



SERMION (NICERGOLINE) IN NEUROLOGICAL PRACTICE: THERAPEUTIC POSSIBILITIES AND FUTURE DIRECTIONS OF APPLICATION

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ABSTRACT

Modern medicine is faced with an ever-growing number of complex clinical cases that require an integrated approach to diagnosis and treatment. Recent studies have demonstrated a significant increase in the incidence of combined pathology, which creates additional difficulties in choosing the optimal treatment tactics and predicting disease outcomes.

Introduction. Cardiovascular pathologies occupy a special place in the structure of morbidity, among which atrial fibrillation in acute myocardial infarction of the lower wall of the left ventricle is of particular interest. According to current research, the incidence of atrial fibrillation in patients with acute myocardial infarction varies from 6% to 21%, which significantly affects the prognosis of the disease and the quality of life of patients. At the same time, the mechanisms of development of this complication remain insufficiently studied, which makes it difficult to develop effective methods of prevention and treatment.

The study of the pathophysiological mechanisms of atrial fibrillation in myocardial infarction of the lower wall of the left ventricle is of particular relevance, taking into account the anatomical features of the blood supply to this area and its innervation. Modern research indicates the existence of complex relationships between the localization of myocardial infarction and the risk of developing rhythm disorders, however, the detailed mechanisms of these interactions require further study.

The introduction of new diagnostic and monitoring methods, the development of molecular cardiology, and the emergence of modern imaging techniques open up new opportunities for understanding the mechanisms of atrial fibrillation in acute myocardial infarction. This creates prerequisites for the development of personalized approaches to the prevention and treatment of this complication.

Currently, there is no unified understanding of all links in the pathogenesis of atrial fibrillation in acute myocardial infarction of the lower wall of the left ventricle, which necessitates comprehensive research in this area. Studying the mechanisms of development of this complication will optimize patient management tactics and improve the prognosis of the disease.



The purpose of this study is to study the mechanisms of atrial fibrillation in patients with acute myocardial infarction of the lower wall of the left ventricle in order to develop effective methods for the prevention and treatment of this complication.

Nicergoline (sermion) is a hydrated semi-synthetic derivative of ergoline (it contains an ergoline core and a bromine-substituted residue of nicotinic acid). The pharmacotherapeutic efficacy of this drug is determined by two main properties: an alpha-adrenoblocking effect, leading to improved blood flow, and a direct effect on the cerebral neurotransmitter systems — noradrenergic, dopaminergic, and acetylcholinergic. Nicergoline is used to treat cerebrovascular insufficiency, cognitive impairment in the elderly, including various forms of dementia, as well as a number of other disorders, mainly of a vascular nature. The drug was developed in the late 60s of the XX century, and in clinical practice it began to be used since the 70s, first in Italy, and then in other countries. Currently, nicergoline is registered in more than 50 countries around the world (in Europe, Asia, Latin America).

In clinical terms, nicergoline was initially considered as a vascular drug acting antagonistically on α 1-adrenergic receptors, and its therapeutic efficacy was associated with vasodilation, decreased vascular resistance, and increased arterial blood flow. Therefore, it was mainly used to treat dementia caused by cerebrovascular insufficiency. However, further studies have shown that nicergoline has a much broader spectrum of action – at the molecular and cellular levels, acting not only on blood vessels, but also on blood cells (platelets) and neurons. Currently, the drug is used for dementias of various origins (Alzheimer's disease, vascular dementia), cerebrovascular disorders (including stroke, transient ischemic attacks, post-stroke disorders, migraine), peripheral vascular disorders (obliterating atherosclerosis of the vessels of the lower extremities), balance disorders of vestibular origin, glaucoma, Parkinson's disease, as well as benign hyperplasia the prostate gland.

When taken orally, the drug has linear pharmacokinetics, which is practically independent of age; it is rapidly and almost completely absorbed in the gastrointestinal tract. Food intake does not have a significant effect on the absorption of nicergoline. Unlike another ergot derivative, hyergine, nicergoline, is excreted mainly in the urine (80%) as metabolites, and only about 20% in the faeces. In healthy volunteers, it was shown that after taking the tablet drug, its maximum concentration in the blood serum is reached within 3 hours, and the half-life is about 15 hours. Nicergoline is usually prescribed at a dose of 30 mg 2 times a day, the duration of the course of therapy is from 2 to 12 months or more. In Asian countries, nicergoline is usually used in smaller doses (however, like other drugs of similar action).

