Sympatholytic & adrenergic blockers
α-receptor Antagonists

Revised by
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OBJECTIVES:

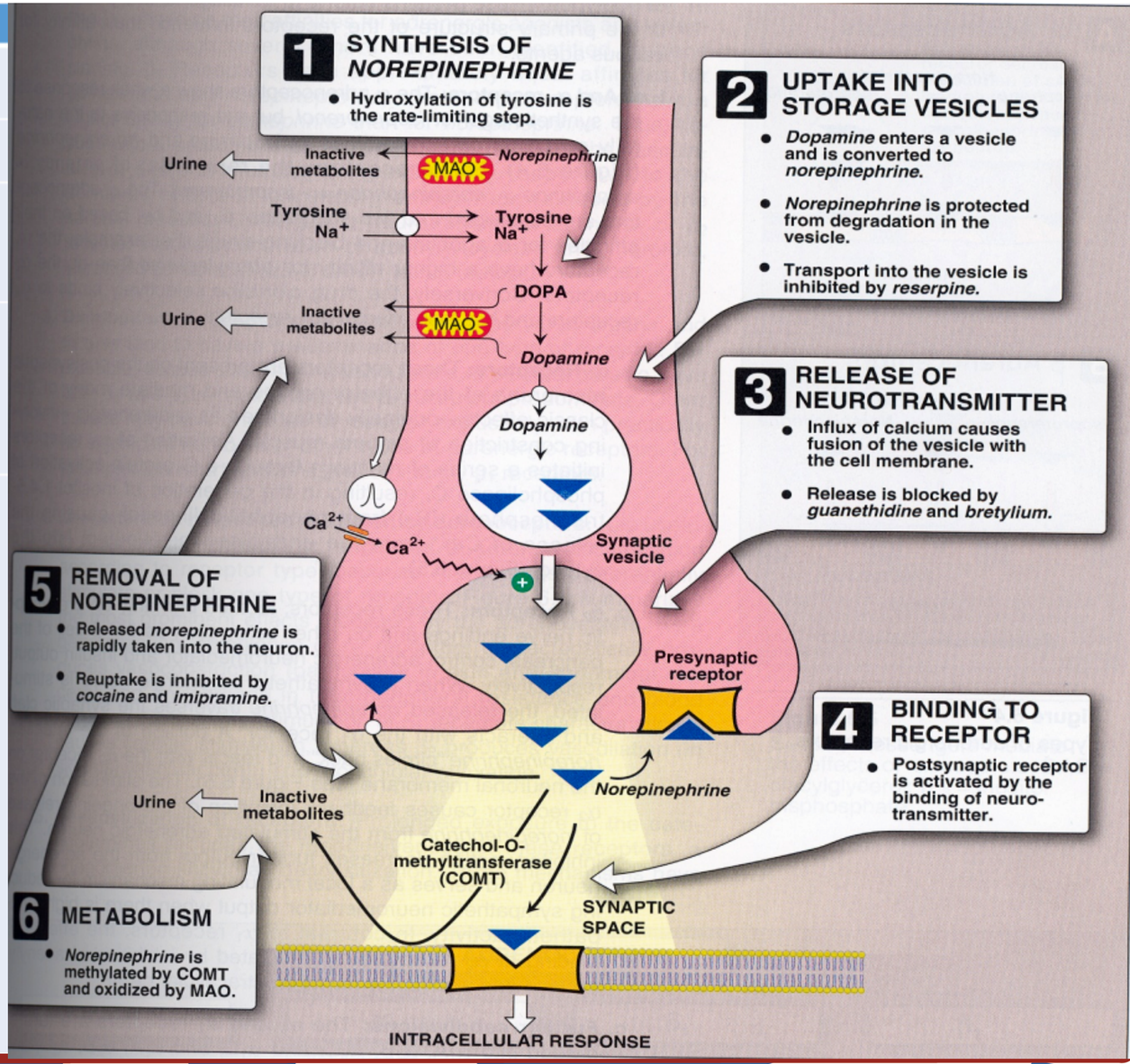
- Describe the different classifications for drugs that can block sympathetic nervous system.
- Describe the kinetics, dynamics, uses and side effects of alpha adrenergic drugs.
- Identify Difference between selective and non selective alpha blockers.
- Know the difference between tamsulosin and other selective alpha receptor blockers.
- Identify the different classifications for beta receptors blockers.
- Describe the kinetics, dynamics, uses and side effects of beta adrenergic drugs.
- Know the preferable drug for diseases as hypertension, glaucoma, arrythmia, myocardial infarction, anxiety, migraine and ect....

