

Beat The Course of Impaired Water and Salt Metabolism in Patients with Heart Failure

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Abstract:

To study the relationship between violations of water-salt homeostasis upon admission to the hospital in patients hospitalized for decompensation of CHF, III–IV FC according to the NYHA classification and a long-term annual prognosis. This prospective follow-up study is based on clinical and anamnestic data and the results of a one-year follow-up of 111 patients – study participants hospitalized for decompensation of CHF in GBUZ City Clinical Hospital No. 24 DZM in January 2015 - February 2016. In patients hospitalized with decompensation of CHF, in the presence of violations of water-salt homeostasis upon admission to the hospital, the relative risk of annual mortality increased by 1.43 times by the end of the follow-up year (HR=1.43; 95% CI: 1.10-1.87; $p<0.01$) compared with patients who had normal levels of sodium and potassium in blood on admission.

Keywords: acute decompensation of HF, pathogenesis, hyponatremia, hypokalemia, hyperkalemia, prognosis.

Introduction

Congestive CHF is a widespread finale for etiologically different forms of diseases of the cardiovascular continuum [1]. At the same time, it is classified as a disabling and growing disease in terms of the number of occurrences for the countries of Europe and the USA [2, 3]. And, despite significant therapeutic successes, CHF still remains a serious public health problem [4], characterized by a high probability of rehospitalization and death, especially in the first months after discharge from the hospital [3, 5], which indirectly leads to a significant economic burden [5].

A number of factors are pathogenetically involved in the decompensation mechanism, while the clinical picture manifests itself as a sharp onset and increase in symptoms and manifestations of CHF [6] (such as shortness of breath, edema, weakness and anxiety [7]), often requiring immediate medical attention [6]. It is worth noting that electrolyte

imbalance at admission is considered to be a common and potentially lethal FR for patients of the intensive care unit [8], nevertheless, its effect on the prognosis and the possibility of use as a predictor in patients with decompensation of CHF at the moment, they are not yet sufficiently studied.

The purpose of the study

To study the relationship between violations of water-salt homeostasis upon admission to the hospital in patients hospitalized for decompensation of CHF, III–IV FC according to the NYHA classification and a long-term annual prognosis

Materials and methods

This prospective follow-up study is based on clinical and anamnestic data and the results of a one-year follow-up of 111 patients-study participants hospitalized for decompensation of CHF GBUZ "GCB No. 24 DZM" in January 2015— February 2016. To collect information about the condition of patients who, for one reason or another, could not come to the consultation after six months and a year after discharge from the hospital, a standard telephone questionnaire of the patients themselves or their family members was used. The study was "taken into consideration" by the local Ethics Committee of the Sechenov First Moscow State Medical University of the Ministry of Health of Russia (Sechenov University).

Inclusion criteria I: verified diagnosis of CHF, hospitalization due to an increase in CHF symptoms, edema. Criteria for non-inclusion /exclusion I: acute (de novo) HF, acute MI during the last month, ACS, massive (de novo) pulmonary embolism, patients with active myocarditis and endocarditis, as well as patients who underwent heart and large vessels surgery and/or endovascular intervention during the last month. In addition, the study did not include patients with cirrhosis of the liver, with chronic kidney disease (CKD) (who regularly receive programmed hemodialysis), as well as alcohol abusers who lead an antisocial lifestyle, who do not understand the goals and objectives of the study due to cognitive impairments. Secondary causes of electrolyte shifts such as vomiting, diarrhea, and diabetic ketoacidosis were taken into account and excluded.

