Antiparkinsonian drugs

Dopaminergic substances

Levodopa (L-DOPA)

Dopamine precursor, supplies dopamine in the basal ganglia. Dopamine does not cross the blood-brain barrier and has no central therapeutic effect after i.v. administration.

The dopamine precursor, **levodopa**, penetrates the brain and is decarboxylated to dopamine, which has a therapeutic effect.

Levodopa is given p.o., the biological half-life is short, about 2 hours. This leads to fluctuations in levels, so the daily dose is usually given in 3 to 4 and sometimes more parts. Unfortunately, only 1-3% of administered levodopa enters the brain unchanged, while the remainder is metabolised extracerebrally, predominantly by decarboxylation to dopamine.

When levodopa is administered with peripheral *dopa-decarboxylase* (DD) *inhibitors* , which do not cross the blood-brain barrier, its metabolism in the periphery is reduced and a greater proportion of the administered substance is available for transfer to the brain. Co-administration of a peripheral DD inhibitor reduces the daily requirement of levodopa to 1/4. Reduction of peripheral dopamine production side effects in the GIT and cardiovascular system. Therefore, levodopa is co-administered more frequently with these peripheral DD inhibitors, i.e. **carbidopa** or **benserazide**.

Levodopa may improve the clinical manifestations of parkinsonism, but is particularly effective in alleviating *bradykinesia* and the resulting difficulties in daily life. The effect on tremor is less pronounced. Levodopa significantly improves the quality of life of patients and also reduces mortality from PD. At the beginning of treatment, about 80% of patients respond favorably to levodopa administration; after 3-4 years of treatment, a gradual decrease in effect is often observed.

Stalevo® (combination: levodopa, carbidoba, entacapone)

Side effects - early

- ***GIT:*** When levodopa is initially administered without DD inhibitors, it causes nausea and vomiting in about 80%.
- ***CVS:*** Arrhythmias , these are not very common, are attributed to increased production of catecholamines on the periphery. Combination with DD inhibitors reduces their incidence.
- ***Psychiatric effect:*** Levodopa may rarely cause schizophrenia - like syndromewith delusions and hallucinations due to increased dopamine activity in the limbic system. Dopa is therefore contraindicated in psychotics.

Side effects - late

- ***Dyskinesias****:* occur in up to 80% of patients with long-term treatment. The most common are involuntary twitching and twisting movements in the face and acres of limbs.
- ***Fluctuation of the response (fluctuation)****:* As the treatment progresses, fluctuations in the clinical response become more frequent. It is sometimes associated with fluctuations in serum concentrations and the effect is then reduced towards the end of the dosing interval (*fading response*). However, there is often no time relationship with the administration of doses, we are talking about an *on-off phenomenon* . There are alternating off periods with significant akinesia with periods on when the momentum is significantly better. The transition between the on-off phases can be sudden, so the patient may stop walking and cannot tear his leg off the ground or get up from the chair in which he sat without difficulty.

Dopamine agonists

- Semi-synthetic derivatives of ergot alkaloids.

Bromocriptine

Bromocriptine is a potent agonist of dopamine *D2 receptors* . It has similar effects as levodopa, also similar side effects with the fact that dyskinesia and on-off phenomenon is less common. It has a longer effect than levodopa, but is more expensive. It can be combined with other antiparkinsonian drugs. Its main significance lies in combination with levodopa.

MAO-B inhibitors

Selegiline (L-deprenyl)

MAO-B is involved in the metabolism of dopamine and tyramine. It is abundant in the basal ganglia. Selegiline, an irreversible MAO-B inhibitor, therefore increases and prolongs the antiparkinsonian effects of levodopa.

Central anticholinergics

They can improve *tremor* and *rigidity* but have little effect on bradykinesia. They alleviate extrapyramidal symptoms caused by neuroleptics.

Side effects

- ***Central**:* drowsiness, bradypsychia, confusion, even delusions and hallucinations.
- ***Peripheral**:* dry mouth, blurred vision, mydriasis, urinary retention, constipation , tachycardia, arrhythmias , increased intraocular pressure.

Drugs that penetrate the CNS well and have less parasymatolytic effects in the periphery compared to atropine are used:

- **Biperiden, orphenadrine; benzatropine ; procyclidine ; diethazine .**

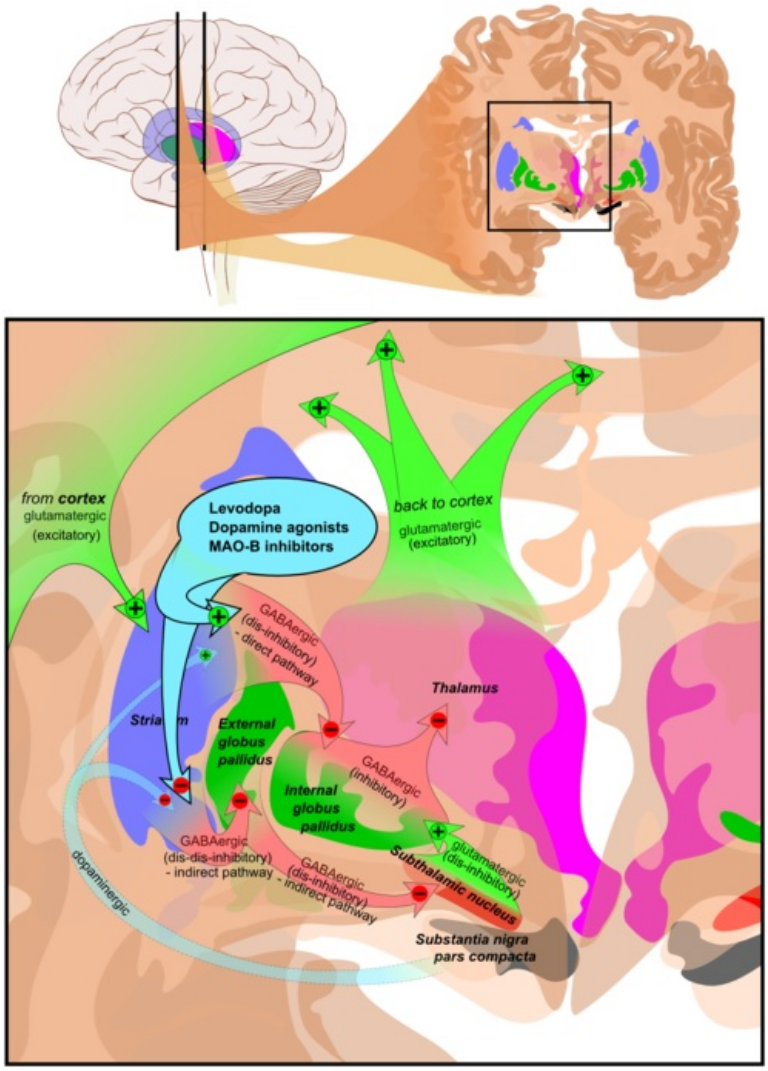
Links

Related articles

- Parkinsonova nemoc/PGS
- Parkinsonský syndrom
- Extrapyramidové syndromy
- Dopamin

Literature

- MARTÍNKOVÁ, Jiřina – MIČUDA, Stanislav – ČERMÁKOVÁ, Jolana. *Vybrané kapitoly z klinické farmakologie pro bakalářské studium : Terapie parkinsonismu* [online]. ©2001. [cit. 2010-07-05]. <https://www.lfhk.cuni.cz/farmakol/predn/bak/kapitoly/cns/parkinson-bak.doc/>.



Circuits of the basal ganglia in treatment of Parkinson's disease.