

Sympatholytic Drugs



ANTIADRENERGIC DRUGS

Centrally acting

Ganglion blocker

Neuronal Blocker

Alpha-blocker

Beta-blocker

1-Centrally acting α_2 - Agonists

- **Clonidine**
- **Methyldopa**
- **Guanafacin**
- **guanabenz**

Mechanism of action of central α_2 agonists

Stimulates central alpha-2 adrenoceptors

reduce sympathetic outflow from the CNS

1-decreased heart rate →
reduction of cardiac output

2-reduce vasoconstriction →
reduction of peripheral vascular
resistance

↓ blood pressure

2-Ganglion Blockers

- Trimethaphan (I.V. infusion).**

3-Adrenergic Neuron Blockers

Guanethidine.

Reserpine.

4-Adrenergic Receptor Blockers

1- Alpha-Adrenergic Blockers

2- Beta-Adrenergic Blockers

1-Alpha-Adrenergic Blockers

Classification

- **Selective α 1-blockers:**

- **Doxazocin**
- **Prazocin**
- **Terazocin**
- **Tamsulosine**
- **Trimazosine**

- **Non Selective α -blockers**

- **Phenoxybenzamine**
- **Phentolamine**
- **Tolazoline**

- **Selective α 2-blockers**

- **Yohambine**

PRAZOCIN

Selective α_1 -blocker

Actions:

- ↗ 1-VD of veins (decrease venous return)
- ↗ 2- VD of arteries (decrease TPR and congestion)
- ↗ 3-Relax sphincter of UB
- ↗ 4- No reflex tachycardia

PRAZOCIN

➤ Therapeutic Uses:

- - Hypertension
- - Benign Prostatic Hypertrophy(BPH)
- - Peripheral vascular disease(PVD)
- - Heart failure

PRAZOCIN

↗ Side Effects:

- ↗ - Orthostatic hypotension (1st dose)
- ↗ - Dry mouth and GIT upset
- ↗ - Headache and drowsiness
- ↗ - Oedma
- ↗ - Rash and pruritis

Tamsulosin

➤ **Selective α 1-blocker**

➤ **Uses:**

➤ **-In Treatment of : BPH**

Beta-Adrenergic Blockers

Classification

Classification

1. According to selectivity:

- Non-selective :block beta1 and beta2
- Cardio-selective: block beta1
- Block alpha and beta receptors : e.g **Labetalol**

2. According to generation:

1st generation: non selective beta-blockers.

2nd generation: cardioselective beta1-blockers.

3rd generation: **vasodilator beta-blockers. They either have:**

- Beta2-agonistic activity: celiprolol & dilevalol.
- Direct V.D & alpha-blocking effect: **carvedilol** &

3-According to (ISA):

Antagonist (no ISA): propranolol, timolol, atenolol & metoprolol.

Partial agonists (have ISA): oxprenolol, pindolol, acebutolol, practolol,

➤ **Non-selective beta blockers**

- **Propranolol**
- **PINDOLOL**
- **NADOLOL**
- **TIMOLOL**

PROPRANOLOL

- **Non selective (blocks $\beta_1 + \beta_2$)**
- **No ISA**

Kinetics:

- **Well absorbed orally (highly lipophilic)**
- **Extensively metabolized in the liver**
- **90-95% bound to PP**
- **Metabolites excreted in urine**

PROPRANOLOL

Actions:

1- **CNS:** ↓ sympathetic flow (Antianxiety)

2- **Respiratory:** bronchoconstriction

3- **C.V.S:**

*Heart: -ve inotropic

↓ O₂ consumption) -ve chronotropic(↓ C.O.P, ↓ cardiac work,

-ve dromotropic

*BL.v: decrease blood flow to the tissues

* blood pressure : β-blockers decrease the blood pressure through:

1. Decrease C.O.P

2. Inhibition of renin release.

3. Resetting of baroreceptors.

4. Presynaptic β_2 -blockade decreases NE release.

5. Central inhibition of sympathetic outflow.

6. Modulation of prostaglandin synthesis in favor of the vasodilator ones as prostacycline

PROPRANOLOL

4- metabolism: Prevents glycogenolysis leads to hypoglycemia

↗ **5- Eye:** β -blockers reduce IOP most probably due to decrease aqueous humour synthesis, but have no effect on pupil size.(timolol)

↗ **6 – increase K release:(Hyperkalemia)**

↗

PROPRANOLOL

Therapeutic Uses:

- **Hypertension**
- **IHD: angina, MI, B blockers acts by:**
 - ↗ **decrease oxygen demand by decreasing cardiac work.**
 - ↗ **Increase oxygen supply by:**
 - ↗ **Increasing diastolic coronary perfusion time.**
 - ↗ **Shifting of subepicardial blood flow to subendocardial flow.**
 - ↗ **Inhibition of platelet aggregation.**

PROPRANOLOL

Therapeutic Uses:

- **Glucoma**
- **Hyprerthyroidism**
- **Ventricular and supra ventricular arrhythmias**
- **Pheochromocytoma with alpha-blockers.**
- . **Prophylaxis in migraine headache.**
- . **Anxiety and essential tremors.**
- **Portal hypertension .**

PROPRANOLOL

Side Effects:

- **Bronchoconstriction**
- **Arrhythmia**
- **Sexual impairment**
- **Fatigue, dizziness, vivid dreams, nightmares**
- **Cold hands and allergic reactions**
- **Prolong insulin hypoglycemia and mask the hypoglycemic symptoms**
- **Increase VLDL, triglycerides, and lower HDL**
- **Oculo-muco-cutaneous syndrome with practolol**

PROPRANOLOL

Precautions & Contraindications:

- Bronchial asthma**
- Partial heart block and A.V block**
- Variant angina**
- Peripheral vascular diseases**
- Used with caution in DM**
- Can not be stopped suddenly as Abrupt discontinuation increases the risk of IHD due to upregulation of beta-receptors.**

Cardio selective beta blockers

selective beta1 blockers

- ↗ - **ATENOLOL**
- ↗ - **METOPROLOL**
- ↗ - **BISOPROLOL**
- ↗ - **ESMOLOL**
- ↗ - **ACEBUTOLOL**

Revision

Summary

Sites functions, Agonists and antagonists of Adrenoceptors

Receptor	Site	Action	Agonists	Antagonists
Alpha 1	Effective organs	VC, mydriasis, spasm of GIT&bladder sphincters, ejaculation.	Phenylephrine Dopamine Noradrenaline Adrenaline	Prazosin Phentolamine Phenoxybenzamine
Alpha 2	Pre & post-synaptic & CNS	Inhibit sympathetic outflow from CNS, decrease release of renin & insulin and inhibit lipolysis	Noradrenaline Adrenaline Clonidine guanfacine guanabenz	Phentolamine Phenoxybenzamine Yohimbine
Beta 1	Heart, presynaptic & kidney	Increase H.R & contr., increase release of NA, renin & lipolysis.	Dopamine Dobutamine Noradrenaline Adrenaline Isoprenaline	<u>Selective β_1 blocker</u> Atenolol Acebutolol Metoprolol Practolol Esmolol
Beta 2	Bronchi, BV, GIT, uterus, bladder & pancreas	Bronchodilation, VD, reax GIT, uterus & bladder, increase release of insulin & glycogenolysis	Salbutamol Isoprenaline Adrenaline noradrenaline	<u>Non Selective β blocker</u> Propranolol Pindolol Nadolol Oxprenolol

Classification of beta blockers, uses and side effects

Drug	Uses	Side effects
<u>Cardioselective β_1 blockers :</u>	MI,	AV block, heart failure, hypotension.
Atenolol	Angina,	Bronchospasm,
Acebutolol	Arrhythmia,	Cold extremities, Fatigue, night mare, depression & hallucination .
.Metoprolol.	Hypertension,	
Practolol	Hyperthyroidism,	
Bisoprolol	Pheochromocytoma with alpha-blockers,	Prolong insulin hypoglycemia and mask the hypoglycemic symptoms.
Esmolol.	Glaucoma,	
	Migraine,	
	Anxiety, tremors&	
	Portal hypertension.	
<u>Non selective β-blockers ($B_{1\&2}$)</u>		
Propranolol.		
Pindolol		
Oxprenolol.		
Nadololol.		
Sotalol.		

• P.A.S. restlessness, tremors, insomnia and anxiety.

Alpha blockers and their uses

α - blockers	Action	Uses
Phentolamine	<ul style="list-style-type: none">• α_1, α_2 blocker• Ach & Histamine like - action• Antiserotonin• Short duration.	<ul style="list-style-type: none">• Diagnosis of pheochromocytoma
Phenoxybenzamine	<ul style="list-style-type: none">• α_1, α_2 blocker• Atropine-like action• Antihistamine & antiserotonin• Long duration	<ul style="list-style-type: none">• Treatment of pheochromocytoma• PVD• Shock
Prazosin	Selective α_1 blocker	<ul style="list-style-type: none">• Hypertension• CHF• PVD• Bladder neck

Thank you