- Titles
- Very important
- Extra information
- Doctor's notes

Remember these from the respiratory block? Yes just go through them for a better understanding of the first two lectures.

In general we can say
1 → excitatory
2 → inhibitory

α-adrenoceptors		β-adrenoceptors			
α_1	α_2	β_1	β_2		β_3
postsynaptic	Presynaptic	postsynaptic	postsynaptic	Presynaptic	postsynaptic
Present in smooth muscles.	-	mainly in heart قلبي هو بيتك الأول و الأخير	mainly in smooth muscles	-	adipose tissue
excitatory in function except in GIT	Inhibition of NE (Negative feedback) α_2 = (a t)wo	excitatory in function	inhibitory in function present هذا بيتك الثاني ارتياح Inhibitory =relaxation	↑ release of NE (Positive feedback) β2 = (P t)wo	
• Vasoconstriction of skin & peripheral blood vessels →↑peripheral resistance → hypertension • Relaxation of GIT muscles • ↑Glycogenolysis • Contraction of: 1- radial muscle of eye → mydriasis 2-pregnant uterus. عشان كذا ما ينفع استخدم أي درق يشتغل على هذا الريسبتور للمرأة المتوقع اجهاضها . 3- sphincter in GIT + urinary bladder راح (أ)جهض طفلي الأول ؟ = α_1		↑ heart rate: *+ chronotropic effect, Tachycardia* ↑ force of contraction : *+ inotropic effect* ↑ *conduction velocity :* *+dromotropic effect* ↑ blood pressure ↑ renin release	• Relaxation of: 1- skeletal & coronary blood vessels (vasodilatation). 2-bronchial smooth muscles 3- GIT muscles (constipation). 4-Urinary bladder 5-Uterus Delay premature labor → عكس الفا١ هنا يفضل استخدامه للمرأة المتوقع اجهاضها لانه يسوي ريلاكسيشن. • ↑blood glucos level(hyperglycemia) • ↑ glucagon release from pancreas • ↑ liver & muscle glycogenolysis • Tremor of skeletal muscles	The 2nd baby is coming. = β_2	↑ lipolysis →↑ free fatty acids



Adrenergic drugs

- Adrenergic stimulants (sympathomimetic)
- Adrenergic Depressants
  - Adrenoceptor Blockers
    - α-adrenergic receptor blockers
    - β-adrenergic receptor blockers
    - α&β adrenergic receptor blockers
  - Adrenergic Neuron Blockers

Sympatholytic

Lytic=inhibition

- Adrenergic neuron blockers
  - -Block neurotransmitter release
  - -Acts pre-synaptically
- Adrenergic receptor blockers
  - -Block receptor itself

Formation of false transmitters

e.g: α-Methyl Dopa

It gives **alpha methyl norepinephrine** (false neurotransmitter) > no action

Depletion of storage sites

e.g. reserpine

Complete removal of NE (no NE stored) the vesicles are empty (no NE release after stimulation)

Inhibition of release and enhance uptake

e.g. guanethiidine

Inhibit the release & prevent reuptake

Stimulation of presynaptic α2 receptors

e.g. clonidine

α-methyl dopa

Inhibit sympathetic system (inhibit the release if NE)

