IMPAIRED RENAL FUNCTION AND ANEMIA IN PATIENTS WITH CHRONIC HEART FAILURE

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Abstract *Chronic heart failure (CHF) accompanies most cardiovascular diseases and is their outcome, remaining unchanged One of the main reasons for the high level of disability and mortality of patients. Increasing heart failure over time exceeds the danger to the patient's life of the disease that caused heart failure. Renal function has a great influence on the prognosis and outcome of CHF. Kidney failure is considered as a factor, determining the survival rate of patients with left ventricular dysfunction. Currently, the diagnosis of renal dysfunction in patients with CHF is based on the determination of concentration Serum creatinine levels, glomerular filtration rate (GFR) and/or the presence of microalbuminuria (MAU) or macroalbuminuria. At the same time, the issue of tubule function and the daily profile of renal function (daily filtration rate) in patients with CHF remains insufficiently studied. Anemia associated with CHF continues to attract the attention of researchers. This is the purpose of this work.*

Keywords: *chronic heart failure, kidney disease, anemia, microalbuminuria, N-acetyl–β-dexosaminidase.*

INTRODUCTION

As the causes of anemia in CHF, along with neurohormonal factors and proinflammatory cytokines that lead to the development of anemia in chronic diseases (AHZ) as a result of iron deficiency, decreased EPO production and suppression of bone marrow function, it is assumed that kidney dysfunction makes a certain contribution to its development. In the study of patients with anemia, 21% were people with iron deficiency, 8% — with a deficiency of other hematopoietic factors (including vitamin B12 and folic acid), 13% — with other specified causes of anemia (including CRF), and in 58% of patients, no specific cause of anemia was found. The condition of the latter was designated as AHZ. It should be emphasized that absolute or relative iron deficiency may occur in patients with CHF both in the presence of CHF and without it; decreased renal function associated with the development of deficiency EPO is often found in CKD. As is known, anemia of any etiology can cause congestive CHF and is associated with a decrease in LV contractility and kidney function, at the same time, anemia itself is a frequent comorbid condition in patients with CHF and CPN. This made it possible to combine the combination of anemia, CHF and CRF with the term COLOR, which has attracted a lot of attention from the medical community in recent years. Published clinical and experimental data confirm the close relationship between anemia, CRF and congestive heart failure. At the same time, each of

the states worsens the course of the other, creating thus, the "vicious circle" of disease progression.

MATERIALS AND METHODS OF RESEARCH

115 patients with CHF were examined, including 76 women and 39 men, whose average age was 60.4±1.2 years. The distribution of patients according to the etiology of CHF: ischemic heart disease (CHD) + arterial hypertension (GB) - 54 patients (47%), CHD – 16 patients (14%), GB – 35 patients (30%), rheumatic heart defects outside the activity of rheumatism - 10 patients (9%). Patients with kidney disease and/or endocrine pathology were not included in the study. All patients were divided into groups depending on the FC CHF according to the NYHA classification (1994). The first group consisted of patients with CHF I FC – 48 people, 45 patients had CHF II FC (group 2), 22 patients had CHF III-IV FC (group 3). The control group consisted of 17 practically healthy people (average age - 60.1 ± 1.3 years). All studies were conducted with the informed written consent of the patients. Renal filtration function was assessed by GFR using the Cockcroft-Gault formula and creatinine clearance using the Rehberg-Tareev method. The daily filtration rate was determined by calculating the GFR using the latter method 8 times during the day every 3 hours, At the same time, the analysis took into account the average values of creatinine clearance during the day and at night. The presence of MAU was determined in all patients. The activity of N – acetyl – β– D– hexosaminidase (NAG) in the morning urine portion was determined as an indicator of the functional activity of the tubules. The daily diuresis was taken into account (the average values of minute diuresis during the day and at night were calculated), the ratio of daily diuresis was calculated. Diuresis/nocturnal diuresis (D/ND), the range of fluctuations in the relative density of urine (OPM) was estimated by Zimnitsky's sample. The presence of anemia was determined by generally accepted criteria using the following indicators: the number of red blood cells, hemoglobin concentration, hematocrit (Ht) values, erythrocyte indices (MCV, MCH, MCHC). We evaluated the parameters of iron metabolism – serum iron (CS), total serum iron binding capacity (GSS), transferrin iron saturation coefficient (CST).