Patients were excluded from the study if they did not want to continue participating in it, or if there was evidence of an active oncological process; with the progression of CKD, requiring the addition of programmed hemodialysis. All the data of the laboratory and instrumental examination were obtained during their routine execution. The creatinine level was determined using the Joffey's kinetic method, the plasma electrolyte level was determined using the Olab-650 analyzer. The body mass index (BMI) was calculated as the ratio (body weight in kg) / (height in meters squared), being considered elevated at values above 25 kg / m². Obesity was diagnosed at BMI values above 30 kg/m². Anemia was diagnosed at a hemoglobin level below 120 g / l for women and 130 g / l for men (according to the standards adopted in GBUZ GCB No. 24 DZM in

2015-2016). To convert creatinine to the usual for Russia mmol / l, it is recommended to multiply the creatinine level in mg/ l by a factor of 88.4 [9]. Acute renal injury was considered an increase in creatinine levels by more than 26.5 mmol/l within 48 hours, which is consistent with national recommendations [10].

Results

All 111 patients included initially had CHF and were hospitalized due to an increase in CHF symptoms and signs of fluid retention in the body. The male to female ratio was about like 51:6; emergency admission to the cardiac rehabilitation unit was required for 63.96% of patients hospitalized with OV FC by NYHA. The average age of patients was 71 ± 12 years; the BMI of patients was 30 ± 6 kg/ m², and 47.75% of patients were obese.

Violations of water-salt homeostasis upon admission to the hospital were recorded with a 33.33% frequency among patients hospitalized for decompensation of CHF, OOO–OV FC according to NYHA. Patients with hyponatremia (17.12% of cases), hypokalemia (12.61% of cases) and hyperkalemia (9.01% of cases) were isolated from the group of patients with impaired water-salt homeostasis upon admission to the hospital. Patients with hypernatremia were excluded from the study due to the appearance of new data for the presence of an active oncological process. The data of clinical and laboratory-instrumental examination indicate the predominance of the frequency of occurrence in the cardiovascular continuum of such comorbid diseases as: hypertension - in 90.09%; it was followed in descending order by: CKD and CHD with 85.59% and 75.68% frequency of occurrence, respectively; then atrial fibrillation in 67.57% of cases.

Features of hemodynamics in decompensated patients with CHF OOO–OV FC with disorders of water-salt homeostasis: upon admission to the hospital, there were no statistically significant differences between groups and subgroups. Indicators of renal function in patients hospitalized for decompensation of CHF and who had violations of water-salt homeostasis upon admission to the hospital were statistically different only when comparing subgroups of patients. The subgroup with impaired water-salt homeostasis upon admission to the hospital was characterized by a statistically significant association of hyperkalemia with a higher creatinine level by 29.36%, urea by 63.75 and, as a consequence, a lower GFR by 42.11%, compared with patients who had normal sodium and potassium levels upon admission to the hospital.

Discussion

The problems of stagnant sleep. According to current ideas, CHF is a manifestation of various forms of cardiac [1] and comorbid extra-cardiac pathology [13], at the final stage of progression of the cardiovascular continuum, manifesting itself as the inability of the myocardium to pump enough blood to meet the body's oxygen needs [1]. The prevalence of CHF in the USA is 5.8 million people [13], which corresponds to 1.8%

of the population; CHF among the population of European countries varies from 0.4 to 2% of the population [14]. On the other hand, in the older age group, taking into account the aging of the population, an increase in the prevalence of CHF is expected by about 20% [15]. The prevalence of clinically pronounced CHF OO–OV FC according to the New York classification among Russian patients is 4.5% according to the Russian study EPOCH (Epidemiological Examination of patients in the European part of Russia), and its prevalence is progressively increasing, increasing by an average of 1.2% (per mille) per year [16].

An example of a particularly specific pathophysiological profile of patients hospitalized for decompensation of CHF, OOO-OV FC according to NYHA and with a violation of water–salt homeostasis may be that in this work hypertension and coronary heart disease, respectively, was not a typical comorbid disease, with a statistically significant five-fold decrease in the odds ratio (OR 0.25; 95% CI: 0.05–1.06; $p=0.0399$ and OR 0.35; 95% CI: 0.13–0.95; $p=0.0331$ for hypertension and coronary heart disease, respectively), compared with patients who had normal levels of sodium and potassium upon admission to the hospital. From a pathogenetic point of view, a decrease in cardiac output during HF leads to activation of the sympathetic nervous system and RAAS [2]. This leads to the maintenance of a high plasma concentration of aldosterone with increased reabsorption of sodium and water in the terminal part of the nephron to maintain perfusion pressure in tissues, as a result, it turns out that renal regulation is the most vulnerable place of sodium/ potassium metabolism [3].