Adrenergic neuron blockers

	α-methyl dopa	Cloindine	Apraclonidine
Mechanism Of Action	1. Forms false transmitter that is released instead of norepinephrine 2. Acts centrally as α2 receptor agonist to inhibit NE release Stimulation of the pre-synaptic α2 receptor	1. Acts centrally as α2 receptor agonist to inhibit NE release. 2. Supresses sympathetic outflow activity from the brain .	Used locally as eye drops . Acts by decreasing aqueous humor formation
Uses	• Drug of choice in treatment of hypertension in pregnancy. With no teratogenic action (pre-eclampsia / gestational hypertension). ممكن نقرأ اسم الدرق " مثل دوبا " والدوبامين موجود بجسمنا طبيعي عشان كذا ما نخاف على الحامل منه	Management of withdrawal symptoms of: • Opiate treatment. (morphine) • Alcohol withdrawal. • Benzodiazepines . (Sleeping pills) • Necotine dependence. (Smoking) الممثل الأمريكي جورج كلوني يخطط يعتزل (ينسحب من) التمثيل لأنه صار مدمن	Treatment of open angle glaucoma ممكن نربط اسم الدرق بمعجزة من معجزات عيسى عليه السلام اللي هي إبراء الأكمه، والأكمه من ولدوا وهم عمي إبراء → Apra الأكمه → Glaucoma may lead to blindness
More information		Little used as antihypertension agent due to rebound hypertention upon abrupt withdrawal. Hypertension comes back and even more severe.	

Adrenergic receptor blockers

Adrenergic receptor blockers or adrenolytics. They block sympathetic actions by antagonizing α or B-receptors.

Types:

α-receptor antagonists.

β -receptor antagonists in details in the next lecture.

Classification of α-receptor Antagonists:

Non-selective antagonists. both α_1 and α_2 not α and β

e.g. **phenoxybenzamine** & **phentolamine**.

ما يدرون فين (phen) يشتغلون بالضبط !

α_1-selective antagonists. post-synaptically

e.g. **prazosin, doxazosin, tamsulosin, terazosin**.

α_2- Selective antagonists. pre-synaptically

e.g. **yohimbine**

Non-Selective α- Adrenoceptor Antagonists

	Phentolamine	Phenoxybenzamine
	ممكن نقرأ الدرق الفينتو لمين ؟ فينتو=فيمتو ، والفيمتو اذا توسخت فيه الملابس ممكن يروح Reversible اسرع Short acting من البنزين او الدهن. "مجرد للربط"	بينما البنزين اذا توسخت فيه الملابس ممكن ما يروح Irreversible ويأخذ وقت Long-acting عشان ينظف "مجرد للربط"
Mechanism Of Action	Reversible blocking of α1 & α2 receptors.	Irreversible block of both α_1 & α_2 receptors Forms stable bond with receptor that's why its irreversible and has a long duration of action.
Duration of Action	Short acting (4 hrs).	Long-acting (24 hrs). *To remember long name>long duration

Pharmacological Actions

1) Vasodilatation of blood vessels (α_1 block).
2) Decrease peripheral vascular resistance
3) Postural hypotension. Increase cardiac output (α_2 block).
4) Reflex tachycardia.
5) Increase in GIT motility and secretions

Reflex tachycardia occurs by two mechanisms:

- Stimulation of *baroreceptor reflex that increase NE release. In heart only
- α2 blockade in heart that abolishes (removes) pre-synaptic negative feedback for NE release. NE will increase

baroreceptor is sensitive to changes in the pressure *blood pressure*, so it'll send signals to CNS to either stimulate or inhibit the Sympathetic NS according to the changes….so in case of hypotension which is decrease in pressure it'll stimulate Sympathetic to increase cardiac output as a result. only in the heart!

Non-Selective α- Adrenoceptor Antagonists

Therapeutic Uses:

Pheochromocytoma (benign tumor in adrenal medulla): Before surgical removal to protect against hypertensive crisis.

For preparation before surgery we give these drugs and sometimes beta-blockers because of high release of E and NE during the surgery that may lead to hypertensive crisis (disaster).

Adverse Effects

-Postural hypotension and syncope.

-Tachycardia.

