**Adrenergic Antagonists**

* The adrenergic antagonists cause direct blocked of adrenergic receptors.
* The adrenergic antagonists display a high degree of receptor specificity. Because this specificity, the adrenergic-blocking agents can be neatly divided into two major groups:

1. Alpha- adrenergic blocking agents (drugs that produce selective blocked of alpha-adrenergic receptors)
2. Beta- adrenergic blocking agents (drugs that produce selective blocked of beta receptors)

Only six alpha-adrenergic antagonist are employed clinically. Because the alpha blockers often cause postural hypotension.

Therapeutic uses for these drugs are limited.

* The alpha-adrenergic blocking agents can be subdivided into two groups.
* One sub-group- the nonselective alpha-blocking agents contains drugs that block alpha₁ and alpha₂ receptors.
* Phentolamine is the prototype for this group.
* The second subgroup represented by prazosin, contains drugs that produce selective alpha₁ blocked.

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| **Category** | **Drugs** | **Receptor Blocked** |
| Alpha-adrenergic  blocking agents | Phetolamins  Phenoxy benzamine  Doxazosin  Prazosin  Terazoin  Tamsulosin | α₁ , α₂  α₁ , α₂  α₁  α₁  α₁  α₁ |
| Beta-adrenergic  Blocking agents | Carteolol  Carvedilol\*  Labetalol  Timolol  Sotalol  Atenalol  Metoprolol  Betaxolol  Acebutolol | β₁ , β₂  β₁ , β₂ (also α₁)  β₁ , β₂ (also α₁)  β₁ , β₂  β₁ , β₂  β₁  β₁  β₁  β₁ |

**Prazosin:**

Actions and uses: Prazosin (minipress) is a competitive antagonist that produces selective blocked of alpha₁- adrenergic receptors.

By blocking α₁ receptors, prazosin can cause dilation of arterioles and veins.

The principal indication of prazosin is hyper tension.The drugs can also decrease symproms of BPH(Benign prostatic hyperplasia)

* Pharmacokinetics:

Prazosin is administered orally.

The drug undergoes extensive hepatic metabolism followed by excretion in the bile.

The half-life is 2 to 3 hours.

* Adverse effects :

Blocked of alpha₁ receptors can cause orthostatic hypotension, reflex tachycardia, inhibition of ejaculation and nasal congestion.

* Preparotions, Dosage, and administration:

Prazosin hydrochloride (minipress) is available in capsules (1, 2, and 5mg) for oral use.

The initial adult dosage for essential hypertension is 1mg taken 2 or 3 times a day.

**Terazosin:**

* Action and uses:

like Prazosin, Terazosin (Hytrin) is a selective competitive antagonist at alpha₁-adrenergic receptors.

The drug is approved for hypertension and BPH (Benign Prostatic Hyperplasia)

* Pharmacokinetics:

Terazosin is administered orally. Terazosin undergo hepatic metablolism followed by excretion in the bile and urine.

Adverse Effects:

like prazosin.

* Preparation, Dosagem and administration:

Terazosin (Hytrin) is available in tablets and capsules (1, 2, 5, and 10mg) for oral use.

Antihypertensive therapy is initiated with a 1-mg dose.

Dosage can be gradually increased as needed and tolerated.

**Doxazosin:**

* Actions and uses: Doxazosin (cardura) is a selective, competitive inhibitor of alpha₁-adrenergic receptors. The drug is indicated for hypertension and BPH.
* Pharmacokinetics: Doxazosin is administered orally. The drug has a prolonged half-life (22hours). Doxazosin undergoes extensive hepatic metabloism followed by biliary excretion.
* Adverse Effects:

Like prazosin.

* Preparation, Dosage and administration:

Doxazosin (cardura) is dispensed in tablets (1, 2, 3, and 8mg) for oral administration. The initial dosage for hypertension or BPH is 1mg once a day.

**Tamsulosin (Flomax)**

* Like doxazosin

**Phentolamine (Regitine)**

* Phentolamine is a competitive adrenergic antagonist, blocks alpha₂ receptors as well as alpha₁ receptors.
* Phentolamine has two applications:

1. Treatment of pheochromocytoma
2. Prevention of tissue necrosis following extravasation of drugs that produce alpha₁- mediated vasoconstriction (e.g., norepinephrine).

Adverse Effects:

Like prazosin, Phentolamine can produce the typical adverse effects

associated with alpha-adrenergic blockade:

Orthostatic hypotension, reflex tachy cardio, nasal congestion and

inhibition of ejaculation.

