pharmacology

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يعطيكم العافية وتين

يعطيكم الف عافية جميعا ،كونوا فخورين بحالكم لانكم وصلتو هون مهما كان نتيجتكم
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الله يوفقكم ويرزقكم اعلى العلامات واعلى درجات الفهم

هلا السلايد الي بالاسود وكلام الدكتور الي بالأحمر
ان شاء الله اني أكون وضحت كل نقطة الكم

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بسم الله ،خلينا نبتدأ ❤️

These drugs their mechanism of action is through increasing the release of NE and epinephrine

And we also could call them central **acting sympathomimetics**

II. INDIRECTLY ACTING SYMPATHOMIMETICS

1. **Amphetamine(this drug has the same action as NE but with a cns action so that means it works on the apha 1 and alpha 2 and beta 1)**

Mechanism of actions: release NE centrally & peripherally →

A. CNS:

- CNS stimulation - alertness - ↓ fatigue

- marked mood elevation(and this amy lead to addiction so you should be careful with giving the drug)

- Appetite Suppression

B. CVS: ↑ arterial blood pressure → **reflex bradycardia**.(here when it works only on a1 without b2 so there is only going to be vasoconstriction so that's going to lead to reflex bradycardia)

Therapeutic uses (CNS):

1-Attention deficit hyperactivity disorder (**ADHD**) in children

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2- **Narcolepsy**.=cnd depression

3. **Obesity** (largely replaced by newer agents e.g. **phenteramine sibutramine**)

these drugs are substitutes because you cant give amphetamine to a patient so he can lose weight and put him in a risk of addiction

Adverse effects:

1. **CNS:**
   - **Psychological dependence** - schizophrenia-like syndrome.
   - Here we have a criteria for saying that this drug is addictive:
   - 1)psychological dependence
   - 2)physiological dependence
   - 3)the patient has withdrawal symptoms if he stops
   - So this drug has all these effects
   - Anorexia & weight loss
   - Insomnia & tremors → depression & fatigue (depletion of CA store).
   - Convulsion → coma & cerebral hemorrhage (severe toxicity)

2. **CVS**: palpitation, arrhythmia, anginal pain and hypertension(anginal pain due its action on the heart wall +inotopic and chronotropic action)

2. **Ephedrine & pseudoephedrine(has a mixed dual action :direct and indirect)**

- Ephedrine acts **directly** (as epinephrine) & **indirectly** (↑ CA release).
- **Less potent & less CNS** effect than amphetamine.

Uses

1. **Nasal decongestant** (ephedrine **&** pseudoephedrine).the drug in red is the more prefered one
2. Topical hemostatic in **epistaxis** (ephedrine)
3. **Spinal shock** (IV) (ephedrine)
4. **Bronchial asthma** (ephedrine)

The last3 action of the drug we use this drug here more than adreline cause adrelinine has way more side effects

So in epistaxis use these drugs also in
Spinal shock and bronchial asthma (here we give them IV not by inhilation so thats why they are prefered

Adverse effects

1. Minimal CNS stimulation → insomnia & anxiety.
2. Minimal CVS stimulation → palpitation, arrhythmia**.**
3. Urinary retention(due to contraction of the sphicter).

3. Cocaine (local anesthetic)has a pain stablizer effect

- **Inhibits CA reuptake → peripheral sympathomimetic** action.
- Readily enters **CNS → amphetamine-like** effect (more intense, more addictive, shorter acting).(here cause the drug is more intense than amphatmine so the addictive effect is gonna be even more higher and since also it has short duration of action so that means that the withdrawl symptomes are going to be even more sever)

Contraindications of sympathomimetic drugs

1. Patients on β blockers (unopposed α-actions → severe hypertension).
2. Hypertensive patients or those with ischemic heart disease (specially decongestants in OTC cold remedies).(here the cardic patient shouldn't take any drug without prescription because even the over the counter cold drugs they have in their component(analgsics,vasoconstricter,antihistamine,and sometimes caffeine to overcome the sedative effect of antihistamine)
3. Adding epinephrine to local anesthetics in cardiac patients & around finger and toes. Because the epi may escape and have a systemic effect
4. Diabetes.
5. Thyrotoxicosis. Thyroxin increases the sensitivity of catochalmines

