CNS
Doctor 2021

Pharmacology
Sheet ( )

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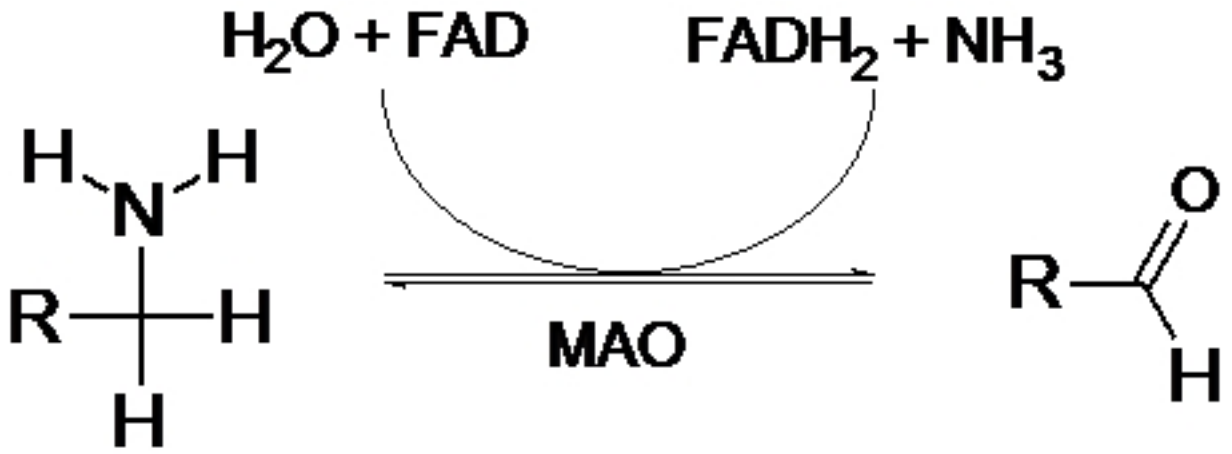
MONOAMINE OXIDASE (MAO) AND DEPRESSION

- MAO catalyze deamination of intracellular monoamines
  - MAO-A oxidizes epinephrine, norepinephrine, serotonin
  - MAO-B oxidizes phenylethylamine
  - Both oxidize dopamine nonpreferentially
- MAO transporters reuptake extracellular monoamine



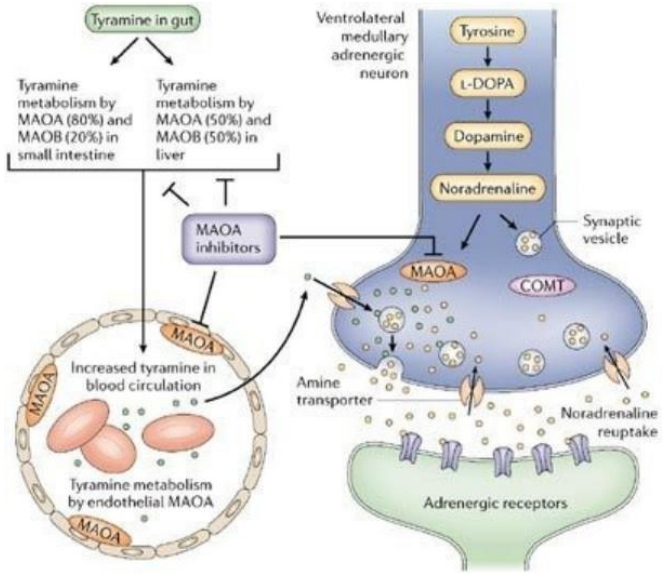
Monoamine oxidase inhibitors (MAOI)

- **Inhibition of intra-neuronal degradation of serotonin and norepinephrine causes an increase in extracellular amine levels.**
- **Phenelzine is a none selective**
- Moclobemide is a reversible and selective inhibitor of MAO-A, used now
- **Selegiline is a selective for MAO-B**, using to regulate the dopamine level within those patients with Parkinson that take levodopa and carpedopa, and the activity decreased (wearing off activity of dopamine), then we augment this by inhibiting the MAO-B.

