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BIOMARKERS OF ENDOTHELIAL FUNCTION AMONG PATIENTS WITH TREATMENT-RESISTANT HYPERTENSION

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Introduction. Cardiovascular diseases remain the leading cause of death, both in the world and in Ukraine in particular. Manually, there are about 9 million cases of death caused by hypertension (HT) in the whole world. One of the earliest target organs expressed in patients with hypertension are arterial vessels. The vascular endothelium, according to modern concepts, is an important endocrine organ. In response to stimulation, the endothelium responds with an increase in the synthesis of vasoactive substances. The most significant of these substances is nitric oxide (NO). Depending on the concentration, NO can be either an in activator or a producer of reactive oxygen species, such as peroxynitrites.

Today, the development of endothelial dysfunction (ED) is considered as one of the independent predictors of an unfavorable prognosis in cerebrovascular diseases. Taking into account the polymodal effect of NO on blood vessels and pro-inflammatory activation, the aspects of the relationship of NO with other biomarkers of ED are promising and at the same time insufficiently studied. Their significance in patients with treatment-resistant hypertension (TRH) is particularly interesting, that has determined the choice of the purpose for this study.

The aim of the study. To determine the levels of biomarkers of endothelial function among patients with treatment-resistant hypertension.

Materials and methods. To achieve this purpose and solve problems, an open, prospective, observational study is conducted. 50 patients with TRH, as well as 70 patients with stage II HT aged 45 to 65 years, were examined. Verification of hypertension was carried out in accordance with the order of the ESC-ESH Guidelines 2018. All patients were compared by age and social status.

Criteria for inclusion in the study: male and female patients from 45 to 65 years of age; discovered TRH; accurate prescription for stage II hypertension of at least 6 months; consent of patients to be followed-up.

Criteria of exclusion from the study: atrioventricular block II-III degrees; congenital or acquired hemodynamically significant heart defects; oncological diseases; alcohol dependence, drug addiction, the presence of mental disorders.

Determination of nitrate and nitrite ions. The method for determining the final stable metabolites of nitric oxide in the blood was performed according to the standard method using Griess' reaction. The amount of nitrites was calculated using nitrogen nitrite.

Determination of endothelin-1. the quantitative content of endothelin-1 was determined by the enzyme-linked immunosorbent assay using the Endothelin-1 ELISA kit (Biomedica, Austria). The plasma endothelin-1 content was expressed in fmol/l.

The results obtained. The level of endothelin-1 between groups of patients was significantly higher in patients with rah than in patients with stage II HT - 1.94 [1.18; 2.56] fmol/l versus 0.98 [0.62; 1.03] fmol/l, respectively, ($p < 0.05$). The level of NO_3 in patients with TRH was 12.30 [10.10; 15.60] mmol/l, which was significantly lower compared to the group of patients with stage II HT ($p < 0.05$). The NO_2 had the lowest value in the group of patients with TRH 6.10 [5.00; 7.20] mmol/l compared to the group of patients with stage II HT - 7.50 [6.20; 9.40] mmol/l, ($p < 0.05$). The median sum of NO_3+NO_2 metabolites in the group of patients with TRH was 18.50 [16.20; 21.40] mmol/l and was significantly lower than the value of this

indicator in the group of patients with stage II HT - 24.50 [20.10 ; 24.30] mmol/l, ($p<0.05$).

Conclusions. Among patients with TRH, there is a decrease in the level of NO metabolites, which characterizes the development of endothelial dysfunction, which is confirmed by an increase in the level of endothelin-1. The assessment of endothelial dysfunction among patients with TRH remains the subject for further scientific study. Determination of biomarker levels of endothelial dysfunction markers as predictors of cardiovascular complications that predict the adverse course of this disease requires further research.