KIDNEY CONDITION IN PATIENTS WITH CHRONIC HEART FAILURE

Khusainova Munira Alisherovna
Khaydarov Sanjar Nizamitdinovich
Uzokov Jurabek Bakhtiyorovich
Karabayeva Gulchehra Khudayberdiyevna
Samarkand State Medical University

ABSTRACT

The purpose of the work. Study of the clinical and functional state of the kidneys, the prevalence and severity of anemia among patients with chronic heart failure (CHF).

Patients and methods. In 77 patients (mean age 60.4±1.2 years) with CHF I-IV FC (NYHA, 1994), the filtration capacity of the kidneys was assessed by the glomerular filtration rate (GFR) using the Cockcroft-Gault formula, the activity of N - acetyl - p - D - hexosaminidase (NAH) in the morning portion of urine as an indicator of the functional activity of the tubules, the presence of microalbuminuria (MAU) was determined, reflecting the function of the endothelium and the glomerular apparatus as a whole. The presence of anemia was determined according to generally accepted criteria results. A significant increase in NAH is characteristic of low FC CHF (FC I-II). In the initial stages CHF in patients there is a slight decrease in GFR, as CHF progresses, filtration decreases significantly, while MAU increases. The concentration of hemoglobin and hematocrit in the blood also decreases with the progression of CHF. Anemia is of an iron-distributing nature. The relationship between the concentration of hemoglobin and the indicators of the functional state of the kidneys has not been revealed. Conclusion. NAH is a marker of early defeat the tubular apparatus of the kidneys. Tubular lesion in patients with CHF precedes glomerular kidney damage. The presence of anemia in patients is associated with the severity of CHF.

Keywords: *chronic heart failure, kidneys, anemia, microalbuminuria, N - acetyl - p - D – hexosaminidase*

INTRODUCTION

The prevalence of chronic heart failure (CHF) continues to grow worldwide, in different countries it affects from 0.4 to 2% of the population. Among people over 50 years of age, the frequency of CHF increases to 6-10%. Despite the successes achieved in prevention and treatment, CHF is associated with high morbidity and mortality rates. Recently, much attention has been paid to its relationship with kidney damage within the so-called cardiorenal continuum. The kidneys are not just

a target organ of heart failure, but play a significant role in the pathogenesis and progression of this disease (the kidney "as a victim and cause of CHF"). An important direction is the timely detection and therapy of conditions that aggravate the severity of CHF, in particular anemia. Its frequency in the population is 10-30%, and with severe CHF, especially in patients with concomitant renal insufficiency, the frequency of anemia can reach 50-80%. This problem has been discussed especially actively recently.

The aim of the work was to study the clinical and functional state of the kidneys and the prevalence of anemia among patients with CHF, depending on the functional class (FC).

MATERIALS AND METHODS

77 patients suffering from CHF were examined, the average age was 60.4 ± 1.2 years. Distribution of patients according to the etiology of CHF: ischemic heart disease (CHD) + hypertension (GB) - 36 patients (47%), CHD - 11 patients (14%), GB - 23 patients (30%), rheumatic heart defects outside the activity of rheumatism - 7 patients (9%). Patients with kidney diseases and/or endocrine pathology were not included in the study. All the subjects were divided into groups depending on the functional class of CHF according to the NYHA classification (1994).The first group consisted of patients with functional class I FC CHF - 22 people, 45 patients were with heart failure II FC (second group), with signs of heart failure III-IV FC - 10 people (3rd group). The control group consisted of 17 practically healthy individuals at an average age of 60.1 ± 1.3 years. The filtration capacity of the kidneys was evaluated - the glomerular filtration rate (GFR) was calculated by the level of creatinine in the blood serum using the Cockcroft-Gault formula. In all patients, the presence of microalbuminuria (MAU) was determined, reflecting, as is well known, the function of the endothelium and the glomerular apparatus as a whole. The activity of N - acetyl - p - D - hexosaminidase (NAH) in the morning portion of urine was also determined as an indicator of the functional activity of the tubules. The daily diuresis was taken into account (the average values of minute diuresis in the daytime and at night were calculated), the daily diuresis/night diuresis ratio (DD/ND) was calculated, the range of fluctuations in the relative density of urine was estimated according to the Zimnitsky sample.The presence of anemia was determined according to generally accepted criteria using the following indicators: the number of red blood cells, hemoglobin concentration, hematocrit values, erythrocyte indices (MCV, MCH, MCHC). The parameters of iron metabolism were evaluated - serum iron (CS), total iron binding capacity of serum (OGSS), transferrin iron saturation coefficient (CST)