Nicergoline increases the synthesis of acetylcholine by activating choline acetyltransferase, increases the release of acetylcholine from presynaptic terminals, reduces the breakdown of acetylcholine by inhibiting acetyl cholinesterase, and also acts on postsynaptic M-cholinergic receptors in the central nervous system. It increases the level of acetylcholine in the cortex and striatum of old animals (rats), while there is no change in the level in young animals. In addition, nicergoline restores the age-related decrease in acetylcholine levels in the hippocampus. The inhibition of acetylcholinesterase when using nicergoline is quite comparable to the similar effect of physostigmine, although it is inferior to the effect of tacrine. A decrease in acetylcholinesterase activity in the brain after intravenous and intraperitoneal administration of nicergoline was confirmed experimentally. The revealed



changes in the acetylcholinergic system in experimental animals were accompanied by better performance of tests for mnestic functions. The additional positive effect of nicergoline is due to its effect on other neurotransmitter systems (adrenergic, serotonergic).

In animals treated with nicergoline, there is an improvement in the performance of tasks related to mnestic activity. At the same time, the degree of improvement increases with an increase in the duration of the course of therapy. The nootropic and antiamnestic activity of nicergoline has been confirmed in models of experimental cerebral ischemia and the use of toxic agents that selectively disrupt mnestic functions. Nicergoline has been successfully used to treat dementias of various origins. The positive effect of the drug in the form of a decrease in the severity of cognitive and behavioral disorders is noted, according to some data, in almost 89% of patients (when prescribing placebo, improvement, usually transient in nature, is noted in 26-50% of cases). In the first studies on the effectiveness of nicergoline in dementia, the Sandoz Clinical geriatric Scale (SCAG) and the General Clinical Impression Scale (CGI) were used for evaluation, and subsequent studies used the Short Mental Status Assessment Scale (MMSE) and the Alzheimer's Disease Assessment Scale (ADAS). The difference in clinical effect between the group of patients treated with nicergoline and those treated with placebo ranges from 5 to 30%, depending on the duration of the course of therapy and the characteristics of the patients included in the study. Clinical research data indicate that nicergoline treatment improves the condition of patients with both Alzheimer's disease and vascular (multiinfarction) dementia on the background of nicergoline therapy. In addition, the drug is effective in dementia of mixed (Alzheimer's and vascular) type. In addition to the immediate positive effect on cognitive functions, a rather rapid decrease in the severity of apathy was noted. Thus, a significant improvement was noted in younger patients and in patients with less pronounced cognitive impairments. In addition, nicergoline therapy is believed to lead to marked improvements in vascular dementia than in Alzheimer's disease or other types of dementia. However, it is possible that this is due to differences in the design of the studies conducted to date. It is interesting to note that the effect of therapy on the latency dynamics of the P300 wave of cognitive evoked potential in vascular (multiinfarction) dementia and Alzheimer's disease does not differ from each other in nature. In patients with dyscirculatory encephalopathy, after a course of nicergoline therapy, an improvement in the subjective state is observed in the form of a decrease or cessation of headaches, dizziness, noise in the head, and fatigue. According to the neuropsychological testing data, a significant decrease in the task completion time according to the Schulte tables was revealed. It is important to note that the positive effect of the drug persisted for a long time after the end of the course of therapy.