-Headache. Due to vasodilation

-Nasal stuffiness or congestion, Due to vasodilatation

-Vertigo & drowsiness.

-Male sexual dysfunction (inhibits ejaculation). because of increased blood flow

Contraindications

precipitate (worsen):

-arrhythmias

-Angina oxygen supply is low and with increased cardiac output it'll make it worse.

contra-indicated in: **patients with decreased coronary perfusion.**

Selective α_1- adrenoceptor Antagonists

Drugs as: **Pr**azosin, **dox**azosin, **ter**azosin.

Duration of Action

Prazosin has short half-life.

Pra as soon as you can اطلع برا بسرعة او نقرا اسم الدرق كذا

Doxazosin, terazosin have long half lives.

long acting لهم فترة طويلة ، (my son=sin)ولدي (Azo) اللي بالشارع آذوا (Dox=dogs) الكلاب (Tera)ترى

TERA the DOX AZO my SIN for a LONG time

pharmacological Actions:

Vasodilatation due to relaxation of arterial and venous smooth muscles.

Fall in arterial pressure with less tachycardia than with non-selective α- blockers. because α2 isn't blocked here

Therapeutic Uses:

- Treatment of hypertension
- Urinary retention associated with benign prostatic hyperplasia. relaxation of urinary bladder's smooth muscles and stopping retention.
- Reynaud's disease causes some areas of your body such as your fingers and toes to feel numb and cold in response to cold temperatures or stress).

Azosin = Azo my son

His name is Reyn aud بالكويتي اسمه ريان العود

Selective α_{1A}–antagonist Tamsulosin

α_1 has two subtypes either α_{1A} which is located mainly in prostate and bladder neck and α_{1B} which is located in the blood vessels. So if we say α_1 we mean both of them like the previous slide but here we mean only α_{1A}

A selective α_{1A}–antagonist.

α_{1A} receptors present in prostate and bladder neck.

Tamsulosin pharmacological Actions:

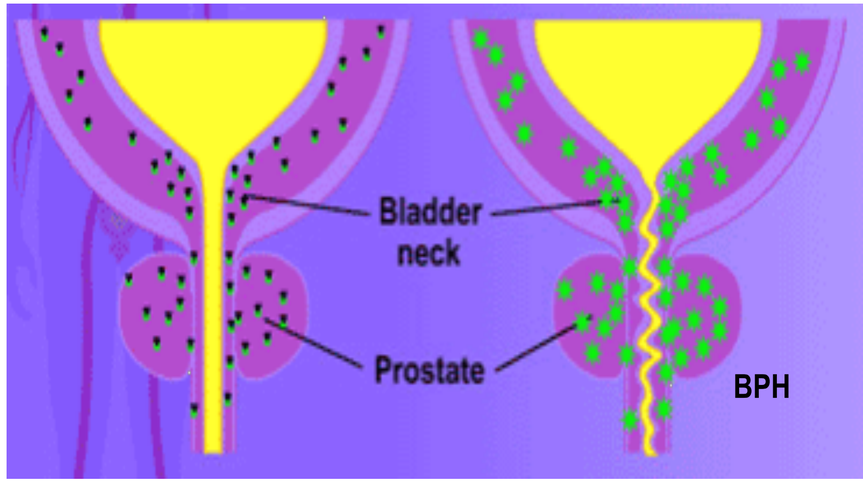
relaxation of smooth muscles of bladder neck & prostate →improve urine flow.

Has minimal effect on blood pressure.

Tamsulosin	Tam is a male who has (BPH) ,finally he find a Solution for that.

USES:

- Treatment of benign prostatic hypertrophy (BPH).
- Help with the passage of kidney stones. size of stones should be less than 4 mm.



Adverse effects of α1- Antagonists

as before with non selective but to a lesser degree.

α_2-selective antagonists

- e.g. **yohimbine**
- Used as aphrodisiac in the treatment of erectile dysfunction.
- Increase **nitric oxide** (vasodilator) released in the corpus cavernosum (tissue of penis) thus producing vasodilator action and contributing to the erectile process. because of increased blood flow

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