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PRACTICAL RELEVANCE OF IMPAIRED WATER AND SALT METABOLISM IN PATIENTS WITH HEART FAILURE

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Abstract:

A prospective study was conducted with the participation of 396 patients hospitalized for decompensation of chronic heart failure. Hyponatremia was diagnosed with a decrease in serum sodium <135 mmol/l, while hyponatremia detected at admission was considered prehospital, and hyponatremia developed during treatment in a hospital setting. In patients with prehospital hyponatremia, the dynamics of sodium levels during hospitalization was analyzed, while in the case of a decrease in sodium levels ≥ 3 mmol/l compared with the baseline value, progressive hyponatremia was diagnosed. The influence of various types of hyponatremia on the course and hospital prognosis of the disease was determined, with the primary endpoint of the study being the combined indicator "death and/or transfer to the intensive care unit". Results. Patients with hyponatremia had more pronounced clinical signs of chronic heart failure. In patients with decompensated chronic heart failure, the presence of prehospital or hospital hyponatremia is associated with a more severe course of the disease and a worsening of the hospital prognosis.

Keywords: hyponatremia, chronic heart failure, decompensation, severity of the disease, prognosis, mortality

Currently, the attention of clinicians of various specialties is attracted by the problem of electrolyte metabolism disorders in inpatient patients. The most common electrolyte anomaly among patients hospitalized for any reason is hyponatremia [1]. It accompanies the course of a number of diseases and is associated with an increase in the duration of hospitalization, the economic costs of treatment and a worsening of the prognosis [2-4]. Among patients hospitalized with decompensation of chronic heart failure (CHF), hyponatremia upon admission to the hospital is detected in 5-35% of cases [5-8], while its prevalence depends on the patient population and the timing of determining the level of sodium in the blood. In most studies devoted to this issue, the prevalence and prognostic significance of reduced blood sodium levels recorded at admission to the hospital were studied [9-13]. At the same time, the incidence and clinical significance of hyponatremia that developed during hospitalization have not been practically studied. Nevertheless, the normal sodium level with a single measurement in the first days of hospitalization does not exclude the possibility of its further decrease against the background of the natural course of the disease and active diuretic therapy.

In addition, the frequency of progression of prehospital hyponatremia during hospital stay also remains unexplored. In this regard, the aim of our study was to assess the clinical and prognostic significance of various types of hyponatremia in patients hospitalized for CHF decompensation.

The purpose of the study. to evaluate the clinical and prognostic significance of various types of hyponatremia in patients hospitalized for decompensation of chronic heart failure.

MATERIAL AND METHODS. A prospective study was conducted with the participation of 396 patients hospitalized at the V.K. Gusak Institute of Emergency and Reconstructive Surgery in connection with decompensation of CHF for the period 2013-2016. The criteria for inclusion in the study were considered to be age over 18 years, hospitalization for decompensation of CHF and signed informed consent. The exclusion criteria were acute coronary syndrome, valvular and septal heart defects, myocarditis, hypertrophic and dilated cardiomyopathy, other conditions associated

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with hyponatremia (burn disease; acute gastrointestinal disorders; liver cirrhosis; nephrotic syndrome, glomerular filtration rate <15 ml/min, adrenal insufficiency, acute hypovolemia), concomitant pathology in the decompensation stage, pregnancy, oncological diseases, alcohol and drug addiction, participation in another clinical trial during the previous 30 days.

At admission to the hospital and during the hospital treatment period, the level of sodium in the blood serum was determined in all patients. The study was performed using ion-selective electrodes on an automatic biochemical analyzer "Cobas C 311". The electrolyte concentration was expressed in mmol/l. Hyponatremia was diagnosed with a decrease in serum sodium <135 mmol/l. The severity of hyponatremia was assessed in accordance with generally accepted recommendations: at sodium levels of 130-134 mmol/l, hyponatremia was regarded as mild, at 125-129 mmol/l — as moderate, and at <125 mmol/l — as severe [14-16]. Hyponatremia detected at admission was considered prehospital, and hospital — developed against the background of treatment in a hospital setting. In order to assess the timing of the development of hospital hyponatremia, electrolyte levels were examined every 3 days. In patients with prehospital hyponatremia, the dynamics of sodium levels during hospitalization was also analyzed, while in the case of a decrease in sodium levels ≥ 3 mmol/l compared with the baseline value, progressive hyponatremia was diagnosed.

