Sympatholytic drug (adrenergic antagonist)

α – receptor blocker:

blockade of α-R →

↓ sympathetic tone on BV →

↓ peripheral resistance →

↓ BP → ↑ HR

1) non selective α-blocker

* **Phenoxybenzamine**

-covalent bond, metabolite is active form

- Block α1(BV)& pre synaptic α2 in heart producing ↑HR (β1)

So it ↓BP but ↑HR

So clinically not used in HT

- used in pheochromocytoma (catecholamine-secreting tumor in adrenal medulla)

-in pre-operation to prevent HT crises & in its management

-Reynaud's diseases

SE:

- postural hypotension

-nasal congestion

-tachycardia & arrhythmia

Due to baroR & block α2 pre synaptic R

-male sexual dysfunction

*Phentolamine:competitive

-used to terminate local anesthesia

-cause postural hypotension

-cause tachycardia (baroR) &
block α2 pre synaptic R

-In pheochromocytoma

2) selective α-blocker

Prazosin ,Terazosin ,Doxazosin
Tamsulosin& Alfuzosin

- competitive blocker of **α-1** R
- P,Te,D used in treatment of hypertension

(because relax sm of artery and veins)

-Tam & A treatment of benign prostatic hyperplasia (BPH)

SE:

-nasal congestion

-exag post hypoT in 1st dose (1/3 or in bed time)

-orthostatic hypotension

-sever HypoT if prazosin used with diuretic & β blockers

-sexual dysfunction

NOTE: Finasteride, dutasteride

inhibit 5 a-reductase then prevent conversion of testosterone to di hydroT

So they used in BPH

yohimbine

-selective α2 blocker

-act centrally ,it increase sympathetic outflow to the periphery

-not used in CNS & CVS disorder

Because it ST them

-used in sexual dysfunction

β - adrenergic blocker (comp)

1-selective or non selective antagonist

2-differ in intrinsic sympathomimetic activity (ISA) & in kinetics.

3- β- blocker not induce postural HypoT (because α R stay active)

Uses:

- angina , arrhythmia , MI , glaucoma , prophylaxis of migraine, CHF,

β- blocker without ISA(pure antag)

A- non-selective β- blocker:

* Propranolol(anderal)

-sustained release prparation

- -ve inotropic & chronotropic eff
-depress AV & SA node

both cause Bradycardia & ↓CO
and ↓ O2 demand

So used in angina

Prepheral vasoconstriction:

-prevent β2 mediated vasodilation

-↓CO → ↓BP → reflex vasoconstr

→↓ preph blood flow (kidney)→

Na retention ↓

No post hypoT (preph resis not affe

Other:

-blocking β2 in lung

-↓glycogenolysis & glucagons sec

I:

-MI

-Angina pectoris

-hyperthyroidism

-glaucoma↓ production of humor

-prophylaxis migraine headache

-hypertension by↓ CO, ↓ sympathetic outflow centrally

Adverse effect:

-bronchoconstriction

-arrhythmia prevented by withd rawell gradually

-sexual impairment (reasons not clear)

-hypoglycemia

CI: Asthma and COPD

DIA:

Cimetidine , furosemide , chlorpromazine enzyme inhibitor Increase its antihypertensive effect

Barbiturate , phenytoin , rifampin are enzyme inducer so decrease its effect

*Timolol and Nadolol

- they potent than propranolol

-Timolol orally and ophthalmic

-Nadolol given orally

- Timolol reduce aqueous humor in eye

-used glaucoma

-in systemic hypertension.

B- Selective β- blocker:

Atenolol (tenormine), Metoprolol , Esmolol , Betaxolol

- all are cardio selective β1 blockers

-block β1 R at dose 50 time less than needs for blocking β2 R

Uses:

- hypertension are useful in :

*hypertensive patients with impaired pulmonary function

*diabetic hypertensive patients who are receiving insuline or oral hypoglycemic agents.

2) β- blocker with ISA

(partial agonist)

* **selective : Acebutolol**

-weakly **ST β1**

-prevent binding of EP & NOR EP on main R

So decrease rat & CO

-used in hypertension

***non selective : Pindolol**

-β1,β2

- used in hypertension

-both drug ↓disturbances of lipid and carbohydrate metabolism

So can be used in diabetic

-they not used in arrhythmia due to its partial agonist effect

β- blocker with α1-blocking eff

Labetalol and carvedilol

-produce prepheral vasodilation

↓ BP

-used in treatment of emergency hypertension

-labetalol used in elderly HT or black HT
(whom with increased Preph vasc resis)
-alternate methyldopa in pregnancy HT
-in hypertensive emergencies

- Carvedilol decrease lipid peroxidation and vascular thickening in HF
- in hypertensive emergencies

Reserpine

-alkaloid

-block Mg/ATPase

-prevent storage of dopamine

-decrease NE release

Slow onset, long duration-