- first line therapy of hypertension

A) Diuretics: mild and moderate HPT alone, and severe one with **vasodilators** and sympathoplegic

1- thiazide: initially-> low co and bv + high pbr

6-8w -> normal co and bv + low pbr

Hypercalcemia

Hazardous in persons taking Digitals, chronic arrythmias.

2-loop diuretics: furosemide, ethacrynic acid, bumetanide

AM and lunch time

Hypocalcemia

Loop diuretics produce greater diuretics but weaker antihypertensive than thiazide.

B) B- adrenergic blocking agents:

A.E: congestive heart failure, hypoglycemia, asthma

1- metoprolol, atenolol: widely used selective antihypertensive

2- pindolol, acebutolol, penbutolol: partial agonist -> decrease vr

3- labetalol, carvedilol: pheochromocytoma

4- esmolol: short half-life-> emergencies hypertension

Sudden withdrawal -> rebound hypertension

C) ACE inhibitors: prils

! Pregnancy

when B-blockers or diuretics are contraindicated or ineffective.

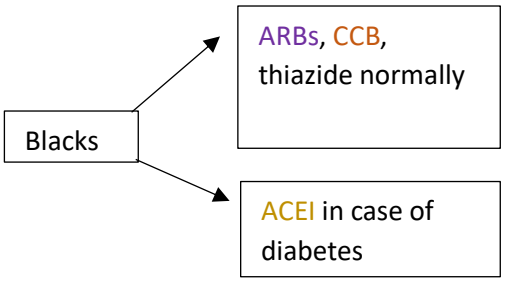
-reduce pbr only by block angiotensin II synthesis (block bradykinin breakdown)

Spironolactone is contraindicated.

-dry cough + angioedema + first dose syncope

✓ chronic kidney disease, diabetes, heart failure

contraindicated in the case of bilateral renal stenosis only.



D) ARBs: sartans

Lower A.E resulting from bradykinin, but can cause fatal renal toxicity, reduce aldosterone, increase k accumulation.

- in HF we use ACEI with ARBs

E) calcium channels blockers: vasodilation effect

✓ Angina, diabetes

1- nifedipine: selective toward vessels, may increase HR

2- diltiazem: moderate chronotropic and inotropic effect (better in HF patients)

3- verapamil: severe // // (constipation)

- Amlodipine: gingival hyperplasia

-nimodipine: cross BBB -> headache

F) selective a1 blockers: sins

chronic hypertension+ benign prostatic hyperplasia

- second line therapy of hypertension:

G) centrally acting adrenergic drugs:

1- clonidine: a2 agonist, mild-moderate hypertension with renal disease

- water and Na retention -> combination with diuretics

- lower HR + CO

- rebound hypertension (life-threating hypertensive crisis)

2- methyldopa: a2 agonist

Decrease PR, no decrease in CO -> variable in treating hypertension with renal insufficiency.

✓ during pregnancy

-doesn't cause water retention

H) vasodilator:

1- Activation of Calcium like: Hydralazine -> moderately severe hypertension

Arteriodilation/ S.E: Lupus-like syndrome

Hydralazine –> B blocker + Thiazide.

Minoxidil -> B blocker + loop diuretic

2- More efflux of K+ like: Minoxidil, Diazoxide

Arteriodilation/ hypertrichosis

best in male patients with renal insufficiency.

3- producers of NO like: Nitroprusside

IV used in emergency hypertension.

Both veins and arteries/ thiocyanosis

for titration purposes, the best drug is nitroprusside (with a short half-life), followed by fenoldopam, and lastly labetalol (with a long half-life).

4- Agonist for dopamine 1 receptors: Fenoldopam

arterial dilation

-drugs for angina:

1) organic nitrates: rapid reduction in o2 demand -> by relaxing coronary arteries

isosorbide dinitrate, isosorbide mononitrate (avoid first pass effect), and Nitroglycerine (dilation of L.vains -> orthostatic hypotension and syncope)

can cause reflex tachycardia -> so give B-blockers.

A.E: headache

- to restore sensitivity -> nitrate free intervals

2) B- adrenergic blocking agents: first line stable angina

-decrease o2 consumption

- stable +unstable + MI

Contraindicated: v. angina, asthma, bradycardia

3) calcium channel blockers:

Nifedipine: v. angina

Verapamil+ diltiazem: decrease o2 demand by slowing HR

Has antiarrhythmic activity

-drugs of heart failure:

1) ACEI: sym or asym

The more hypertrophy =the worse the HF

-decrease VR-> increase HR

-decrease angiotensin II

- all stages of LVF

2) B- adrenergic blocking agents: low doses

-Bisoprolol, carvedilol or nebivolol

-chronic heart failure due to left ventricular systolic dysfunction.

Dobutamine: B1 adrenergic agonist/ increase inotropic activity for acute HF

We give noradrenaline to inhibit its B2 effect when given IV

3) Diuretics: decrease symptoms by decrease extracellular volume and decrease venous return

Thiazide-> only mild

- We are afraid of hyponatremia

Combined with ACEI + ARBs+ spironolactone to help in hypokalemia.

4) aldosterone antagonist:

Spironolactone-> prevent NA and water retention + decrease K secretion -> hyperkalemia.

-moderate to severe HF

-CNS effects

-eplerenone in case of gynecomastia

5) inotropic drugs (digitalis):

-Increase inotropic and decrease chronotropic

- low therapeutic index

digoxin: competitive with K -> increase intracellular Ca / increase vagus activity.

- in severe LVSF -orally -emergency - low K -> intoxication

A.E: xanthopsia

combination of hydralazine and nitrate is reasonable for patients with reduced LVEF.

Newer antianginal drugs:

1) Ivabradine: selectively inhibits the If current-> Decreases O2 demand

- used in HF with B blockers

A.E: luminous phenomena (due to blockage of Ih)/ bradycardia / blurred vision / headache

2) Ranolazine: selectively inhibits the late sodium influx in the myocardium

-targets the consequences of ischemia

-slightly increased QT interval

-contraindicated: severe liver disease.

3) Trimetazidine: switches the cardiac energy metabolism from fatty acid oxidation to glucose oxidation by Inhibition of the reduction of (ATP)

-causes symptoms of Parkinsonism/ restless leg syndrome

4) Nicorandil: has two functioning parts, (it's a nitrate like drug with positive K+ channel (ATP) effect)

A.E: gastrointestinal, skin and mucosal ulcerations