THE ROLE OF THIOTRIAZOLINE IN THE ORGANISM

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ABSTRACT

The paper considers the synergy between the nootropic drug piracetam and the metabolic agent thiotriazoline that maintains energy metabolism and survival of neurons and other types of cells. Piracetam, a nootropic drug, a chemical pyrrolidone derivative, is used in neurological, psychiatric, and narcological practice. There is evidence on the positive effect of piracetam in elderly and senile patients with coronary heart disease. This drug is supposed to stimulate redox processes, to enhance glucose utilization, and to improve regional blood flow in the ischemic brain regions. Due to its action, the drug activates glycolytic processes and elevates ATP concentrations in brain tissue. Thiotriazoline is a compound that has antioxidant, anti-ischemic properties. The co-administration of piracetam and thiothriazoline is an innovation area in the treatment of stroke and other brain damages, especially in insulin resistance and high blood glucose levels. The paper considers the neurobiological properties of thiotriazoline and piracetam, which synergistically exert neuroprotective and neurotrophic effects.

As a result of the conducted researches it is established that with the development of experimental contact dermatitis and experimental pneumonia there is an increase in the level of stable metabolites of nitric oxide, increase of activity of total NO synthase and, at the same time, inhibition of L-arginine activity in the blood, thus these indicators were most expressed on the late stages of her forming of combine pathology(18^{th} day). The use of thiotriazoline in curative aims stipulated the decline of stable NO metabolites on 31.9% ($p \leq 0.05$), NOS in blood on 26.6% ($p_1 \leq 0.05$) and increase of content L-arginine on 34.5% ($p_1 \leq 0.05$) at experimental contact dermatitis

and experimental pneumonia as compared to the group of animals that did not yield to influence of this preparation.

At the same time, thiotriazoline activates the antioxidant system of enzymes and inhibits the processes of lipid peroxidation in ischemic areas of the myocardium. Thiotriazoline activates antiradical enzymes, contributes the economization of the consumption of tocopherol. The drug inhibits the formation of the initial and final products of the lipid peroxidation reaction in pathologically altered tissues. It protects the structural and functional integrity of the cardiomyocyte membranes, and also reduces myocardial sensitivity by adrenergic cardiostimulatory effects of catecholamines and prevents progressive inhibition of myocardial contractile function. Thiotriazoline increases the resistance of cardiomyocytes to hypoxia. Based on the results of the treadmill test, thiotriazoline significantly increased the duration of the load and the maximum achievable heart rate at the peak of the load, and also it reduced the overall average level of displacement of the ST segment and the level of systolic blood pressure. There are several differences between thiotriazoline and riboxine. Riboxine has a lesser effect on the cumulative shift level of the ST segment and the maximum heart rate and does not affect the level of hypertension. Acquired data are indicated that thiotriazoline has the correct antiischemic effect, and myocardial contraction becomes the most economical. The results of the stress test were confirmed by data from a 24-hour ECG monitoring, according to which in the future thiotriazoline there was a significant reduction in the time of myocardial ischemia and the duration of individual episodes of ischemia. 63 In conclusion, the first drugs for anti-ischemic therapy were vitamins of group B, but their effectiveness was refuted in clinical trials. The next drug was trimetazidine, since it has a high cytoprotective effect. This drug is especially effective in patients with stable angina. But thiotriazoline is a new anti-ischemic drug that includes anti-ischemic, metabolic and antioxidant activity with minimal side effects. Summing up, given the good tolerability, efficacy and safety, thiotriazoline can be recommended as a remedy of metabolic therapy for the treatment of IHD in the elderly.

Trimetazidine is a metabolic agent of proven efficacy in improving myocardial ischemia and angina. A comparative international multicenter randomized trial, assessed anti-anginal anti ischemic efficacy and safety of Trimetazidine (60 mg/d) and Thiotriazoline (600 mg/d) in symptomatic patients with chronic ischemic heart disease receiving the first line therapy. The study assessed the efficacy of the two drugs on total exercise duration, time to 1-mm ST segment depression, the number of angina attacks and nitroglycerin tablets consumed amount. Both drugs have demonstrated clinical efficacy equal for all primary and secondary endpoints.

COVID-19 leads to disruption of the blood coagulation system, to thrombosis, hypercoagulability, as a result, to an increased risk of strokes and heart attacks. During

COVID-19, endothelial dysfunction develops associated with NO deficiency with decrease in the level of SH compounds. Tiazotic acid (Thiotriazoline) has immunomodulatory, anti-inflammatory, antioxidant, anti-ischemic, cardio- and endothelioprotective, antiplatelet, hepatoprotective activity. Our studies conducted at the National Research Medical Center "University Clinic of ZSMU" with the participation of 57 patients (from 30 to 65 years old) with post-COVID syndrome, who received thiotriazol with basic therapy in either tablets (200 mg each) or suppositories Dalmaxin (0.2 g each) twice a day for 30 days. Inclusion criteria for the study were a positive PCR test for COVID-19; if the PCR test was negative, then the presence of IgM COVID-19 or IgG COVID-19 (with radiologically confirmed pneumonia). The following biochemical parameters were studied: C-reactive protein - by immunoturbodimetric method; D-dimer - by enzyme immunoassay; ferritin - by immunochemiluminescent method; endothelial NO-synthase (eNOS) - by ELISA method; alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyltransferase (GGT), total bilirubin; international normalized ratio (INR) and determination of platelet aggregation. During treatment with thiotriazoline, significant increase in the eNOS content was recorded, which indicated the presence of endothelioprotective activity of the drug. Thiotriazoline significantly reduced the level of D-dimer in the blood of patients, and also led to the normalization of INR. The established effects testified to the presence of antiplatelet and fibrinolytic action of thiotriazoline and its ability to reduce the risks of heart attacks and strokes in post-COVID syndrome. Thiotriazoline led to an objective improvement in general clinical parameters in patients with post-COVID syndrome, complaints of palpitations disappeared, blood pressure stabilized.

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