Such fluctuations are important, besides, there is evidence [3] that a decrease in potassium levels during hospitalization has an unfavorable prognostic value after discharge of patients hospitalized for decompensation of CHF, which does not depend on either the initial potassium level or its level at discharge from the hospital. The hyperkalemia subgroup was statistically significantly characterized by an increase in the level of urea by 63.75 and creatinine by 29.36% and, as a consequence, a decrease in GFR by 42.11% compared with patients who had normal levels of sodium and potassium upon admission to the hospital. Sodium homeostasis. The plasma level of sodium directly depends on the secretion of antidiuretic hormone (ADH) in the posterior pituitary lobe [19], the concentration of which in CHF increases in response to a decrease in blood pressure when the sympathetic nervous system (SNS) is activated by stimulation of baroreceptors [20]. However, it should be borne in mind that according to experimental data, the regulation of ADH secretion on the one hand and SNS and RAAS on the other function differently in essence in different patients with CHF [20]. Activation of ADH secretion leads to an increase in the reabsorption of free water in the collecting tubes of nephrons, which ultimately leads to the appearance of hyponatremia [19]. Dysnatremia is a marker of a significantly compromised prognosis in CHF, regardless of LVEF [21].

Potassium homeostasis. On the other hand, if we talk about potassium homeostasis, it is worth noting that potassium is primarily an intracellular ion and even slight

fluctuations in serum concentration in absolute values (within 1 meq /l [25], which corresponds to 1 mmol /l [9]) lead to a 25% shift in the ratio intracellular to extracellular concentrations [25]. Physiological endogenous or exogenous pharmacological increase in the level of insulin or catecholamines stimulating β_2 receptors most often contributes to a significant redistribution of potassium in favor of the intracellular space [25]. There was also a negative correlation between potassium levels and plasma renin and norepinephrine activity [18]. On the other hand, hypokalemia, which occurs as a consequence of intracellular potassium redistribution outside the state of alkalosis, hyperinsulinemia and hypercatecholema, is very rare [25], and it is rather a consequence of an increase in aldosterone levels as a consequence of neurohormonal activation in CHF on the one hand, or the iatrogenic effect of diuretic therapy on the other [26]. It is characterized by an increase in the frequency of life-threatening arrhythmias [5], and sudden cardiac death due to accelerated depolarization, increased automatism and elongation of the action potential [27].

According to the literature [5], the incidence of hypo- / hyperkalemia was studied in a large cohort of patients with CHF (n = 6,073) and is about 15%, and for hypokalemia – 11% (at $K < 4.0$ mmol / l) and 4% for hyperkalemia (at $K > 5.5$ mmol / l). In this study, hypokalemia was detected in 12.61% of cases and hyperkalemia in 9.01% of cases, and as mentioned above is associated with the development of life-threatening arrhythmias in patients with CHF, however, if patients with initial hypokalemia revealed a statistically significant difference in average potassium values by 27.27% from the conditionally normal potassium level (in the control group: patients with baseline normonatremia and normokalemia), then in patients with baseline hyperkalemia, even large differences (31.81%) did not reach a statistically significant difference, possibly due to the small number of observations. According to the results of one-year follow-up in this work, it was found that violations of water-salt homeostasis upon admission to the hospital was a predictor of an unfavorable long-term prognosis for patients hospitalized for decompensation of CHF. In total, 33.33% frequency of occurrence of violations of water-salt homeostasis of sodium and potassium was detected upon admission to the hospital. It is worth noting that at the same time, the chloride level was statistically significantly lower by 3.81% initially in patients with hyponatremia upon admission to the hospital (and this trend was not observed in hypo-/ hyperkalemia).

