
بسم الله الرحمن الرحيم

Sympatholytic drugs;

- Adrenergic Blockers.
- Adrenergic antagonists.
- Adrenergic receptor antagonists.
- Adrenoceptor antagonists.

by

DR. Muhammad Sarwar

Adrenoceptors;

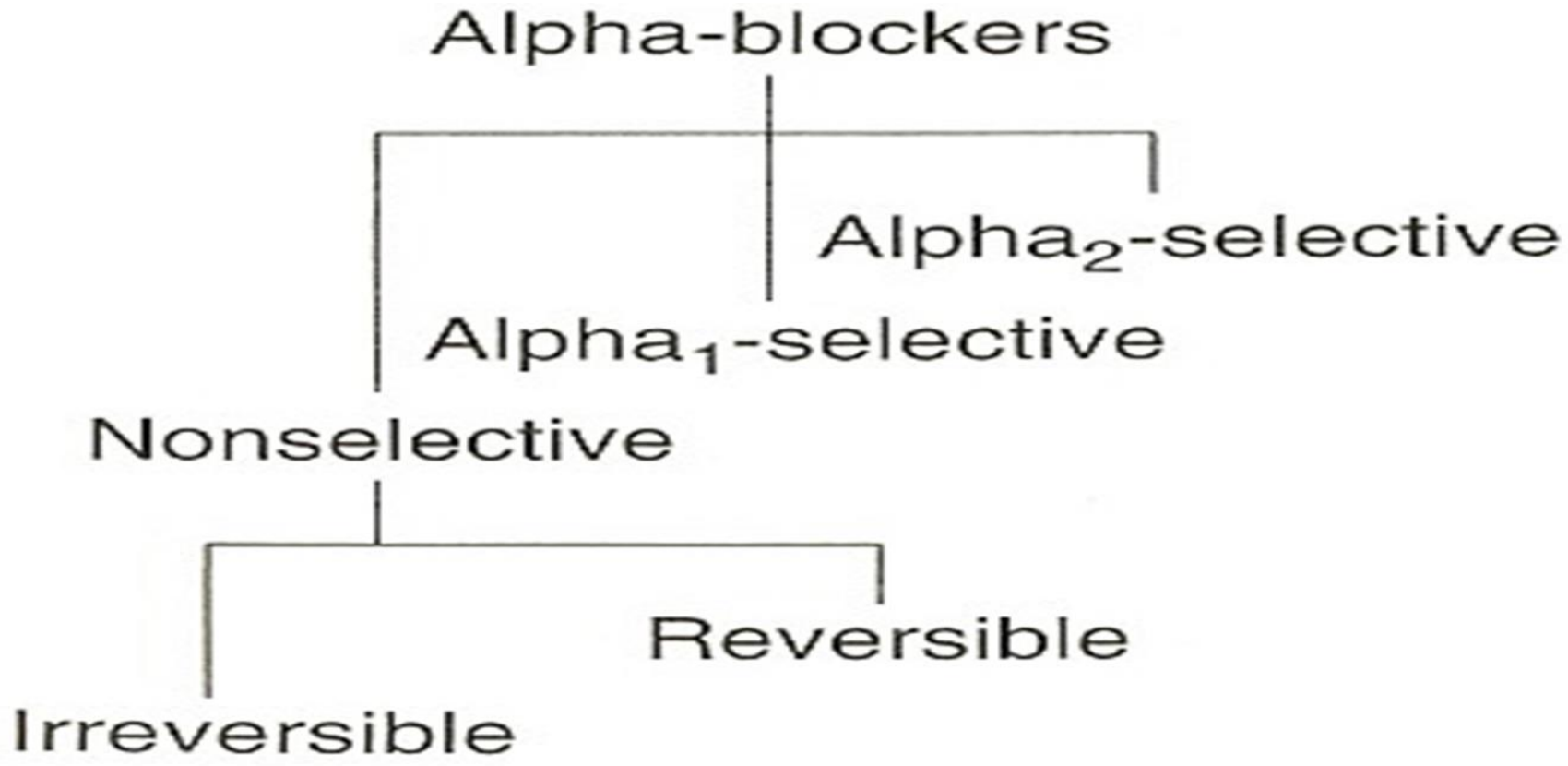
• α_1 … Blood vessels	Vasoconstriction
Pupillary dilator m.	Mydriasis
Prostate	Contraction
• α_2 … presynaptic terminals	Inhibition
β-Cells of Pancreas	Inhibition of insulin release
• B_1…. Heart	Stimulate
Juxtaglomerular cells	Renin release
• B_2…..	
• Respiratory smooth m	Relax
• Uterine smooth muscle	Relax
• Vascular smooth muscle	Relax
• Skeletal muscle	K uptake
• B_3….. Fat	Stimulate lipolysis
• D_1….. Renal blood vessels	Vasodilation

