

• Goodman and Gilmans The Pharmacological Basis of Therapeutics, 13th Edition

VISION & MOTO

- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine





Integration Model

For Basic Sciences Interactive Lectures

Prof. Umar's Clinically Oriented

Learning Objectives

At the end of the lecture, students of 3rd Year MBBS will be able to ;

01 Classify alpha adrenergic blockers

- O2 Describe the mechanism of action and therapeutic uses of alpha adrenergic blockers
- **O3** Discuss adverse effects of alpha adrenergic blockers
- 04 Explain the basis of "epinephrine reversal"

ADRENOCEPTOR ANTAGONISTS

Agents that inhibit responses mediated by adrenoceptor activation are called a drenoceptor antagonists, adrenergic antagonists or adrenergic blocking agents (α and β adrenergic antagonists)

These agents reduce the effects produced by both sympathetic nerve stimulation and by exogenously administered adrenomimetics

PRE- LECTURE ASSESSMENT

- 1. What is the primary clinical use of alpha blockers?
 - a) Treatment of hypertension
 - b) Treatment of diabetes
 - c) Treatment of depression
 - d) Treatment of insomnia
 - e) Treatment of peptic ulcer disease

2. Which of the following is an example of a selective alpha-1 blocker?

- a) Propranolol
- b) Terazosin
- c) Clonidine
- d) Prazosin
- e) Tamsulosin

3. Alpha blockers work by primarily blocking which type of receptors?

- a) Beta receptors
- b) Alpha-1 receptors
- c) Alpha-2 receptors
- d) Dopamine receptors
- e) Muscarinic receptors

4. Which of the following is a common side effect of

alpha blockers?

- a) Bradycardia
- b) Hypotension
- c) Hyperglycemia
- d) Tachypnea
- e) Hypoglycemia

5. Which of the following drugs is used in the treatment of

benign prostatic hyperplasia (BPH) due to its alpha-1

blocking action?

- a) Metoprolol
- b) Tamsulosin
- c) Lisinopril
- d) Amlodipine
- e) Simvastatin

6. Which of the following alpha blockers is commonly

used for the treatment of pheochromocytoma?

- a) Doxazosin
- b) Terazosin
- c) Phenoxybenzamine
- d) Metoprolol
- e) Clonidine

7. Which of the following is the most likely cause of "first-

dose phenomenon" with alpha blockers?

- a) Sudden drop in blood pressure
- b) Increased heart rate
- c) Severe headache
- d) Bronchospasm
- e) Hyperkalemia

8. Which of the following is a contraindication for using alpha blockers?

- a) Hypotension
- b) Hypertension
- c) Asthma
- d) Renal impairment
- e) Tachycardia

9. Which of the following is a long-acting alpha-1 blocker

that is often prescribed for hypertension?

- a) Prazosin
- b) Terazosin
- c) Doxazosin
- d) Clonidine
- e) Tamsulosin

10. Which of the following alpha blockers is primarily used in the treatment of post-traumatic stress disorder (PTSD) for its action on alpha-1 receptors in the brain?
a) Prazosin
b) Phenoxybenzamine

- c) Tamsulosin
- d) Doxazosin
- e) Clonidine

CLASSIFICATION ACCORDING TO REVERSIBILITY OF ACTION (Duration of Action)



Reversible (Competitive blockers- short acting)

- Prazosin
- Terazosin
- Trimazosin
- Doxazosin
- Urapidil
- Phentolamine
- Tolazoline



Irreversible (Non-Competitive blockers-long acting) Phenoxybenzamine

ACCORDING TO RECEPTOR SELECTIVITY

Selective α -Blockers

Α.

i) Selective α₁ Blockers
Prazosin
Doxazosin
Alfuzosin
Terazosin
Bunazocin
Tamsulosin
Urapidil
Indoramin

ii) Selective α_2 Blockers Yohimbine Tolazoline

CLASSIFICATION

CORE

ACCORDING TO RECEPTOR SELECTIVITY

B.

Non-selective / Both α_1 & α_2 Blockers

Phentolamine Phenoxybenzamine Dibenamine

Mixed α and β Blockers Labetalol Carvedilol



C.

