Antidepressants

Antidepressants affect the pathologically decreased depressed mood and other symptoms of depressive syndrome - psychomotor depression or restlessness, fear, phobia , anhedonia (inability to experience joy), disinterest, sleep disorders and appetite. They are also used outside the field of psychiatry. They mainly suppress algic syndromes, regardless of whether the patient is simultaneously with depression or not.

The analgesic effect can be achieved by approximately half the dose of the antidepressant effect and also in a shorter time (5 days compared to the 2 weeks on average needed to develop the antidepressant effect). The analgesic effect is probably caused by the activation of the descending suppression system, which has its originin the medulla oblongata and projects to all segments of the spinal cord . It is activated by norepinephrine and serotonin .

Current scientific knowledge has led to the idea that depression is associated with a decrease in catecholamines (noradrenaline and dopamine) as well as serotonin at the synapses of the limbic system . As a result of the low concentration of mediators in the synapse, the amount and sensitivity of receptors on the postsynaptic membrane increases (up regulation).

Antidepressants are drugs that adjust deficit and hypersensitivity by various mechanisms. According to these mechanisms, they are divided into monoamine reuptake inhibitors (formerly thymoleptics) and aminooxidase inhibitors (MAOIs, formerly thymoeretics).

Monoamine reuptake inhibitors

Drugs belonging to this group (formerly called thymoleptics) inhibit the reuptake of norepinephrine, dopamine and serotonin from the synaptic cleft to the presynaptic end. This increases the concentration of the mediator in the synaptic cleft. Gradualy the number and hypersensitivity of receptors decrease (down regulation). Adjustment of conditions in the synaptic cleft requires 10 or more days . Therefore, the patient should be warned in advance about the slowly developing effect of treatment so that the patient does not lose confidence in the treatment procedure.

The first generation (tricyclic antidepressants)

- **nortriptyline, norimipramine, dosulepin, amitriptyline, imipramine and clomipramine**.

The disadvantages are side effects:

1. QT prolongation (cardiotoxicity) - increased incidence of severe ventricular arrhythmias ;
2. anticholinergic effects result in dry mouth, tachycardia, accommodation disorder, constipation and urinary retention, risk of glaucomatous attack (in angle-closure glaucoma); in the elderly it can lead to cognitive and memory impairment ;
3. antihistamine effects lead to sedation , increased appetite and weight gain; on the heart (especially in current cardiopathy) they can prolong or block AV conduction and cause arrhythmias;
4. antiadrenergic effects lead to postural hypotension and subsequent tachycardia.

The second generation

Antidepressants with a stronger effect and better tolerability compared to the 1st generation . Their effect doesn`t have anticholinergic or cardiotoxic impact.

- **maprotiline, mianserin, trazodone, viloxazine**

The third generation antidepressants are selective serotonin reuptake inhibition (SSRI = selective serotonin reuptake inhibitor)

The third generation inhibits the uptake of only one neurotransmitter and is further divided into: - **serotonin reuptake inhibiting antidepressants** (SSRIs and SARIs), - **noradrenaline reuptake inhibiting antidepressants** (NARI), and - **dopamine reuptake inhibiting antidepressants** (DARI)

- SSRIs: **fluvoxamine , fluoxetine , sertraline , paroxetine , citalopram , escitalopram** and **SARI** (trazodone, nefazodone - not available in the Czech Republic)
- NARI: **reboxetine, atomoxetine**
- DARI: **amineptine** (Survector - not available in the Czech Republic)

They are currently the *drugs of choice* in the treatment of depression. They are administered for a long time, and are considered prophylaxis of recurrence.

The advantage is a slight effect on adrenergic and cholinergic fibers. The side effects of this generation includes those corresponding to increased serotonin neurotransmission, ie. nausea , vomiting , fatigue, diarrhea - serotonin syndrome . Sexual disorders are also more common . Overall, however, their tolerability is considered very good.

The fourth generation

The fourth generation include for example selective serotonin and norepinephrine reuptake inhibitors (SNRIs), such as **venlafaxine**. They are characterized by a minor side sedative effect. 4th generation antidepressants include antidepressants that affect dopamine and norepinephrine (DNRI) signaling , such as **bupropion** .

Monoamine oxidase inhibitors MAO-I

Drugs belonging to this group (formerly called thymoeretics) act intracellularly - **they prevent the degradation of neurotransmitters inside the cell**. Inhibition of MAO has similar effects as inhibition of reuptake at the presynaptic end membrane. Intracellularly increased concentration of neurotransmitters leads to their increased secretion into the cleft and to down regulation of hypersensitive adrenergic and serotonin receptors.

The original MAOIs acted irreversibly and non-selectively (MAO-A and MAO-B isoenzymes). The treatment had side efects including hypertension or hypertensive crisis with the simultaneous consumption of foods high in **tyramine** (a precursor of catecholamines) - such as cheese, chicken liver, wine, beer, sour milk products, yogurt, etc. In the last 10 years, interest in this group has increased again. It turned out, for example, that with age, the activity of MAO increases and is associated with a higher frequency of depression in the elderly. At the same time, it was found that MAO-type A plays a major role in the degradation of serotonin and noradrenaline. MAO-B degrades more dopamine and tyramine, selectively inhibited by selegiline .

Modern substances therefore show a specific reversible and short-term effect on MAO-A , called RIMA (reversible inhibitors of monoamine oxidase-A):

- **moklobemide**, **brofaromine** a **toloxatone**.

Due to the short-term inhibition, it is not necessary to follow dietary restrictions, they also does not have a hepatotoxic effect. **Side effects :** insomnia, dizziness, occasionally postural hypotension, drug interactions (significantly reduced). In terms of drug interactions, we cannot administer them at the same time with psychostimulants (amphetamine, ephedrine, dopamine, norepinephrine), antidepressants, 1 to 3 generation (a interval of several weeks must be chosen between started and stopped treatment). The effect of anticoagulants and antidiabetics, etc. increases due to a decrease in their biodegradation .

References

Related articles

- Psychofarmaka
- Deprese
- Inhibitory zpětného vychytávání serotoninu
- Antipsychotika

Sources

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References

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