Classification of Sympatholytics;

- **α blockers;** e.g., **Prazosin,** Doxazosin, Terazosin.
- **β blockers;** e.g., **Propranolol, Timolol, Pindolol.**
- **Block both α and β;** e.g.,
  - Labetalol and Carvedilol (**β >> α_1**)
- **Adrenergic neuron blockers;** e.g.,
  - **Reserpine, Guanethidine**, bethanidine.
- **Centrally acting sympatholytics;**
  - **Methyldopa, Clonidine**.
- **Peripheral dopamine blockers;** – no clinical significance

α blockers;

These agents cause **blockade of α mediated responses** to sympathetic nervous system & exogenous sympathomimetics.



Classification of α blockers;

- **α_1 selective antagonists; (α_{1A}, α_{1B}, α_{1D})**

  α_1 >>>> α_2

  - **Prazosin, Doxazosin, Terazosin,** Indoramin
  - **Tamsulosin (α_{1A}), Alfuzosin (α_{1A}), (for BPH).**

- **α_2 selective antagonists; (α_{2A}, α_{2B}, α_{2C})**

  - **Yohimbine. (α_2 >> α_1)**

- **Non selective antagonists; (block α_1 & α_2)**

  - **Reversible;**
    - Phentolamine (competitive, reversible, $\alpha_1 = \alpha_2$)
  - **Irreversible;**
    - Phenoxybenzamine ($\alpha_1 > \alpha_2$)

- **Blockers of both α and β Receptors;**
  - **Labetalol, Carvedilol ($\beta_1 = \beta_2 \geq \alpha_1 > \alpha_1$)**
- **Other drugs with α antagonist activity;**
  - **Neuroleptic drugs;**
    - chlorpromazine, Haloperidol.
  - **Antidepressant;**
    - Trazodone (also block α_1).

Relative selectivity α antagonists;

- **Prazosin, Terazosin, Doxazosin.** $\alpha_1 >>>> \alpha_2$

- **Phenoxybenzamine** $\alpha_1 > \alpha_2$
- **Phentolamine** $\alpha_1 = \alpha_2$
- **Yohimbine** $\alpha_2 > > \alpha_1$

Pharmacokinetics of α-blockers;

- **Well absorbed** after oral administration.
- Undergo **extensive hepatic metabolism**.
- The main difference between agents is in **elimination half-life**;
  - **short** with **Indoramin** and **Prazosin** and
  - much **longer** with **Doxazosin** and **Terazosin.**

Pharmacodynamics;