The effect of nicergoline is dose-dependent, which is confirmed by the results of electrophysiological research methods. On the background of nicergoline therapy in patients with dementia, α - and β -activity on the EEG increases in combination with a decrease in θ — and Δ -waves, which, in turn, correlates with improved attention and memory. Cognitive improvement occurs in parallel with an increase in blood flow velocity in the middle and anterior cerebral arteries, as well as in the right parietal region. It should be noted that nicergoline is considered as an effective drug for the treatment of various types of vascular dementia, including multiinfarction dementia. With an increase in the duration of the course



of treatment from 6 months to 12 months, the effectiveness of therapy also increases. In addition, the progression of cognitive disorders slows down against the background of nicergoline treatment, and the differences between the group of patients receiving nicergoline and those receiving placebo increase with increasing study duration. In this regard, the results of evaluating the effectiveness of nicergoline during long-term (24 months) therapy in patients with leukoencephalopathy on the background of hypertension, but without dementia, are very indicative. In the group of patients receiving the drug, there was a slowdown in the progression of cognitive disorders, and according to some neuropsychological parameters (memory, attention), their improvement was noted. The effectiveness of the drug in moderate to severe Alzheimer's disease was confirmed in a multicenter, double-blind, placebo-controlled randomized trial conducted in 33 European centers (Italy, Sweden, Great Britain, Belgium and Germany). Another indication for prescribing this drug is post-stroke disorders. In addition to improvements in the cognitive sphere, which is confirmed by the data of the P300 wave study of cognitive evoked potential, patients also showed a decrease in the severity of post-stroke motor defect. The most significant result was observed in patients with a lower degree of hemiparesis. Thus, the use of nicergoline in stroke patients improves the course of the rehabilitation period, accelerates the recovery of both cognitive and motor functions, and ultimately has a positive effect on the quality of life of patients. There are few studies on the effectiveness of nicergoline in Parkinson's disease, but there has also been a decrease in the severity of cognitive, emotional, personal, and behavioral disorders during therapy with this drug. The positive effect of nicergoline has also been noted in migraines. It consists in reducing the severity of headaches and stopping seizures. Indications for the appointment of nicergoline are also balance disorders caused by vestibular dysfunction. Experimental research data indicate the ability of this drug to improve the compensation of vestibular disorders due to its dopaminergic effect. In patients with balance disorders and dizziness as the leading symptom, positive dynamics in the condition, accompanied by an improvement in the quality of life, is noted in 44-78% of cases. The results of the clinical evaluation were confirmed by posturography data. In patients with dyscirculatory encephalopathy, after a course of nicergoline therapy, there was a decrease in dizziness, a decrease or disappearance of shakiness during the Romberg test. The drug is well tolerated. In particular, the nature, frequency, and severity of adverse reactions in patients receiving nicergoline are quite comparable to the effects of placebo. However, even if side effects do occur, they tend to decrease as therapy continues. Among the side effects that are quite typical for the entire class of ergot derivatives, complaints of dry mouth, constipation, and diarrhea should be noted. With oral administration of the drug, systolic and diastolic blood pressure do not change significantly, and only sometimes decrease slightly (without a statistically significant difference with patients receiving placebo). With a single intravenous injection of nicergoline, a decrease in blood pressure was detected as early as the 5th minute, which returned to its baseline level by the end of the first hour. In this regard, some caution is emphasized when administering nicergoline intravenously to patients of older age groups. Patients with initially high blood pressure may experience a bursting headache after administration of the drug. As found by B. Winblad et al., in the group of patients receiving nicergoline, side effects requiring discontinuation of treatment were observed in 8.5% of



cases, in the group receiving placebo — in 8.3% of cases. Against the background of nicergoline therapy, there are no statistically significant changes in vital functions and laboratory parameters, with the exception of a slight increase in serum uric acid levels in some cases, which is not accompanied by any clinical symptoms. However, this should be taken into account in patients with a history of gout.

Conclusions: Thus, nicergoline has been used in clinical practice for almost 40 years. During this time, significant experience has accumulated in the use of this drug in various pathogenetic conditions. And if initially nicergoline was considered as an exclusively "vascular" drug, leading to an improvement in cerebral blood flow due to its antagonistic effect on α 1-adrenergic receptors, then later a significantly wider range of its effects was demonstrated. Nicergoline has a positive effect on cholinergic and catecholaminergic neurotransmitter systems, inhibits platelet aggregation, improves cerebral metabolism by increasing oxygen and glucose utilization, and has anti-apoptotic, antioxidant, and neurotrophic activity. All this makes it possible to consider nicergoline not only as a symptomatic remedy, but also as a remedy with a neuroprotective effect. The combination of efficacy with good tolerability makes the drug sermion (nicergoline) very popular, especially in neurogeriatric practice.

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