* **a good rule you can use for knowing the contraindications of a certain drug if the the patient already has a condition that this drug is going to exaggerate then don't use it)**

Sympatholytic Drugs

I. Centrally-Acting Sympatholytics

1. Methyl dopa

Mechanism:

- Prodrug → metabolized in the brain to α-methyl NE which stimulates **central α_2** receptors in brain stem (NTS) → ↓ central sympathetic outflow.

Uses: Antihypertensive especially in **pregnancy**.(**safe on the mother and the baby)**

Adverse effects: (limit its use)

1. **Sympatholytic**: **S**edation - **S**exual dysfunction(no ejaculation) -1) Dry mouth - 2)Diarrhea 3) Peptic ulcer aggravation – 4)Bradycardia.
   These*2,3,4* action the explanation to why we see them is due to :
   We blocked the sympathtic so now the upper hand is to the para
   But action number one is due to somtthing. Centerally with theNTS or the a2 is a presynaptic autoreceptor so it decrese the release of ach
2. **Salt and water retention → Tolerance & Weight gain.**
3. Hepatitis, hemolytic anemia, systemic lupus (immune based).
4. Depression (↓ DA, ↓ 5HT synthesis).
5. Parkinsonism & Hyperprolactinemia (↓ DA). **See the next page for explnation**

2. Clonidine

Mechanism of Action

1. Activates **central α_2** and **Imidazoline** receptors → ↓central sympathetic outflow → ↓ BP.(central alpha 2 found in NTS and imidazoline found in vasomotor center)
2. Acts on **peripheral presynaptic α_2** receptors → ↓ NE release.
3. Stimulates **peripheral postsynaptic α_2** receptors → ↓ renin & aldosterone.

Uses

1. Preanesthetic medication (sedative & analgesic).so I need less **Morphine to use before surgery**
2. **M**orphine withdrawal see next page for explanation
3. **M**enopausal hot flushes.
4. **M**igraine prophylaxis

   } ↓ Sympathetic discharge

5. Hypertensive urgencies.

I. Centrally-Acting Sympatholytics

1. **Methyl dopa**

These drugs will work on the alpha 2 receptor so they work as an agonist but will have a sympatholytic effect.

Right now we already know that tyrosine under the effect of hydoxylase will change to DOPA and then under the action of decarboxylase it will change to dopamine

So this drug is given in the methyl dopa form so it will transform into the methyldopamine form and then into the methyl NE form

So it gives a false neurotransmitter

The explnation why sodium and water retention occurs is due to the there is no VC and then gain weight will happen and the tolerance

What do we mean by tolerance?

Right now we gave the drugs cause lets say the patient already has hypertension then there was water retention which will lead to increse in the blood pressure يعني شطبو عمل بعض

2. Clonidine

2. Morphine withdrawal

Right now any drug that causes drowsiness on the cns just like morphine its wuthdrawl symptom is gonna be the oppisite so we use this drug to decreas the sympathatic effect

Like amphytamine the drug causes - CNS stimulation - alertness – so. Its withdrawl symptomes is gonna be ↑ fatigue .....

There is a difference when we say that the patient is in a hypeertensive emergency and the patient is in a hypertensive urgrncy

Hypertensive emergency	Hypertensive urgency
Systolic Bp over 210 with target organ damage	Systolic Bp over 210 with no target organ damage
Iv drug should be used	Oral drug could be used

Adverse effects

1. **Sympatholytic**: Sedation - Sexual dysfunction - Dry mouth - Diarrhea Peptic ulcer aggravation – Bradycardia.
2. **Salt and water retention → Tolerance & Weight gain.**
3. **Rebound hypertension**: treated by α & β blockers e.g. labetalol.