and serum ferritin.Statistical processing was carried out using the computer program "Statistica for Windows 6.0". The differences were considered significant at $p<0.05$. The data is presented in the form X±m, where X is the average value of the value, m is its standard error.

RESULTS

Table 1

Glomerular filtration rate indicators (X±m)

Groups of examined	CHF FC I, n=22	CHF II FC, N=45	CHF III and IV FC, N=10	Control group, N=17
GFR (according to the Cockcroft-Gault formula), ml/min	81,9=4,2*	80,5=5,3*	42,2=5,5***	97,5=3,1

The level of serum creatinine in patients with CHF I FC was 85.5±4.2 mmol/l, with II FC - 89.9 ± 3.2 mmol, with III-IV FC - 107.2 ± 8.4 mmol / l, in the control group - 80.2 ± 1.2 mmol /l, while significant differences between the indicators of the control group and patients with III-IV FC.When determining GFR, significant differences were revealed between the data of the control group and patients with CHF of varying severity. Moreover, GFR significantly decreased with the increase of FC CHF (Table. 1).The level of MAU in the group of patients with I FC CHF was 10.39±1.60 mg/day, in the group with II FC MAU was 10.61±1.56 mg/day, with III-IV FC 36.83±4.40 mg/day, in the control group - 6.70±3.50 mg/day.

From the data presented, it can be seen that MAU was detected in the group of patients with III-IV FC CHF, while the difference in MAU indicators between the group of patients with III-IV FC CHF and the control group turned out to be significant ($p<0.001$).When studying the activity of NAG in urine, it was revealed that the studied indicator had maximum activity in patients with I FC CHF, and as the severity of CHF worsened, the activity of the enzyme gradually decreased.

An increase in the level of NAH in urine was found in 71% of patients with I FC, in 67% of patients with II FC and in 60% of patients with III-IV FC. The NAH index in patients with I and II FC CHF significantly exceeded that in the control group (Table 2). A decrease in daily diuresis was observed in all patients, amounting to 92% at FC I, FC II - 85%, FC III-IV - 72% of the average value in the control group. The decrease in daily diuresis occurred mainly due to a decrease in the rate of diuresis during the daytime ($p<0.001$, Table 3).

Table 2

Activity - acetyl - p - D - hexosaminidase in urine (X±m)

Groups of examined	CHF FC I, n=22	CHF II FC, N=45	CHF III and IV FC, N=10	Control group, N=17
Activity - acetyl - p - D - hexosaminidase in urine mmol/hour per 1 mmol of creatinine	106,3±28,8 *	72,3±7,6*	48,0±5,4 39,	8±4,6*

Table 3

Average indicators of diuresis and the range of fluctuations in the relative density of urine according to the Zimnitsky sample (X=m)

Groups of surveyed	Daily diuresis (in ml)	Average rate of minute diuresis		The range of fluctuations in the relative density of urine
		during daylight hours	during at night hours	
Control group, n=17	1291,8±86,8	0,93±0,07	0,83±0,06	13,4±1,88
HSN I FC, n=22	1046,8±46,1*	0,64±0,03***	0,82±0,04	14,3±0,71
HSN II FC, n=45	972,0±37,0**	0,58±0,03***	0,8±0,04	12,5±0,67
HSN III-IV FC, n=10	826,2±35,0***	0,54±0,03***	0,62±0,04**	11,2±0,74

A statistically significant decrease in night diuresis relative to the corresponding indicator in the control group was registered only in patients with III-IV FC. Shifts in the diurnal rhythm of diuresis, compared to the average values of the DD/ND ratio, are significantly more pronounced at I and II FC.

