
بسم الله الرحمن الرحيم

Sympatholytic drugs;

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

by

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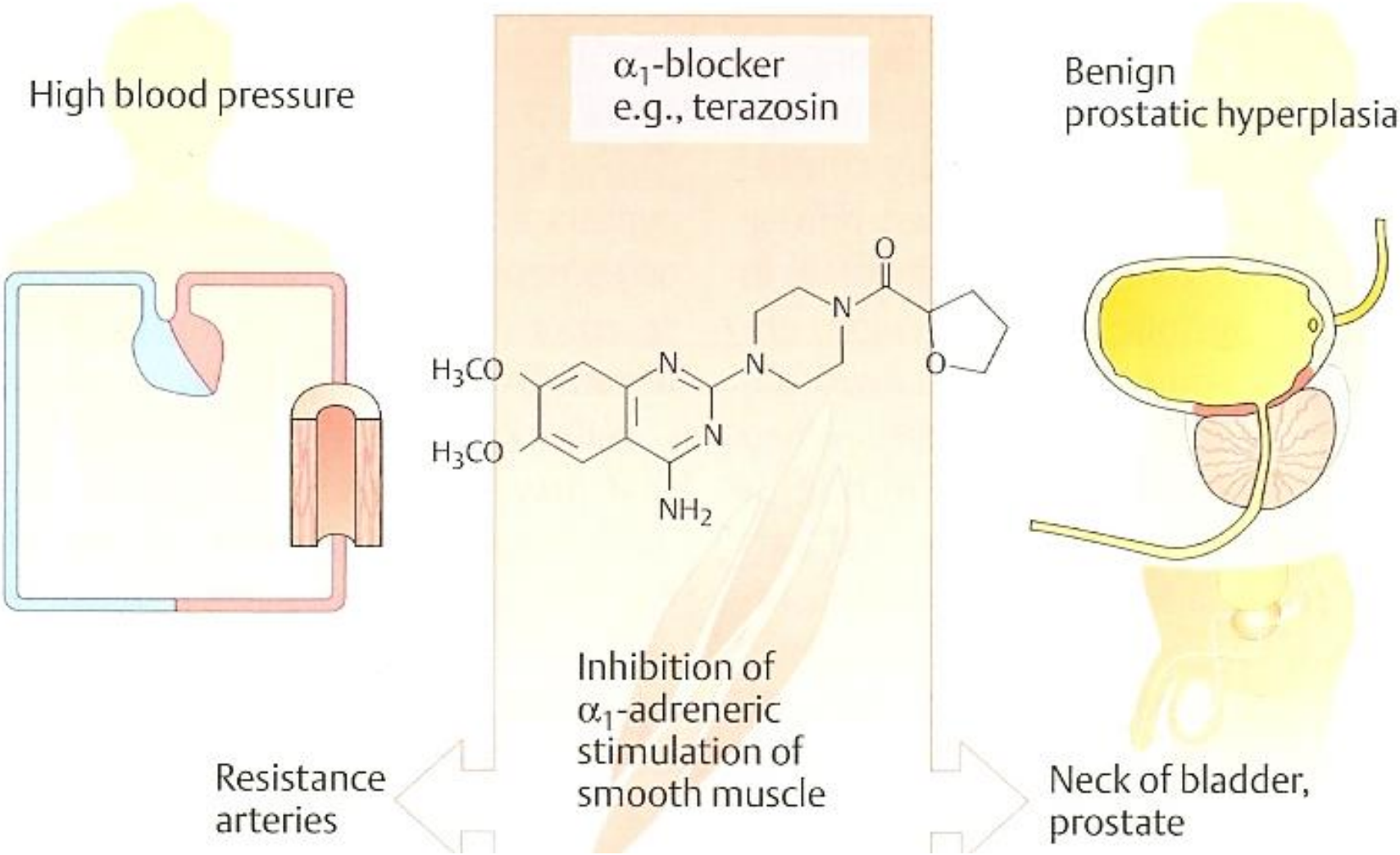
Clinical uses of α-blockers;

. Indications for α_1-sympatholytics



Clinical uses of α blockers;