THE RESULTS AND THEIR DISCUSSION

The serum creatinine level in patients with CHF I FC was 85.5 ±4.2 mmol/l, with FC II - 89.9 ± 3.2 mmol/l, III-IV FC – 107.2 ± 8.4 mmol/l, in the control group – 80.2 ± 1.2 mmol/ l, while there were no significant differences between them. indicators of the control group and patients with III-IV FC. When determining GFR, differences were found between the data in the control group and in patients with CHF II FC and III-IV FC. GFR significantly decreased as the CHF FC increased. In 38% of patients with I FC, GFR exceeded 90 ml/min/1.73 m2, at II FC - in 25% of patients, and normal GFR values were absent in patients with III-IV FC HSN. A moderate decrease in GFR (60-89. 9 ml/min/1.73 m2) was observed in 38% of patients with FC I, FC II – in 39%, FC III-IV – in 58% of patients. Marked decrease in GFR (30-59. 9 ml/min/1. 73m2) at FC I was detected in 19% of cases, at FC II – in 33%, at FC III–IV - in 33% of cases. Y 4% In the examined patients with FC I,

in 3% – with FC II and in 8% – with FC III-IV, GFR was less than 30 ml/min/1.73 m2. In patients with FC I, the average CP in the daytime was reduced by 51%, in patients with FC II - in 61%, in 76% of patients with III-IV FC. All calculated daily average KP values differ significantly from the average values of the control group. The average GFR at night, remaining at the level of normal and subnormal values in patients with I FC, is significantly reduced when FC III-IV. The analysis of the daily filtration profile revealed the following. GFR was significantly higher at night than during the day and was determined in 72% of patients with FC I, 73% with FC II and 66% with FC III-IV, i.e. in patients with low classes of CHF, the predominance of GFR at night It is registered more often and reliably: in patients with FC I, the average difference between GFR during night and daytime hours is 21.3%, in patients with FC III-IV-16.0%. Studies of NAG in urine have shown it The maximum activity was in patients with stage I CHF, and as the severity of FC worsened, the enzyme activity decreased. Thus, an increase in the level of NAG in urine was found in 71% of patients with I FC, in In 67% of patients with II FC and in 60% of patients with III-IV FC. NAG values in patients with FC I and FC CHF II significantly exceeded the indicators of the control group. The daily rhythm of diuresis, when compared The mean values of D/N were significantly more impaired in patients with I and II FC. Thus, DD/ND in patients of this group was 0.89±0.07 (in the control group – 1.2±0.08), in patients with II FC – 0.84±0.04, and in patients with III-IV FC – 0.98±0.06. The OPM fluctuation range also depended on FC Swiss franc. Less than 7 was determined in 7% of patients with FC I, in 19% - with FC II and in 23% - with III-IV FC. In the group of patients with FC I, the hemoglobin concentration was 139.6 ± 2.7 g/l, FC II – 136.2 ± 1.8 g/l, FC III-IV - 122.0 ±6.4 g/l, in the control group -139.4 ±4.8 g/l. Significant differences have been identified between the indicators in the control group and in patients with III-IV FC. The number of patients with hemoglobin levels less than 120 g/l increases with the progression of CHF according to FC: at FC I - 0%, at FC II-0%. In 5% of cases (3 out of 45 people), in 30% of cases (3 out of 10 people) with III-IV FC. When studying the parameters of iron metabolism (LV, OHSS, CST) and analyzing the number of red blood cells, blood pressure values and erythrocyte indices, there were no significant differences between patients with CHF in the group as a whole and the control group. At the same time, patients with III-IV FC had a decrease in hypertension to 0.35, while in patients with I and II FC it was 0.40. The correlation between the indicators was studied for hemoglobin and renal functional status (GFR, MAU, NAG, serum creatinine). No reliable relationship has been established. According to available data, the pathology of tubules and interstitium is considered a late manifestation of nephropathy in CHF, secondary to glomerular lesion. In recent years, it has been shown that damage tubules and interstitium are not only a manifestation, but also an independent factor in the development and progression of renal failure in many nephropathies. It is known that the determination of enzyme activity in urine can serve as an important criterion for the degree of damage to the renal tubular apparatus in various pathological processes. Depending on the degree of damage to the urine, enzymes with different intracellular localization are