To compare two samples of continuous variables that are subject to the normal distribution law, we used paired and unpaired Student t-criteria, with Wilcoxon criteria different from the normal distribution law. To compare more than two samples subject to the normal distribution law, a one—factor analysis of variance was used and, if there was a statistically significant difference between the groups, a pair comparison using the Scheffe criterion, and with the control group, the Dunnet criterion. If the distribution law differed from the normal one, a rank univariate Kruskal-Wallis analysis of variance was performed, and if there was a statistically significant difference between the groups, a comparison using the Dunn criterion was performed.

THE RESULTS OF THE STUDY. Patients with hyponatremia were significantly ($p < 0.05$) older than those with normal sodium levels, among them patients with anemia, concomitant chronic obstructive pulmonary disease, type 2 diabetes mellitus and impaired renal function were more common. There were no significant differences in body mass index, prevalence of concomitant hypertension, atrial fibrillation, myocardial infarction between the groups. Patients with hyponatremia had more pronounced clinical signs of CHF. According to echocardiography, they had a smaller ejection fraction and more pronounced diastolic dysfunction of the left ventricle compared to normonatremic patients. Analysis of drug therapy showed that patients with hyponatremia were more likely to receive thiazide and thiazide-like diuretics compared to patients with normonatremia. In the group with hospital hyponatremia, in addition, the frequency of administration of mineralocorticoid receptor antagonists was higher compared to the other groups of patients.

A detailed analysis of diuretic therapy during the active phase revealed differences in the doses of drugs: patients with hyponatremia higher doses of hydrochlorothiazide, indapamide and spironolactone were prescribed compared to patients with normal sodium levels. The highest doses of spironolactone were taken by patients with hyponatremia that developed during hospitalization. To assess the impact of various types of hyponatremia on the course and hospital prognosis of the disease, the frequency of development of the combined primary endpoint "death and/or transfer to the intensive care unit" and its individual components was analyzed. Patients with hyponatremia were more likely to develop adverse outcomes, and their hospital stay was longer compared to those with normal blood sodium levels. The reasons for the transfer to the intensive care unit were analyzed, and if there were several indications for the transfer, the leading one was chosen as the reason for the analysis.

It was revealed that patients with hyponatremia, compared with patients with normal sodium levels, developed gi more often during hospitalization-potency or hypoperfusion of organs requiring treatment in the intensive care unit. Among people with prehospital hyponatremia, it is more common to-the occurrence of refractoriness to diuretics was observed. According to the results of pathoanatomic studies, cardiovascular diseases were the leading causes of hospital mortality in both groups of patients, while cardiovascular mortality was higher among patients with hyponatremia. Persons with reduced sodium levels died more often than patients with normal electrolyte levels due to the progression of heart failure, while the statistical significance of the differences was achieved due to a subgroup of patients with prehospital progressive hyponatremia. It is noteworthy that death against the background of increasing symptoms of decompensation of CHF among this cohort of patients was several times higher than in the subgroups of patients with hospital and prehospital non-progressive hyponatremia and reached 31.3%.

Regression analysis adjusted for age, comorbid pathology and the severity of CHF showed that the presence of hyponatremia was associated with a significant increase in the risk of death and transfer to

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the intensive care unit. At the same time, prehospital hyponatremia had a greater prognostic value in relation to an unfavorable outcome compared to hospital. It is noteworthy that the progression of the existing
upon admission, hyponatremia significantly increased the risk of the end point. At the same time, hospital non-progressive hyponatremia retained its influence in the multifactorial model only on the risk of developing a combined endpoint, while its prognostic value in relation to individual components of the latter did not reach statistical significance.