- **Treatment of Hypertension.**
- **Benign prostatic hypertrophy (BPH).**
- **Pheochromocytoma.**
- **Peripheral vascular disease.**
- **Reversal of intense local vasoconstriction.**
- **Erectile dysfunction.**

Treatment of Hypertension;

- **Prazosin, doxazosin and terazosin;**
  - Are used as **add-on drugs** in **difficult-to-treat** hypertension.
  - **Severe hypertension** in case of **overdose with indirect sympathomimetics** such as cocaine, amphetamines or phenylpropanolamine.
  - **Rebound hypertension** on sudden cessation of clonidine.
- An additive antihypertensive effect occurs when given with either a **diuretic or a β blocker.**
- **First dose hypotensive response;**
  - An exaggerated orthostatic hypotensive response to the first dose of α_1 selective agents in some patients.
  - The first dose is usually small and taken before going to bed.

Treatment of Pheochromocytoma;

- **Phenoxybenzamine** (irreversible α blocker);
  - **in preparation for surgery,**
  - **in chronic treatment of inoperable or metastatic tumour.**
- **Reversible or irreversible α blocker?**
  - Phenoxybenzamine /Phentolamine.
  - In the treatment of pheochromocytoma a massive release of catecholamines from the tumour may overcome a reversible block.
- **β receptor antagonists may be required after alpha antagonists.**
- **Nitroprusside** --- short duration of action, given in infusion and its dose can be readily titrated.
- **Calcium channel blockers.**
- **Phenoxybenzamine other uses;**
  - **Carcinoid tumour** -- it has serotonin blocking effects.
  - **Mastocytosis** – it has H_1 antihistamine effects.

- **Benign prostatic hypertrophy;**
  - **Tamsulosin, Alfuzosin.**
    - **selective α_{1A}** –receptor antagonists.
  - **α_1 antagonists** – prazosin, doxazosin.
- **Peripheral vascular disease like Raynaud's phenomenon;**
  - Efficacy not well documented.
  - Phentolamine, prazosin.
  - Calcium channel blockers may be preferred.
- **Reversal of Local vasoconstriction;**
  - **Phentolamine is** infiltrated into ischemic tissue to reverse intense local vasoconstriction in **accidental local infiltration of potent alpha agonist such as NE.**

- **Erectile dysfunction;**
  - **Phentolamine or yohimbine** by direct injection to cause penile erection in men.
  - used in combination with a nonspecific vasodilator papaverine.
  - Long term ---fibrotic reaction.
  - Prostaglandins, **Sildenafil**, a cyclic GMP **phosphodiesterase inhibitor** and apomorphine are now preferred.

α_2 selective antagonists –Yohimbine ($\alpha_2 >> \alpha_1$)

(Little clinical usefulness)

- Orthostatic hypotension --- ↑ NE release.
- Male erectile dysfunction.
- can reverse the antihypertensive effects of an α_2 agonist such as clonidine.

Adverse effects;

- **Postural hypotension.**
- **Reflex tachycardia.**
  - It is more marked with non-selective agents (Phenoxybenzamine & Phentolamine) and α_2 blockers.
  - It is less common and less severe with α_1 selective blockers.
  - The agents that also block α_2 presynaptic receptors augment release of NE and will further stimulate β receptors in the heart.
- **Tendency to retain sodium and fluid.**
- **Male sexual dysfunction** --- **Inhibit ejaculate** (more marked with phenoxybenzamine & phentolamine)
- **Dizziness, a lack of energy.**

Tachycardia with α blockers;

- Why tachycardia is more marked with α_2 blockers & nonselective agents (Phenoxybenzamine & Phentolamine)? & It is less common & less severe with α_1 selective blockers?
- **The agents that block α_2 presynaptic receptors in the heart augment release of NE and will further stimulate β receptors in the heart.**
  - **In patient with coronary disease angina may be precipitated by the tachycardia.**

Antagonism

Phentolamine

- **Reversible.**
- **Competitive antagonist**, dissociate from the receptors & the block can be surmounted with sufficient high concentration of agonists.
- **Short acting.**

Phenoxybenzamine

- **Irreversible.**
- Binds **covalently** to α receptors, do not dissociate and cannot be surmounted.
- **Long acting.**


Thank You