

ADRENERGIC ANTAGONISTS

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DEFINATION AND TYPES

➤ These drugs occupy & **block** adrenergic receptors in competition with NA & adrenaline. They are of **two** classes:

1. Alpha – blockers

2. Beta – blockers

1. Alpha – blockers: these are divided to

A. Selective α -blockers (block either α_1 or α_2 receptors)

B. Non-selective α -blockers (block both α_1 & α_2 receptors)

α BLOCKERS

Alfuzosin UROXATRAL

Doxazosin CARDURA

Phenoxybenzamine DIBENZYLINE

Phentolamine REGITINE

Prazosin MINIPRESS

Tamsulosin FLOMAX

Terazosin HYTRIN

Yohimbine YOCON

β BLOCKERS

Acebutolol SECTRAL

Atenolol TENORMIN

Betaxolol BETOPTIC-S, KERLONE

Bisoprolol ZEBETA

Carteolol CARTROL

Carvedilol COREG, COREG CR

Esmolol BREVIBLOC

Labetalol TRANDATE

Metoprolol LOPRESSOR, TOPROL-XL

Nadolol CORGARD

Nebivolol BYSTOLIC

Penbutolol LEVATOL

Pindolol VISKEN

Propranolol INDERAL LA, INNOPRAN XL

Timolol BETIMOL, ISTALOL, TIMOPTIC

1. PHARMACOLOGICAL ACTIONS OF ALPHA BLOCKERS

1. CVS:

Blockade of α_1 vasoconstrictor receptors produces **vasodilatation** & decrease in arterial blood **pressure**. This is associated with **stimulation** of the heart **rate**.

2. Eye:

Blockade of α_1 receptors in the radial muscle of the iris leads to **miosis**.

3. Headache, nasal congestion (vasodilatation of the cranial & nasal vessels)

THERAPEUTIC USES

1. Hypertension
2. Hypertensive crisis
3. Pheochromocytoma hypertension
4. Benign prostatic hypertrophy to relax bladder sphincter muscle & reduces urine retention
5. Peripheral vascular disease e.g. Raynaud's syndrome (spasm of the upper limb blood vessels on exposure to cold weather).

ADVERSE EFFECTS

1. Postural hypotension
2. Tachycardia (more with nonselective alpha-blockers)
3. Failure of ejaculation.
4. Headache, sedation, nasal congestion

INDIVIDUAL ALPHA BLOCKERS

- 1. Doxazosin:** selective α -1 blocker suitable for once daily administration in hypertension & benign prostatic hypertrophy (BPH).
- 2. Phenoxybenzamine:** irreversible nonselective oral long acting α -blocker useful in treatment of phaeochromocytoma (tumour of the adrenal medulla secreting excessive adrenaline & NA causing hypertension).
- 3. Phentolamine:** nonselective reversible injectable α -blocker useful in **hypertensive crisis** associated with high catecholamine levels in blood as in **phaeochromocytoma**.

2. BETA – BLOCKERS

1. **Cardioselective β -Blockers:** (atenolol, metoprolol).
 2. **Non-selective β -Blockers:** β_1 & β_2 -receptors (propranolol)
 3. **Mixed α & β blocker** (Labetalol)
- These agents block beta-effects of adrenaline & NA. Cardioselective β -blockers have higher affinity to cardiac β_1 - than for β_2 -receptors. Non-selective β -blockers block β_1 & β_2 -receptors.

PHARMACOKINETICS OF BETA BLOCKERS

- Most beta-blockers can be given orally once daily or more.
- **Lipid-soluble compounds (e.g. propranolol):**
 - Cross blood brain barrier (BBB) into the CNS
 - Produce more central effects than the water soluble agents.
 - Highly metabolized in the liver
 - Safe in renal impairment
- **Water-soluble drugs (e.g. atenolol):**
 - Excreted unchanged in urine
 - Have longer $t_{1/2}$ & accumulate in renal disease
 - Should be avoided in renal impairment

PHARMACODYNAMICS OF BETA BLOCKERS

1. **CVS:** These agents decrease heart rate, myocardial contractility, cardiac output & O₂ consumption. They decrease renin release by kidneys.
2. **Bronchi:** producing bronchoconstriction & may precipitate in asthmatic attack.
3. **Eye:** producing a reduction in intraocular pressure (IOP)

THERAPEUTIC USES OF BETA BLOCKERS

1. CVS indications:

- **Essential hypertension**
- **Angina pectoris:** Beta-blockers are cardioprotective by reducing cardiac work & myocardial O₂ demand.
- **Acute myocardial infarction (AMI)** to reduce infarction size & to prevent new infarction.
- **Arrhythmias** like ectopic beats & tachycardia

2. **Glaucoma:** timolol eye drops reduces production of aqueous humour & the high IOP

3. **Hyperthyroidism** to reduce manifestations of sympathetic over-activity in the disease.

5. CNS indications:

- **Migraine** prophylaxis
- **Chronic anxiety** to control excessive sympathetic manifestations of anxiety

ADVERSE EFFECTS OF BETA BLOCKERS

1. Bradycardia
2. Bronchospasm & precipitation of asthmatic attack
3. Cold extremities due to peripheral vasoconstriction
4. Nightmares with lipid soluble agents

Sudden withdrawal of β -blockers should be avoided.

CONTRAINDICATIONS OF β -BLOCKERS

1. Asthma
2. Heart block
3. Severe heart failure (although small doses of selective beta-blockers were found to be useful in mild heart failure)
4. Late pregnancy

INDIVIDUAL BETA-BLOCKERS:

1. **Atenolol** (selective)
2. **Propranolol** ((nonselective)
3. **Timolol** (nonselective)
4. **Metoprolol** (selective)
5. **Pindolol** (nonselective)

THANKS