Drugs with α blockade as adverse effect

Neuroleptic drugs (Chlorpromazine , Haloperidol) Antidepressant (trazodone) Ergotamine Dihydroergotamine

CLASSIFICATION



CLASSIFICATION ACCORDING TO GENERATIONS

01 02, 03

First Generation (Non selective)

Phentolamine Phenoxybenzamine

Second Generation

Terazosin Doxazosin Alfuzosin*

Third Generation

Tamsulosin Silodosin

MECHANISM OF ACTION

- Prevention of α receptor mediated events through
 - Reversible blockade
 - Irreversible blockade
- Inhibition of uptake of NE by presynaptic adrenergic terminal
- Action at other receptors
 (5HT, histamine & acetylcholine)



CORE





CARDIOVASCULAR SYSTEM

- Inhibit the vasoconstrictor effect of norepinephrine by selectively inhibiting the activation of postsynaptic α1 (arteries & veins) receptors by circulating and/or neutrally released catecholamines
- This results in fall in peripheral vascular resistance ensuing drop in BP
- Due to blockade of α1 receptors in veins of lower limbs dilatation →↓ venous tone → pooling of blood on standing Postural / orthostatic Hypotension → dizziness, fainting syncope
- Reflex tachycardia due to baroreceptor reflexes
- More marked if presynaptic α2 receptors in the heart are blocked leading to more stimulation of heart by NE

CARDIOVASCULAR SYSTEM







CARDIOVASCULAR SYSTEM

EPHINEPHRINE REVERSAL PHENOMENON OF DALE

Reversal in the effect of large doses of epinephrine on blood pressure from a pressor response mediated by α_1 receptors to a depressor response, mediated by β_2 receptors by prior administration of α blocker.





Urinary bladder:

Blockade of $\alpha_{1A} \& \alpha_{1D}$ receptors in prostate ---Decreased smooth muscles tone in prostate and neck of bladder ---- \uparrow urine outflow Apoptosis in prostate smooth muscle

Metabolic Effects:

 \uparrow insulin secretion from islet cells (α_2 blockers)

Eye:

Miosis (α1 pupillary dilator muscle)

Other Effects:

个 HDL Nasal stuffiness 个 intestinal motility

THERAPEUTIC USES

Selective α Adrenergic Blockers

<u>α1</u> Adrenergic Blockers

- 1. Urinary Obstruction (Benign Prostatic Hyperplasia)
- 2. Chronic Hypertension
- 3. Hypertensive Emergencies
- 4. Peripheral Vascular Spastic Disease
- 5. Congestive Cardiac Failure

<u>α2</u> Adrenergic Blockers

- 1. Postural Hypotension
- 2. Diabetic Neuropathy

Non selective α Adrenergic Blockers

- 1. Pheochromocytoma
- 2. Local vasoconstrictor excess
- 3. Reversal of tissue anesthesia
- 4. Sexual dysfunction

Pathophysiology of Pheochromocytoma

Pheochromocytoma



HORIZONTAL INTEGRATION- PATHOLOGY

ADVERSE EFFECTS

Selective α Adrenergic Blockers

- Postural Hypotension & syncopal episodes First dose phenomenon
- QT interval prolongation (Alfuzosin)
- Intraoperative floppy iris syndrome (Tamsulosin)
- Retrograde ejaculation

* Non selective α Adrenergic Blockers

- Hypotension
- Reflex Cardiac stimulation (tachycardia, arrhythmias and MI)
- Nasal stuffiness and congestion
- Nausea

Sedation

Phenoxybenzamine

- Diarrhea (Phentolamine)
- Retrograde ejaculation

Family medicine

- 1. Role of family physician is very important in a patient on alpha blocker as they require regular monitoring of their blood pressures.
- One of the most common side effects of alpha blockers is orthostatic hypotension. Family physicians educate patients on how to manage dizziness and lightheadedness, such as rising slowly from sitting or lying down.
- 3. They provide guidance on avoiding dehydration, alcohol consumption, and any other factors that might exacerbate side effects.



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Kim, S.J., Park, S.G., Pak, S., Lee, Y.G., Cho, S.T. and Kwon, O., 2022. Predictive factors for alpha blocker use after transurethral prostatectomy: Can preoperative urodynamic outcome predict alpha blocker medication after surgery?. *Plos one*, *17*(9), p.e0274399.

ARTIFICIALINTELLIGENCE

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