S12: Antihypertensives

BP = PVR × C.O.; C.O. = SV × HR

if alter just 1 (or multiple) = ↔ BP

∴ use these as targets

⇒ must know which one is driving the HTN in your patient

⇒ ↕ outflow / centrally Acting

⇒ Arterioles } Dilation / constriction

⇒ Venules

⇒ Diuresis (loss of Na^+ = loss of H_2O) ↓ volume

⇒ cardiac output (C.O.) → chrono/inotropy drugs

Main classes

β-blockers (↓ C.O.)

Centrally Acting Drugs (↓ ↕)

CCB (Calcium channel Blockers) (vasodilating Fx + ↓ C.O.)

ACE-i (vasodilating + Renal Fx) }

ARB (vasodilating + Renal Fx) }

Diuretics

∴ Thiazide

∴ Loop

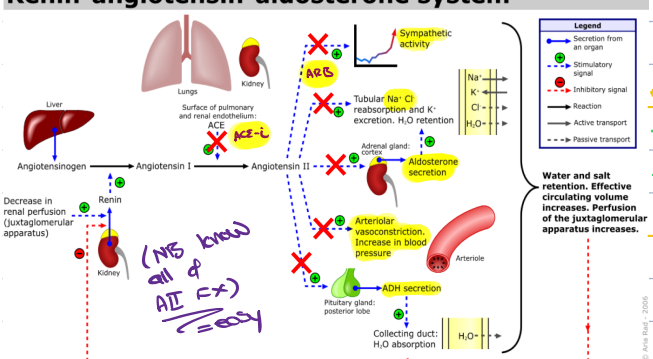
∴ K^+ sparing (Aldosterone Antagonists) } Renal Induce H_2O loss

ACE-i & ARB → (↓ RAAS)

MOA → ACE-i (ACE Enzyme inhibition)

→ ARB (R. Blocker = no Fx)

Renin-angiotensin-aldosterone system



(NB know all of AII Fx) = easy

⇒ ACE-i → Enalapril, Perindopril } Enzyme inhibition

⇒ ARB → Losartan, Valsartan } R. Inhibition

NB Hypotension = Risk for all Antihypertensives

⇒ overall ACE-i & ARB has the same Fx on the RAAS system. ↳ induce diuresis

↳ Relax aa. in PVS

[NB Renoprotective Fx of ARB / ACE-i]

↳ AII constricts Efferent arteriole in Glomerulus = ↑ Glomerular pressure

⇒ ACE-i & ARB oppose this constriction = Renoprotective

∴ Good for DM & HTN (↓ Abnormal protein leaking) → Bad sign of kidney disease

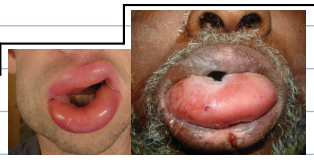
Adverse Fx of ARB & ACE-i

ACE-i → Dry cough | Angioedema | Hyperkalemia

ARB → Hyperkalemia (↑ K^+)

↓ ECG d's (T-wave)

Bradykinin = also broken down by ACE-Enzyme ∴ if inhibit = accumulates = Dry cough + Angioedema (vasodilation)



↳ Lip + tongue swelling

β-blockers (βb)

Oppose & Stimulation of the Heart

(β_1 | β_2 | β_3 R.)

⇒ negative chronotropy

⇒ negative inotropy ↓ C.O. [Loop, Henle]

MOA: Bind R. = prevent R Stimulation

↳ slows Automaticity of SA node

↳ ↑ Diastolic time = Ventricle workload ↓

↳ "cardioselective"

β-blockers [prefer use β_1 selective]

Atenolol (β_1 selective)

Propranolol (non-selective)

Carvedilol (β & K blocking)

↳ More used in Heart failure patients.

Adverse Fx: (most common)

[Bronchoconstriction & fatigue]

cold extremities / dyslipidaemia

have L type, T type, N type

CCB: Calcium channel Blocker:

MOA: Bind L-type Ca^{2+} channels

(block Ca^{2+} entry into cells) more on aa. side

= Relax smooth muscle (↓ PVR)

= Slow cardiac conduction: ↓ Rate

: ↓ contractility

↳ overall ↓ Myocardial O_2 Demand

Drugs (2 classes)

Dihydropyridines (act only on vasculature)

→ Amlodipine

→ Nifedipine

Non-Dihydropyridines (act on PVR & ♡)

→ Verapamil

→ Diltiazem

CCB Adverse Fx

Ankle oedema ↓

Headache } Dilation of vessels

Flushing

Diuretics

3 classes: DCT (reaches Max efficacy)

Thiazide diuretics (low ceiling diuretics)

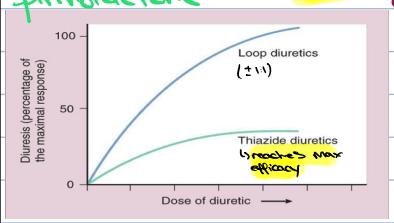
Hydrochlorothiazide (HCTZ)

Loop Diuretics (High-ceiling diuretics)

Furosemide → Has vasodilatory Fx too (specific to furosemide)

Aldosterone Antagonists (K^+ sparing)

Spironolactone (collecting Duct)



Adverse Fx:

Thiazide Diuretics (HCTZ)

↳ Hypokalemia

↳ Hyperuricaemia = (Gout)

↳ Glucose intolerance

↳ (DM ∓ use HCTZ)

[↑ furosemide]

Loop Diuretics:

Hypokalemia (more severe)

Hypocalcaemia & Hypomagnesaemia } (loss Ca^{2+} / Mg^{2+})

Ototoxicity (Hearing)

Aldosterone Antagonists:

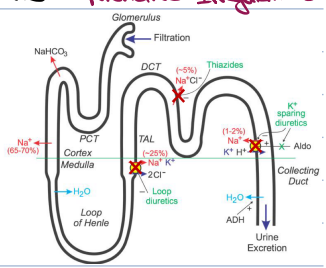
Hyperkalemia (K^+ sparing)

Oestrogen-like Fx

↳ male = Erectile dysfunction = Gynaecomastia

↳ female = Menstrual Irregularities

Aldosterone = ↑ Fibrosis = ∴ Antag = ↓ Fibrosis



Stepwise Approach (EDM)

1) Lifestyle modifications → most NB step!

2) Low dose HCTZ

3) Low dose HCTZ + ACE-i or CCB

4) Low dose HCTZ + ACE-i + CCB

5) Low dose HCTZ + ACE-i + CCB + β-blocker

NB only give ARB if intolerant to ACE-i - NB

Compelling Indications:

Medicine treatment choices with compelling indications

Compelling indications	Medicine class
Angina	β -blocker Calcium channel blocker
Post myocardial infarction	β -blocker ACE-inhibitor
Heart failure	ACE-inhibitor Carvedilol Spironolactone Hydrochlorothiazide or furosemide
Left ventricular hypertrophy	ACE-inhibitor
Stroke	Hydrochlorothiazide Calcium channel blocker
Diabetes type 1 or 2 with/without evidence of microalbuminuria or proteinuria	ACE-inhibitor, usually in combination with a diuretic
Chronic kidney disease	ACE-inhibitor, usually in combination with a diuretic
Isolated systolic hypertension	Hydrochlorothiazide Calcium channel blocker
Pregnancy	See Chapter: Obstetrics.