- **Side effects: Blood pressure problems** (clear and you should take aware of)**, Dietary requirements, Weight gain, Insomnia, Edema.**

- **Monoamin oxidase theory:** if you inhibit the amino oxidase, you will produce more epinephrine, norepinephrine, serotonin and more dopamine. MAO-A oxidizes epinephrine and norepinephrine, so it will be targeted to increase serotonin, while to increase dopamine, MOA-B will be targeted.
- Treating of depression depends on increasing dopamine, serotonin and norepinephrine, and that's we will get when use monoamin oxidase inhibitors.
- In term of depression we use MOA-A inhibitors, Moclobemide is the drug that is used for depression.
- There is a drug-drug interaction; because of the presence of MAO-A within the circulation and the liver, so we avoid using this drugs (also because of the tyramine and cheese effect)
- Using of these drugs was decreased; because the other selective drugs are better. But these drugs are still used because of they are not selective which is needed in case of refractory toward the treatment when other drugs have no effect on the patient (resistance).
- We use this drug also with the atypical depression, it occurs in teenagers, the appearance is fine and no problems are noticed, but internally this patient is very depressed, but not as the first drug of choice, we use them after trying the other drugs.
- Don't give with serotonin. !!ما ترفع السيريتونين بدوائيين

The important about MAO inhibitors is the cheese, atypical depression and the selectivity.



Buproprion

- It is not a drug to be used alone, it is good for use as an augmenting agent, by giving SSRI with it, so produce an activity on level of serotonin in addition to dopamine, norepinephrine. It is as giving MAO inhibitors but without its effect on blood pressure and without the cheese effect.

- Mechanism of action likely reuptake inhibition of dopamine and norepinephrine, so no worry about the serotonin syndrome.

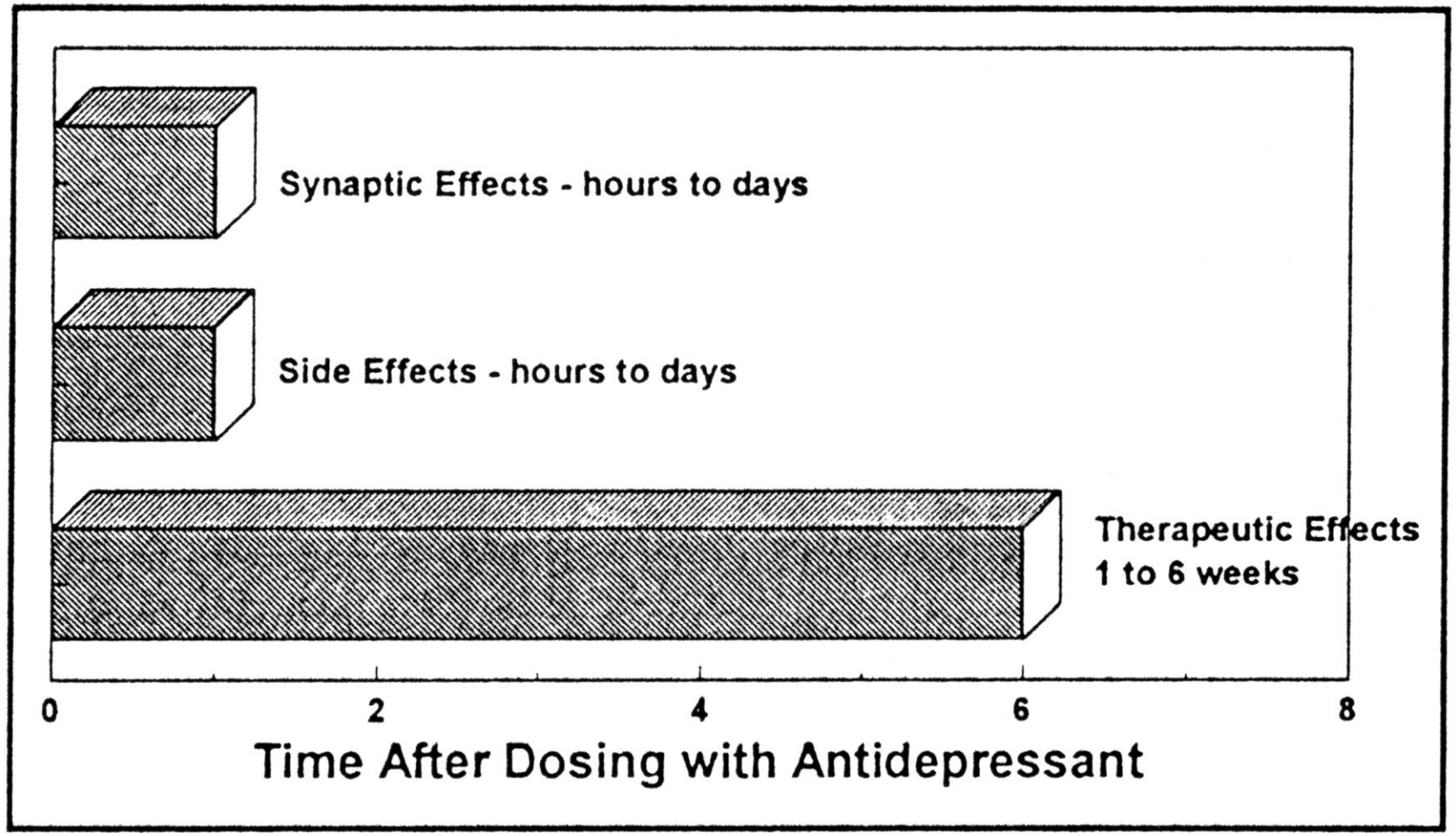
- No weight gain, no sexual side effects, no sedation (-> because it doesn't decrease dopamine) or cardiac interactions.