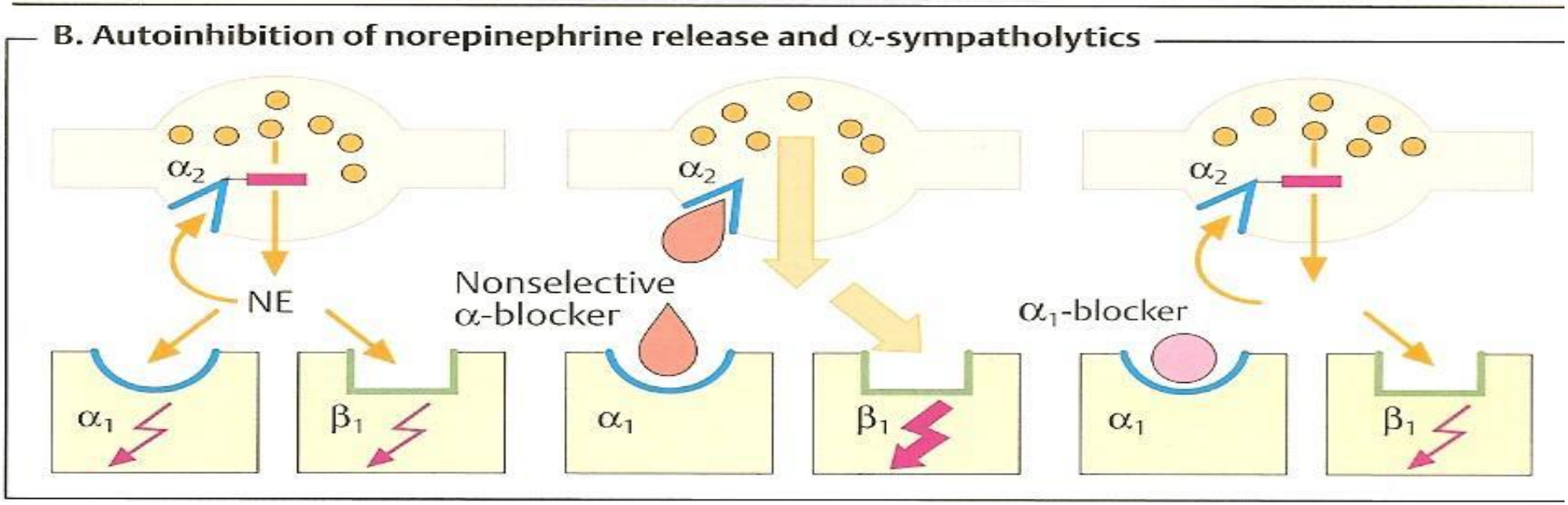
- **Mechanism of action;**
  - **Prazosin, Terazosin and Doxazoxin** act at **α_1 receptors.**
    - **Cause competitive blockade α_1-mediated responses** to sympathetic nervous system & exogenous sympathomimetics.
  - **Phentolamine** causes **competitive blockade of both α_1 & α_2 receptors.**
  - **Phenoxybenzamine** binds **covalently** to **α receptors.** (slight α_1 selectivity).

Pharmacological effects;

- **Predominantly cardiovascular;**
  - **Sympathetic tone (Arteriolar & venous tone)** is due to **α_1 receptors on vascular smooth muscles.**
  - **α_1 blockers inhibit vasoconstriction**, so **vasodilatation** occurs in arterioles and veins.
  - leading to **↓ total peripheral resistance and a fall in BP,** which is more in **upright position (Postural, orthostatic hypotension).**
  - **Baroreceptor reflexes** oppose fall in BP, so there is **increase in the heart rate (Reflex tachycardia) & cardiac output** and also **fluid retention.**

- **Urinary bladder;**
  - **α_1 blockers inhibit contraction of trigon** & **sphincter muscles** of urinary bladder thus **decreasing the resistance to urinary outflow.**
- **Pancreas;**
  - They **facilitate insulin secretion.**
- **Minor effects of α blockade;**
  - Miosis.
  - Nasal stuffiness.
  - No significant direct cardiac effect.

- **α_2 antagonists (Yohimbine);**
  - Activation of **α_2 receptors presynaptically** inhibit release of NE from peripheral nerve endings.
  - Activation of **α_2 receptors in Ponto-medullary** region centrally inhibits sympathetic activity and causes a fall in BP.
  - **Yohimbine blocks α_2 receptors**, thus **increasing the release of NE from sympathetic nerve endings**, which activates α_1 and β_1 receptors postsynaptically causing **rise of BP.**




Thank You