Thus, DD/ND in patients with I FC was 0.89±0.07 (in the control group - 1.2±0.08; $p<0.05$), with II FC - 0.84±0.04 ($p<0.01$).V patients with III-IV FC - 0.98±0.06 ($p>0.05$).The range of fluctuations in the relative density of urine in most patients remained within the normal range (7-30). Less than 7 it was determined in 7±3% of patients with I FC, in 19±4% - with II FC, and in 23±5% - with III-IV FC. In general, shifts in all groups by average values are statistically insignificant.In the group of patients with I FC, the hemoglobin concentration was 139.6 ± 2.7 g/l, with II

FC - 136.2 ± 1.8 g/l, with III-IV FC - 122.0 ± 6.4 g/l, in the control group - 139.4 ± 4.8 g/l. There were significant differences between the indicators in the control group and in patients with III-IV FC ($p < 0.05$). The number of patients with hemoglobin levels less than 120 g/l increases with the progression of CHF: with FC I - 0%, with FC II - in 5% of cases (in 3 people out of 45), in 30% (in 3 people out of 10) with FC III-IV.In the study of indicators of iron metabolism (SJ, OZHSS, CST) and the analysis of the number of red blood cells, hematocrit values and erythrocyte indices revealed no significant differences between patients with CHF in the group as a whole and the control group (Table. 4).

Table 4

Indicators of iron metabolism, hemoglobin concentration, values of hematocrit and erythrocyte indices (X±m)

Indicators	For the group of patients with CHF, as a whole	I FC, n=22	II FC, n=45	III-IV FC, n=10	Control group, n=17
SI	20,1 ± 1,3	20,5 ± 1,0	20,2 ± 0,8	19,6 ± 2,1	21,9 ± 1,4
TIBCS	77,5 ± 2,8	74,6 ± 1,5	77,7 ± 1,9	80,3 ± 4,9	79,3 ± 3, 3
TCI, %	25,3± 1,8	26,5 ± 2,0	26,0 ± 1,1	23,5 ± 2,5	27,9± 2,0
ABV	4,6 ± 0,1	4,8 ± 0,1	4,7 ± 0,1	4,3 ± 0,2	4,8 ± 0,3
HCE	83,5 ± 1,4	83,3 ± 0,9	84,1 ± 0,9	83,0 ± 2,4	82,3 ±1,1
CHB	29,0 ± 0,7	29,4 ± 0,5	28,9 ± 0,4	28,5 ± 1,2	29,3 ± 0,5
CHBC	345,5 ± 3,2	352,6 ± 3,3	343,4 ± 1,8	343,4 ± 4,5	356,8 ± 1,7
hematocrit	0,4 ± 0,01	0,4 ± 0,01	0,4 ± 0,01	0,4 ± 0,02	0,4 ± 0,02

Table 5

Analysis of the relationship between hemoglobin indicators and the functional state of the kidneys

Indicators	I FC, n=22		II FC, n=45		FC III-IV, n=10	
	r	p	r	p	r	p
Hemoglobin and NAH	0,77 >	0,05	- 0,02 >	0,05	- 0,46 >	0,05
Hemoglobin and MAU	0,25 >	0,05	- 0,13 >	0,05	- 0,82 >	0,05
Hemoglobin and GFR	0.42 >	0.05	0.07 >	0.05	0.11 >	0.05

At the same time, there was a decrease in hematocrit in patients with III-IV FC to 0.35, whereas in patients with I and II FC it was 0.40 ($p<0.05$).When determining the level of serum ferritin, significant differences were revealed between the indicators in the control group and in patients II, III-IV FC. In the control group, the serum ferritin level was 51.0 ± 18.1 ng/ml, in patients with CHF II FC - 87.5 ± 17.5 ($p < 0.05$), III- IV FC - 152.0 ± 20.3 ($p <0.01$). The correlation between hemoglobin indicators and the functional state of the kidneys (GFR, MAU, NAH) was investigated. A reliable relationship has not been established (Table 5).