- It is a weak drug.

- Low induction of mania, it increases dopamine and NE so don’t use in bipolar

- Does not treat anxiety unlike many other antidepressants and can actually cause anxiety, agitation and insomnia; because it increases dopamine and norepinephrine.

- Needs 4 to 6 weeks to produce its activity.



Onset of action of antidepressants. Synaptic effects and side effects of antidepressants begin before therapeutic effects are observed.

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- Following the initiation of the antideppresant dryg treatment there is generally a therapuetic lag lasting for 3-4 weeks.

- 8 weeks trial, then you allow to switch to another antidepressant.

- Partial response then add one another drug from different class.

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- if the initial treatment was successful then 6-12 maintenance periods.

- If the patient has experience two episodes of major depression, then it is advisable to give an anti depressant life long.

Tricycle antidepressant (Amitriptyline)

- **TCAs inhibit serotonin, norepinephrine, and dopamine transporters, slowing reuptake.**
- **with a resultant increase in activity.**
- **Muscarinic acetylcholine receptors, alpha-adrenoceptors, and certain histamine (H1) receptors are blocked.**

Side effects:

(1) drug-induced Sedation

(2) Orthostatic hypotension

(2) Cardiac effects

(3) Anticholinergeric effects dry mouth, constipation,blurred vision, urinary retention

- These drugs appeared after monoamin oxidase inhibitors. Using of them decreased nowadays.
- **Mechanism of action:** reuptake inhibition of dopamine, serotonin and norepinephrine, which increases their activity in the synapse.
- in addition to being a good antidepressants, they bind to many other receptors leading to side effects that is associated with this binding:

1. Muscarinic receptors ->
2. alpha-adrenoceptors -> inhibition of adrenoreceptors leads to orthostatic hypotension.
3. certain histamine (H1) receptors -> histamine released is blocked, leading to sedation.

- They effect on vagal nerve leading to an important toxicity effect on heart, the heart will lose its normal rhythm, there will be an elongation in QT and QRS intervals.
- When talking about the effect of these drug on the heart, we are ether talking about the side effects of the drug which is represented in some palpitation and tachycardia, or about the toxicity of the drug that will cause very fast arrhythmia with QRS elongation, but not torse de point.
- It is used in case of resistance against to all other drugs. But don't combine with serotonin to avoid serotonin syndrome They may be used in fibromyalgia, where all the body is in pain because the patient is depressed and depression affects the pain management.
- -TCA has drug-drug interaction
- -and has S.E bcz of its non selectivity