Specific for Clonidine

Here cause the patient has been on long time trying to decrease the sympthatis discharge so when he stops the body will increase the discharge causing rebound hypertension

II- Alpha Adrenoceptor Antagonists

Classification

Non-selective		Selective	
Irreversible Long acting	**Reversible Short acting**	**Alpha$_1$ Selective**	**Alpha$_2$ Selective**
Phenoxybenzamine ($\alpha_1>\alpha_2$) مش مهم	($\alpha_1 = \alpha_2$) مش مهم + **Direct VD**	Prazosin, Doxazosin, Terazosin, Tamsulosin	Yohimbine

Other α Blockers: labetalol- carvedilol.

They have an alpha blok and beta block action together

Selective α_1 blockers

I. Cardiovascular actions

1. **Mixed vasodilators:**
   a. Arteriodilators→↓ peripheral resistance→ ↓blood pressure.
   b. Venodilators→↓ venous return→ postural hypotension.so this could be considdered an an adverse effect
2. **Tachycardia**: ~~more with nonselective agents (they block presynaptic α_2 receptors, → ↑ NE release → stimulate cardiac β_1 receptors)~~. مش مهم الشرح

Reflex tachycardia due to vasodilation

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3. **Fluid retention on chronic use** (compensatory ↑ in blood volume).

II. Other actions

- Block α receptor at base of **bladder & prostate** →↓ resistance to urine flow→ useful in benign prostatic hyperplasia (BPH).
- Relaxation of **vas deferens**→ inhibition of ejaculation.(sexual dysfunction) AE
- **Miosis - Nasal congestion (stuffiness).**

Therapeutic uses of α blockers

1. **BPH**.
2. **Essential hypertension**. (***with hyperlipidemia***) not effect the lipid profile
3. **Hypertensive emergencies**

- **In most** hypertensive emergencies (labetalol)
- **Clonidine rebound & pheochromocytoma (phentolamine+βB /or/ labetalol)**
- As we said before that colindine needs to be withdrawaled gradually and to combine that with a blocker and b blocker
- So what can you do ?
- You can give labetalol (which combine the two effects)
- Or give a (a blocker)alone with b blocker alone
- 3)or give alpha blocker only alone
- **But you cant give b blocker alone its contraindectaed cause the alpha receptor will still be open so that epi can bind to and cause hypertensive crisis.**

4. **Extravasation of α-agonists** (prevent VC & dermal necrosis).

As we know one of the actions that we could use by using an alpha agonist is: Added to local Anesthetics to prolong their action. So sometime it could go to the suroounding tissue so to prevent that we give this drug the alpha blocker

4. **Raynaud's disease**: Ca^{2+} channel blockers are preferred.
5. **Pheochromocytoma**: medical treatment: **before surgery or if inoperable**

(phenoxybenzamine is preferred; irreversible blocker).

Adverse Effects of αblockers

1. **1st dose postural hypotension**:to prevent that start ↓ by giving small dose (1 mg) at bed time.
2. **Tachycardia** (marked with non-selective agents).
3. **Impaired ejaculation and sexual dysfunction**.
4. **Nasal congestion**, **flushing**, **headache**.

All VD will cause this effect + that it will cause reflex tacycardia except ACEI caus ethey also decrese rthe sympathatic outflow

Tamsulosin

- High affinity for **α_{1A}** receptors (responsible for prostate smooth muscle contraction) than α_{1B} receptors (responsible for VC) →↑efficacy in benign prostatic hyperplasia with less effect on blood vessels than other selective $\alpha_1$blockers→ **minimal change in BP**. So we can only use this drug if the patient doesn't have any hypertensive condition

Selective α2 blockers

- **Yohimbine**: used as an **aphrodisiac** →↑NE release→ stimulates ejaculation
- Cause the main action for a 2 receptor is to decrease the sympathetic outflow so here the opposite will happen

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