sequentially isolated. Thus, with a slight and moderate degree kidney damage in urine increases the activity of enzymes associated with hand cells (cytoplasmic and lysosomal). With significant damage to the kidneys, an increase in the content of mitochondrial enzymes in the urine is observed, which, as a rule, corresponds to cell necrosis. NAG is a lysosomal enzyme, the increased activity of which is characteristic of damage to the proximal tubules. The established maximum activity at the first CHF FC may indicate minor kidney damage, and a decrease in the rate of increase in CHF FC It can be considered as an increasing damage to the renal tubular apparatus. Most researchers associate the presence of MAU with impaired glomerular filter function and increased intraclubular pressure. The increased permeability of the glomerular filter may be due to generalized vascular endothelial dysfunction, a change in the charge of the anionic components of the glomerular basement membrane. The role of proximal reabsorption of albumin and its degradation during passage through the tubules in the genesis of MAU requires further study. Currently, there is no clear answer to the question of which part of the kidney is affected by MAU. The analysis of the obtained data showed that in patients with CHF, against the background of the absence of protein in a single morning portion of urine, determined by conventional methods, there is damage to the glomerular apparatus of the kidneys, as evidenced by the detected MAU. The degree of MAU correlates with the exacerbation of CHF FC. Given the significant increase in the activity of NAG, compared with the control group, already at the first FC CHF and the detection of MAU only in patients with III-IV FC, it can be assumed that in patients with CHF, damage to the tubules precedes damage to the glomeruli. The degree of decrease in GFR it corresponded to an increase in FC CHF: at I – II FC - slightly, at III-IV FC - significantly. Other studies have also shown that glomerular filtration in CHF is maintained at a fairly high level for a long time, significantly decreasing only in patients with severe CHF decompensation. We found that with CHF, the daily rhythm of renal filtration function also changes. Significant (compared to the control group) decrease GFR in the daytime was observed in all the examined groups. Significant decrease in GFR at night (relative to the control group) is determined only in patients with III-IV FC. In addition, patients with In FC I and II, the difference between the mean GFR values during the daytime and at night (towards a relative increase in filtration at night) is recorded with a higher level of confidence than in patients with FC III. In other words, patients with FC I and II have a distinct “decrease” in the daily clearance of endogenous creatinine. It is known that an increase in filtration at night is associated with an improvement in the kidneys are at rest and in a horizontal position. There is a definite relationship between the value of GFR and the level of serum creatinine (CC), namely, an increase in CC with a decrease in GFR, but this relationship is not linear. With a moderate decrease in GFR (in patients with I, II FC CHF), GFR increases unreliably and clearly increases only in patients with III-IV FC. This fact once again confirms the opinion that An indicator of kidney damage, especially in the early stages of CHF, is GFR rather than QOL. Natural The predominance of ND over DD was observed only in patients with I-

II FC. Despite the coming oliguria, the average range of OPM fluctuations was within the normal range. At the same time, in patients with III-IV FC In FC, there was an increase in the number of cases with a reduced range of OPM fluctuations. The hemoglobin concentration in patients with CHF decreases significantly as FC worsens: from 139.6 g/l to 122.0 g/l. As FC worsens, the number of patients with a hemoglobin concentration of less than 120 g/l also increases. The level of hypertension is considered an independent factor of mortality in CHF. Reducing hypertension by 1% increases mortality by 2% during the year. In patients with CHF, we observed a decrease in hypertension at III-IV FC.

CONCLUSIONS

1) In patients with CHF I-II FC, significant tubular dysfunction was established, as evidenced by an increased content of N-acetyl-β-D-hexosaminidase in urine, a marker of early damage to the renal tubular apparatus. GFR in patients with FC I does not change significantly, in patients with FC II there is a decrease in the average daily filtration rate. The circadian rhythm of GFR is disrupted: glomerular filtration decreases during the daytime and increases at night – the so-called "decomposition" of the daily clearance of endogenous creatinine.

2) As CHF worsens, there is a significant decrease in GFR, microalbuminuria increases, these changes were most significant in patients with III-IV FC. The daily filtration curve is monotonous: the same decrease in glomerular filtration day and night.

3) The concentration of hemoglobin in the blood and the hematocrit index also decrease with deterioration of the functional state of patients. No correlation was found between the concentration of hemoglobin and indicators of the functional state of the kidneys.

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