Some patients worsen with Beta blockers – so withdraw them


METOPROLOL 50 mg
30 comprimate


Rx PRESCRIPTION DRUG
30 film-coated tablets
Bisoprolol STADA® 5 mg
Bisoprolol fumarate 5 mg
STADA


Carvedilol 6.25mg
Tablets
28 tablets
SANDOZ

Aldosterone antagonists

Spironolactone and Epleronone

Pathophysiological role of Aldosterone in CHF

- Increases Sodium and water retention, hence increases preload
- Fibroblast proliferation in myocardium
- Fibrotic transformation of myocardium
- Ventricular remodelling
- Contributes to symptoms and progression of disease
- Hypokalemia and hypomagnesemia can cause cardiac arrhythmias

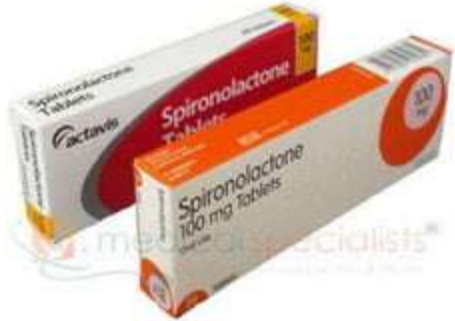
Role of aldosterone antagonists in CHF

- Provide symptomatic and disease modifying benefits
- Indicated in mild to moderate HF as add-on to ACEIs + Beta blockers
- Randomized trials show evidence of survival benefit over and above that provided by ACEIs + Beta blockers

Role of aldosterone antagonists in CHF

- Spironolactone may cause gynecomastia in some patients where it may be replaced by Epleronone

- Doses higher than the recommended doses can be dangerous because of hyperkalemia



Images shown for illustration purpose only
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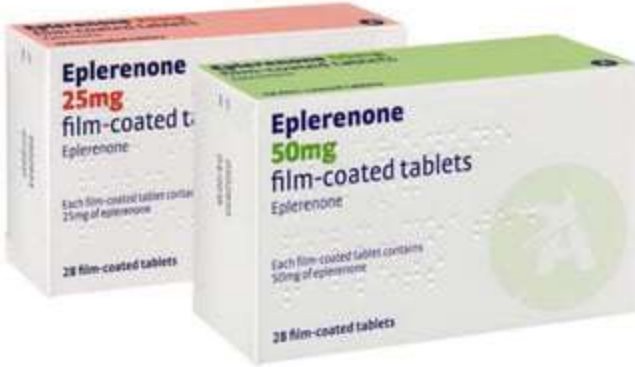
Eplerenone
25mg
film-coated t
Eplerenone
28 film-coated tablets
Eplerenone
50mg
film-coated tablets
Eplerenone
Each film-coated tablet contains
50mg of eplerenone
28 film-coated tablets

Thank you

Stay healthy