Most often, hospitalization with decompensation of CHF is primarily associated with the gradual progression of congestive phenomena, and not with a decrease in cardiac output, leading to an increase in LV preload [13]. Increased LV filling pressure contributes to the progression of CHF, leading to subendocardial ischemia and myocardial cell damage [13]. However, as mentioned earlier, the mechanisms underlying the regulation of the ADH system on the one hand and SNS and /or RAAS on the other may be different in nature in patients with CHF [20] already at the initial stages of progression of the pathology of the cardiovascular continuum.

Over the past 20 years, the prognosis of outpatient patients with CHF has improved significantly; significant progress has been made in treatment, however, a high level of rehospitalization persists and in the age group over 65, CHF is still the most common cause of repeated hospitalizations of patients [13]. And the very hospitalization for CHF is a predictor of an unfavorable prognosis, especially since up to 18% of CHF decompensations occur during the first month after discharge from the hospital [28], and slightly less than 3% (417 patients out of 14,374 thousand) with terminal CHF survive until the fourth episode, according to the registry DPTOMOZE-HF [24]. According to some data, the annual mortality of patients after discharge from the hospital reaches 15%, and rehospitalization reaches 30% in the period from 30 to 60 days after discharge from the hospital [13]. A large Russian multicenter study ORACLE-RF (the first open study of acute decompensation syndrome of HF and concomitant diseases in the Russian Federation) reports a mortality rate of patients with congestive CHF from 13% to 43% by the end of the month and year after discharge from the hospital [28]. Such a high mortality rate, according to current ideas, is explained by complex multiple organ damage [14, 16].

In this study, 19.82% total mortality was detected within a year after discharge from the hospital; in the presence of hyponatremia and /or dyskalemia at admission to the hospital, an increase in the relative risk of annual mortality was revealed by 1.43 times (HR=1.43; 95% CI: 1.10–1.87; $p<0.01$), compared with patients, who had normal levels of sodium and potassium upon admission. In the hyponatremia subgroup, there was a statistically significant increase in the relative risk of death by 1.4 times (HR=1.41; 95% CI: 0.99–2.01; $p<0.05$), compared with patients who had normal levels of sodium and potassium at admission to the hospital. In the hypo-/hyperkalemia subgroups, there was a statistically significant increase in the relative risk of death by 1.4 and 2.3 times, respectively (for hypokalemia and hyperkalemia respectively (HR 1.39; 95% CI: 0.93–2.07, $p<0.05$; and HR 2.23; 95% CI: 1.04–4.78; $p<0.05$), according to compared with patients who had normal levels of sodium and potassium at admission to the hospital.

Conclusion

This study first of all revealed an association between electrolyte imbalance at admission and annual mortality. In patients hospitalized for decompensation of CHF, OOO–OV FC according to NYHA with violations of water-salt homeostasis of sodium and /or potassium upon admission to the hospital, there is an increase in the relative risk of annual mortality by 1.43 times by the end of the follow-up year (HR=1.43, 95 % CI: 1.10-1.87, $p<0.01$), compared to patients who had normal levels of sodium and potassium upon admission to the hospital. Neither hypertension, nor coronary heart disease – not typical in frequency of occurrence for patients hospitalized for decompensation of CHF, OOO–OV FC according to NYHA with violations of water-salt homeostasis of sodium and potassium upon admission to the hospital, with a statistically significant decrease in frequency of occurrence by 4 and 3 times,

respectively (OR=0.25; 95% CI: 0.05–1.06; $p=0.0399$ and OR=0.35; 95% CI: 0.13–0.95; $p=0.0331$), compared with patients who had normal levels of sodium and potassium at admission.

In the subgroup of patients with hyponatremia at admission to the hospital, there was a statistically significant increase in the relative risk of annual death by 1.41 ra (HR=1.41; 95% CI: 0.99–2.01; $p<0.05$), compared with patients who had normal levels of sodium and potassium at admission to the hospital. In the subgroup of patients with hypo-/hyperkalemia, there was a statistically significant increase in the relative risk of annual death by 1.4 and 2.2 times, respectively: HR=1.39; 95% CI: 0.93–2.07; $p<0.05$ and HR=2.23; 95% CI: 1.04–4.78; $p<0.01$), compared with patients who had normal levels of sodium and potassium at admission. The hyperkalemia subgroup was statistically significantly characterized by an increase in the level of urea by 63.75 and creatinine by 29.36% and, as a consequence, a decrease in GFR by 42.11% compared with patients who had normal levels of sodium and potassium upon admission to the hospital.