Because of its ability to block alpha₂ receptors, phentolamine

produces greater reflex tachycardia then prazosin.

Preparations, Dosage, and administration:

Phentolamine is dispensed in solution (5mg/25ml) for IM and IV administration. The dosage for preventing hypertension during surgial excision of a pheochromocytoma is 5mg (IM or IV).

To prevent necrosis following extravasation of IV norepinephrin the region should be infiltrated with 5 to 10 mg of phentolamine diluted in 10ml of saline.

**Phenoxy benzamine: (Dibenzyline)**

* Like phentolamine.

**Beta-Adrenergic Antagonists:**

* The beta-adrenergic antagonists can be subdivided in to two groups:

1. Non selective beta blockers. (represented by propranolol).
2. Cardioselective beta blockers. (represented by metaprolol)

**Propranolol: (Inderal)**

* Propranolol was the first beta-adrenergic blocker to receive widespread clinical use and remains one of our most important beta-blocking agents.
* Propranolol blocks beta₁ and beta₂ receptors, and is the prototype of the non-selective beta-adrenergic antagonists.
* **Pharmacologic Effects**
* By blocking cardiac beta₁ receptors, propranolol can reduce heart rate, decrease the force of ventricular contraction, and suppress impulse conduction through the AV node.
* The net response to these effects is a reduction in cardiac output.
* By blocking beta₁ receptors in the kidney, propranolol can suppress secretion of renin.
* Blockade of beta₂ receptors has three major effects

1. Blockade of beta₂ receptors in the lung can cause broncho constriction.
2. Blockade of beta₂ receptors in the certain blood vessels can produce vasoconstarction.
3. Blockade of beta₂ receptors in the skeletal muscle and the liver can cause inhibition of glycogenolysis.

* Pharmacokinetics:
* Propranolol is highly lipid soluble and therefore can readily cross membranes.
* The drug is well absorbed following oral administration.
* Propranolol is widely distributed to all tissues and organs, including the central nervous system.
* Propranolol is inacticated by hepatic metabolism and the metabolites are excreted in the urine.
* **Therapeutic uses:**

propranolol Blockade β₁ In heart :

hypertension, angina pectoris, cardiac sysrhythmia.

* Adverse Effects:

1. Bradycardia. Beta₁ blockade in the heart can cause bradycardia. Heart rate should be assessed before each dose. If necessary, heart rate can be increased by administering atropine and isoproterenol.
2. Atrioventricular heart block. By slowing conduction of impulses through the AV node.
3. Heart failure. In patients with cardiac disease.
4. 4. Rebound cardiac excitation. Abrupt with drawal of propranolol can cause rebound excitation of the heart, resulting in tachy cardia and dysrhythmias.
5. 5. Bronchoconstriction.
6. 6. Inhibition of Glycogenolysis.
7. 7. CNS Effects. Depression, hallucinations.

Drug interaction:

1. Calcium channel blockers.
2. Insulin

* Preparations: Propranolol hydrochloride (Inderal) is available in two oral formulations.

1. Tablets (10 to 90mg)
2. Sustained-release capsules (60 to 160 mg). The drug is also available in solution (1mg/ml) for IV administration.

Dosage :

for treatment of hypertension. The initial dosage is 40mg twice a day. The usual adult dosage for angina pectoris is 160mg/day.

**Metoprolol, (Lopressor, Toprol XL)**

* Is the prototype of the cardioselective beta-adrenergic antagonists.
* These drugs are preferred to the non selective beta blockers for patients with asthma or diabetes.
* Pharmacologic Effects:

blocking cardiac beta₁ receptors heart --------------

- reduces heart rate.

- force of contraction

- impulse velocity through the AV node.

Blocking beta₁ receptors ---- reduces secretion of renin.

* Pharmacokinetics: metoprolol is moderately lipid soluble and well absorbed following oral administration.

Elimination is by hepatic metabolism and renal excretion.

* Therapeutic uses: 1/ hypertension

2/ angina pectoric

3/ myocardial infarction

* Adverse Effects: bradycardia, reduction of cardiac output, AV heart block, heart failure, and rebound cardiac excitation.
* Preporations, Dosage and Administration:

Metaprolol is available is standard oral tablets (50 and 100mg) under the trade name Lopressor and in sustained-release oral tablets(50, 100 and 200 mg). -Under the trade name Toprol XL, the drug is also available in solution (1mg/ml) for IV administration. The initial dosage for hypertension is 100mg/day in single or divided doses.