**Sympatholytic drug (adrenergic antagonist):**

- **α – receptor blocker:**
  
  - Blockade of α-R → ↓ sympathetic tone on BV → ↓ peripheral resistance → ↑ BP, HR

1) **non selective α-blockers:**

- *Phenoxybenzamine*
  
  - Produce covalent bond with α-1 post synaptic and α-2 pre-synaptic R

  **Effect:**
  
  - CVS: increase HR
  - Used in treatment of pheochromocytoma (catecholamine-secreting tumor in adrenal medulla)
  - In pre-operation to prevent hypertensive crises
  - Raynaud's diseases

  **SE:**
  
  - Postural hypotension
  - Nasal congestion
  - Tachycardia & arrhythmia
  - Male sexual dysfunction

- *Phentolamine:*
  
  - Used to terminate local anesthesia
  - Cause postural hypotension
  - Cause tachycardia by blocking α-2 of cardiac sympathetic nerve.

2) **selective α-blocker**

  **Include:**
  
  - Prazosin, Terazosin, Doxazosin & Tamsulosin
    
    - Competitive blocker of α-1 R
    - Used in treatment of hypertension (because relax sm of artery and veins)
    - Treatment of benign prostatic hyperplasia
    - Used in combination with diuretics (return Na & H2O)
    - Doxazosin longest duration, excreted by intestine

  **SE:**
  
  - Nasal congestion
  - Orthostatic hypotension
β - adrenergic blocker
- these drugs are selective or non-selective antagonist
- they differ in intrinsic sympathomimetic activity (ISA) (in CNS effects) & in kinetics.
  - β-blocker not induce postural hypotension (although it lower BP) because α-R stay active.
  - these drugs used in treatment of angina, C. arrhythmia, myocardial infarction (MI), glaucoma, prophylaxis of migraine headache and in hyperthyroidism.

1) β-blocker without ISA (pure antagonist)
A- non-selective β-blocker:

* Propranolol (anderal)
  - prototype, given orally, iv
  - (-ve inotropic & chronotropic effect.
    - depress AV & SA node } Bradycardia & decrease CO and O2 demand decrease
  - decrease BP so decrease blood flow then increase Na+ retention
  - prevent β2-mediated vasodilatation
  - blocking β2 in lung leading to bronchial smooth contraction
  - decrease glycogenolysis
  - decrease glucagon secretion

CI:
Asthma and COPD

SE:
Insomnia, bradycardia, bronchospasm, sexual impairment, arrhythmia in sudden stop of drug.

DIA:
Cimetidine, furosemide, chlorpromazine, they interfere with its metabolism so with its antihypertensive effect.
Barbiturate, phenytoin, rifampin are enzyme inducer so decrease its effect

I:
-MI
-Angina pectoris
-hyperthyroidism
-glaucoma
-migraine
-hypertension

*Timolol and Nadolol
- they potent than propranolol
- Timolol orally and ophthalmic , Nadolol given orally
- Timolol reduce aqueous humor in eye
- used in treatment of open angle glaucoma
- in systemic treatment of 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
- Esmolol short acting, iv, used in acute arrhythmia during surgery

Uses:
- hypertension are useful in:
  * hypertensive patients with impaired pulmonary function
  * diabetic hypertensive patients who are receiving insuline or oral hypoglycemic agents.
- Ischemic heart diseases

2) β- blocker with ISA (partial agonist)

* selective:

Acebutolol
  - β1 selective blocker, partial agonist
  - used in hypertension and ventricular arrhythmia

* non selective:

Pindolol
  - partial agonist
  - both used in hypertension
  - both drug decrease disturbances of lipid and carbohydrate metabolism

**β- blocker with α1-blocking effect.**

Labetalol and carvedilol
- produce prepheral vasodilation so decrease BP
  - used in treatment of emergency hypertension