Discussion. The results of the study confirm the literature data that hyponatremia is a frequent violation of the water-electrolyte balance in patients hospitalized for decompensation of CHF. According to the data obtained by us, in general, its frequency reached 33.3%, while in 48.5% of patients it occurred at the pre—hospital stage, and in 51.5% - during treatment in the department. Hospital hyponatremia developed on average by the end of the first week of hospital stay. Interestingly, by the time of discharge, spontaneous normalization of sodium levels occurred only in 7.8% of patients, in 25% of patients, on the contrary, progression of hyponatremia was observed. In the prevailing majority of cases, patients with decompensated CHF developed mild hyponatremia, while the frequency of moderate and severe hyponatremia was low (84.8% and 4.6%, respectively). It is believed that a decrease in blood sodium levels in CHF is a variant of hypervolemic hypernatremia and is caused mainly by a violation of water excretion by the body [22, 23]. At the same time, the pathophysiological basis for the development of hyponatremia in this case is excessive neurohumoral activation in conditions of a decrease in cardiac output. Despite the absolute excess of water in the extracellular space of the body during decompensation of CHF, the effective volume of circulating blood remains low, which through the system of baroreceptors promotes non-osmotic stimulation of the secretion of antidiuretic hormone and effectors of the renin-angiotensin-aldosterone system. Such neurohumoral activation is compensatory in nature and is aimed at normalizing perfusion pressure by limiting the excretion of sodium and water. The release of antidiuretic hormone directly enhances the reabsorption of water in the collecting tubules of the kidneys, whereas angiotensin-2 and norepinephrine limit the delivery of water to the kidneys by reducing their perfusion and, consequently, contribute to a decrease in its
division [24]. In addition, a decrease in cardiac output and a high level of angiotensin-2 are powerful stimuli for thirst, which leads to an
increase in water consumption.

The degree of neurohumoral activation in CHF, and hence the risk of hyponatremia, as a rule, correlates with the severity of cardiac
dysfunction, which is confirmed in our study. Indeed, patients with hyponatremia had more severe clinical (FC according to NYHA,
severity of congestion, test distance with 6-minute walking) and echocardiographic (degree of systolic and diastolic dysfunction) signs of CHF compared to patients with normal blood sodium levels. It cannot be excluded that active diuretic therapy also makes a certain contribution to the development of hospital hyponatremia. Thus, according to the results of our study, patients with hyponatremia received thiazide, thiazide-like diuretics and spironolactone significantly more often and in higher doses. It is noteworthy that the highest doses of spironolactone were taken by patients with hyponatremia that developed during hospitalization. Of course, ensuring adequate sodium and diuresis is the most important factor in preventing the symptoms of CHF decompensation, and with the development of signs of hypervolemia, it is a necessary condition for their elimination. Nevertheless, it is worth remembering that the use of diuretic therapy may be accompanied by the development of undesirable side effects, among which various electrolyte disorders, including hyponatremia, occupy a leading position. According to the literature, hyponatremia is most often observed when using thiazide and thiazide—like diuretics, less often - loop and potassium-sparing [22]. Thiazide diuretics have a mixed mechanism of hyponatremic action: they enhance the effect of antidiuretic hormone at the level of collecting tubes and at the same time stimulate natriuresis. The development of hyponatremia when using spironolactone, in addition to the natriuretic effect of the drug, is associated with its ability to block the release of sodium from the cell, which leads to an increase in the intracellular electrolyte content and a decrease in its concentration in the blood.

Thus, active diuretic therapy in patients with decompensated CHF, especially with the use of thiazide, thiazide-like diuretics and high doses of spironolactone, should be carried out with caution, under the control of blood electrolyte levels, which is regulated by modern guidelines [21]. It remains unclear whether hyponatrimia per se is a factor determining the deterioration of the prognosis in CHF, or it only acts as a laboratory marker of the severity of the disease. To answer this question, further large-scale research is needed. However, in any case, a decrease in blood sodium levels can serve as a simple and reliable tool for risk stratification in patients with decompensated CHF, as it is associated with a deterioration in the hospital prognosis of the disease and an extension of the hospitalization period.

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CONCLUSION. Hyponatremia is a frequent violation of the water-electrolyte balance in patients hospitalized for decompensation of CHF. In general, its frequency reaches 33.3%, while in 48.5% of patients it develops at the pre-hospital stage, and in 51.5% during treatment in the department. By the time of discharge, spontaneous normalization of sodium levels occurs only in 7.8% of patients, in 25% of patients, on the contrary, there is a progression of hyponatremia. The presence of both prehospital and hospital hyponatremia is associated with a more severe course of CHF, deterioration of the hospital prognosis and lengthening of hospital stay. The progression of hyponatremia present at admission significantly increases the risk of death and transfer to the intensive care unit.

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