References

1. Kemp WL, Brown TG, Burns DK. Pathology: the big picture [In-ternet]. 2013 [cited 2018].
2. Filippatos TD. Hyponatremia in patients with heart failure. World Journal of Cardiology. 2013;5 (9):317
3. Salah K, Pinto YM, Eurlings LW, Metra M, Stienen S, Lombardi C et al. Serum potassium decline during hospitalization for acute decompensated heart failure is a predictor of 6-month mortality, independent of N-terminal pro – B-type natriuretic peptide levels: An individual patient data analysis. American Heart Journal. 2015;170 (3):531–542. e1.
4. DeWolfe A, Lopez B, Arcement LM, Hebert K. Low serum sodium as a poor prognostic indicator for mortality in congestive heart failure patients: low serum sodium and mortality. Clinical Cardi-ology. 2010;33 (12):E13–7.
5. Hoss S, Elizur Y, Luria D, Keren A, Lotan C, Gotsman I. Serum potassium levels and outcome in patients with chronic heart failure. The American Journal of Cardiology. 2016;118 (12):1868–74.
6. Teerlink JR, Alburikan K, Metra M, Rodgers JE. Acute decompensated heart failure update. Curr Cardiol Rev. 2015;11 (1):53–62.
7. Mareev V. Yu., Ageev F. T., Arutyunov G. P., Koroteev A. V., Revishvili A. S. National recommendations of VNOK and SSHF on the diagnostics and treatment of chronic heart failure (third review) Approved by OSSN Conference, December 15, 2009. Russian Heart Failure Journal. 2010;11 (1):3–62.]
8. Lindner G, Exadaktylos AK. Störungen des Natriumhaushalts beim Notfallpatienten: Salz in der Suppe der Notfallmedizin. Der Anaes-thesist. 2013;62 (4):296–303.

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9. Laboratory medicine: the diagnosis of disease in the clinical laboratory. Second edition. Laposata M, editor. -New York: McGraw-Hill Education Medical; 2014. 480 p.
 10. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney inter.* 2012; (2):1–138.
 11. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Journal of the American Society of Echocardiography.* 2015;28 (1):1–39. e14.
 12. 1R: a language and environment for statistical computing [Inter-net]. [cited 2018].
 13. Deubner N, Berliner D, Frey A, Güder G, Brenner S, Fenske W et al. Dysnatraemia in heart failure. *European Journal of Heart Failure.* 2012;14 (10):1147–54.
 14. Ganiger H, Ravishankar AG. Dysnatraemia in heart failure: a descriptive study. *Int J Scientific Study.* 2015;3 (6):81–5.
 15. Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness: The ESCAPE Trial. 2005;294 (13):1625-33.
 16. Gheorghiade M, Rossi JS, Cotts W, Shin DD, Hellkamp AS, Piña IL, et al. Characterization and Prognostic Value of Persistent Hyponatremia in Patients With Severe Heart Failure in the ESCAPE Trial. *Archives of Internal Medicine.* 2007;167 (18):1998.
 17. Fonarow GC, Abraham WT, Albert NM, Gattis WA, Gheorghiade M, Greenberg B et al. Organized program to initiate lifesaving treatment in hospitalized patients with heart failure (OPTIMIZE-HF): rationale and design. *American Heart Journal.* 2004;148 (1):43–51.
 18. Rastegar A. Serum Potassium. Walker HK, Hall WD, Hurst JW, editors. *Clinical Methods: The History, Physical, and Laboratory Examinations* [Internet]. 3rd ed. -Boston: Butterworths; 1990 [cited 2018].