DISCUSSION

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, enzymes with different intracellular localization are sequentially released into the urine. Thus, with a slight and moderate degree of kidney damage in the urine, the activity of enzymes associated with the brush border (cytoplasmic and lysosomal) increases. With significant damage to the kidneys, an increase in the content of mitochondrial enzymes in the urine occurs, which, as a rule, corresponds to cell necrosis. NAH is a lysosomal enzyme, the increased activity of which is characteristic of damage to the proximal tubules. The maximum increase in its activity at the first FC of CHF corresponds to minor renal damage, a decrease in the activity of NAH with the progression of CHF can be regarded as an increasing damage to the tubular apparatus of the kidneys. The MAU test is considered today as an early marker of kidney damage, glomerular apparatus and endothelial dysfunction. Analysis of the data obtained 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 degree of MAU detected by MAU correlates with an increase in FC CHF (III-IV FC). Given the significant increase in the activity of NAH, in comparison with the control group, already at I FC CHF, and the detection of MAU only in patients with III-IV FC, it can be assumed that in patients with CHF, tubular lesion precedes damage to the glomeruli.To a certain extent, the results of the GFR analysis correspond to this. When determining GFR, it was revealed that the degree of decrease in GFR correlates with an increase in FC CHF: at I-II FC - slightly, at III-IV FC - significantly, which can probably be explained by the inclusion of intrarenal compensatory mechanisms aimed at supporting filtration in the early stages of CHF.

The role of the renin-angiotensin-aldosterone system is not excluded in this sense. It is known that angiotensins are the main mediators of renal vasoconstriction, have an active vasoconstrictive effect not only on afferent, but also on efferent arterioles and, thereby, maintain the pressure necessary for glomerular filtration.There are certain relationships between the value of GFR and the level of serum creatinine (SC): an increase in SC with a decrease in GFR, but this relationship is not linear. With a moderate decrease in GFR (patients with I-II FC CHF), the GFR increases slightly and begins to increase sharply only in patients with III-IV FC, when the GFR decreases to 42 ml/min. This fact once again confirms the opinion that GFR, not SC, is an indicator of kidney damage, especially in the early stages of CHF. With the increase in symptoms of heart failure, a decrease in daily diuresis was observed.

The natural predominance of ID over DD was noted only at the early stages of the development of heart failure. Despite the onset of oliguria, the range of fluctuations in the relative density of urine was observed within the normal range. At the same time, in patients with III-IV FC, an increase in cases was observed, with a reduced range of fluctuations in the relative density of urine.The concentration of hemoglobin in patients with CHF significantly decreases as heart failure increases: from 139.6 g/l in patients with I FC to 122.0g/l in patients with III-IV FC. As heart failure progresses, the number of patients with a hemoglobin concentration of less than 120 g/l increases. It is believed that the level of hematocrit is an independent factor of mortality in CHF. A decrease in hematocrit by 1% increases mortality by 2% in those the end of the year. Among patients with CHF, a decrease in hematocrit was observed at III-IV FC. Thus, in patients with III-IV FC (the average hematocrit was 0.35), the risk of death increases compared to patients with I and II FC (hematocrit - 0.40).Taking into account the normal indicators of iron metabolism (LV, CST, OHSS), elevated ferritin levels in patients with III-IV FC and an increasing decrease in hemoglobin concentration as CHF deepens, it can be assumed that anemia in these cases refers to iron redistributive, which is caused by a violation of the movement of iron from the depot to the blood plasma and further to erythrocaryocytes. When examining patients with CHF, we did not find a relationship between the functional state of the kidneys and the level of hemoglobin.

CONCLUSION

1. N - acetyl - p - D - hexosaminidase is a marker of early damage to the renal tubular apparatus, its significant increase is characteristic of low FC HSN (FC I - II). In other words, as a tubular lesion in patients with CHF precedes glomerular kidney damage. At the initial stages of CHF in patients , there is a slight a decrease in the

glomerular filtration rate, as CHF progresses, filtration decreases significantly, and microalbuminuria simultaneously progresses.

2. The concentration of hemoglobin in the blood and the indicator hematocrit also decreases with the progression of CHF. Anemia is of an iron-distributing nature. The relationship between the concentration of hemoglobin and the indicators of the functional state of the kidneys was not revealed.

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