# ADRENERGIC ANTAGONISTS

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# CONTENTS

# 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 $\alpha_1$ or $\alpha_2$ receptors**)**

**B. Non-selective α-blockers** (block both $\alpha_1$ & $\alpha_2$ 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 $\alpha_1$ vasoconstrictor receptors produces **vasodilatation** & decrease in arterial blood **pressure**. This is associated with **stimulation** of the heart **rate.**

**2. Eye**:

Blockade of $\alpha_1$ 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, bisoprolol ).
2. **Non-selective β-**Blockers: **$\beta_1$ & $\beta_2$-**receptors (**propranolol**)
3. Mixed α & β blocker (Labetalol)

- These agents block beta-effects of adrenaline & NA. Cardioselective β-blockers have higher affinity to cardiac **$\beta_1$**- than for **$\beta_2$**-receptors. Non-selective β-blockers block **$\beta_1$** & **$\beta_2$**-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 ½ & 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 broncho-constriction & 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 $O_2$ 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