

SPECIFIC PROPERTIES OF THE DRUG AMANTADINE AGAINST VIRUSES AND IN PARKINSON'S DISEASE

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Abstract. Long-term therapy of Parkinson's disease (PD) with dopaminergic agents is naturally accompanied by the appearance of symptom fluctuations and dyskinesias, and these complications are an extremely important factor that adversely affects the quality of life.

Keywords: Parkinson's disease, substantia nigra, levodopa therapy, NMDA receptors, Amantadine sulfate (PK-Merz), striocortical connections, amantadine hydrochloride.

СПЕЦИФИЧЕСКИЕ СВОЙСТВА ПРЕПАРАТА АМАНТАДИН В ОТНОШЕНИИ ВИРУСОВ И ПРИ БОЛЕЗНИ ПАРКИНСОНА

Аннотация. Длительная терапия болезни Паркинсона (БП) дофаминергическими средствами закономерно сопровождается появлением флуктуаций симптоматики и дискинезий, и эти осложнения являются крайне важным фактором, отрицательно влияющим на качество жизни.

Ключевые слова: болезнь Паркинсона, черная субстанция, терапия леводопой, NMDA-рецепторы, амантадина сульфат (ПК-Мерц), стриокортикальные связи, амантадина гидрохлорид.

In 2017, it was 200 years since the famous English physician James Parkinson described the disease that was later named after him [1]. However, despite such a significant history of studying Parkinson's disease (PD), this disease remains a serious challenge for clinical and fundamental neurology to this day. As is known, the leading motor manifestations of PD (hypokinesia, muscle rigidity, resting tremor) are caused by the death of dopamine neurons in the substantia nigra of the midbrain, degeneration of the nigrostriatal pathway and destabilization of the functional network of subcortical nuclei. A decrease in the inhibitory effect of dopamine on striatal neurons leads to a relative predominance of the activity of the cholinergic systems of the brain. Of additional importance is the excitotoxic effect of excess concentrations of glutamate, caused by the disintegration of striocortical connections due to damage to the dopaminergic mesocortical pathway. While recognizing the successes achieved, it should be emphasized that in the long term, the treatment of patients with PD is associated with a number of complex problems that are still far from being resolved.

Motor complications of long-term levodopa therapy are of significant importance in assessing the course of PD and mark the onset of the advanced stage of the disease. In the pathophysiological mechanisms of levodopa-induced dyskinesias, the key role is played by the hyperactivity of glutamatergic receptors located on the medium spiny neurons of the striatum: in dyskinesias, hyperphosphorylation of NMDA receptors is noted, which leads to an increase in synaptic efficiency and activation of the corticostriatal glutamatergic pathway. It has been shown that dyskinesias and fluctuations of symptoms significantly impede the motor activity of patients and are among the leading factors that reduce the quality of life. In its chemical structure, amantadine is a tricyclic aminoadamantane 1-aminoadamantane hydrochloride (1-adamantylamine hydrochloride). It is a white or white with a slight yellowish tint crystalline powder with a bitter taste. Amantadine also exhibits a number of other important properties:

- increased dopamine synthesis in nigral neurons;
- increased release of dopamine (and other monoamine) vesicles into the synaptic cleft and blocking the reuptake of dopamine by presynaptic terminals;
- increased sensitivity of dopaminergic receptors to the neurotransmitter;
- mild anticholinergic effect.

Amantadine is generally well tolerated in patients of all ages, although it should be used with caution after 70–75 years of age. Side effects are rare and may include swelling (usually of the shins and feet), dry mouth, mottling of the skin, sleep disturbances, episodes of agitation, and hallucinations. Today, two main forms of amantadine are known - amantadine hydrochloride and amantadine sulfate. Amantadine sulfate (PK-Merz) is characterized by a more stable concentration in the blood and the absence of any significant "peak dose" effect, so even with long-term use, it has a stable, persistent antiparkinsonian effect. Another major advantage of amantadine sulfate (PK-Merz) is the availability (in addition to the standard tablet form) of a liquid form for infusion administration. The infusion form of PK-Merz is the first and currently the only antiparkinsonian drug that can be used parenterally.

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