EARLY PREDICTORS OF RENAL DYSFUNCTION IN PATIENTS WITH CHRONIC HEART FAILURE

Study was aimed at an early detection of subclinical disorders in renal function in patients with chronic heart failure (CHF). Fifty-two patients with ischemic heart disease (IHD) with post-infarction cardiосclerosis were examined. All the patients underwent complex clinical examination, a level of serum creatinine, residual nitrogen and urine enzymes. Determination of urine enzymes level in CHF patients may be considered as diagnostic approach for an early diagnosis of renal dysfunction.

Keywords: Chronic heart failure, renal dysfunction, urine enzymes, glomerular filtration rate

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Introduction

Chronic heart failure (CHF) is one of the prevailed, progressing and prognostic unfavorable diseases of cardiovascular system as well as one of the mostly occurred causes for hospitalization. About 50% of CHF patients despite of application of combined therapy died during 5 years after onset of clinical symptoms.

The most occurred cause of CHF is ischemic heart disease (IHD) that accounts for 54-68.6%. It was established that presence of renal dysfunction in CHF patients is predictor of unfavorable clinical prognosis even more valuable than severity of heart failure (HF) and Left ventricular ejection fraction (LVEF) (Bock and Gottlieb, 2010; Eilers, Liu, Gruber, and Niemann, 2010). Distribution of renal dysfunction in CHF varied from 25% up 60% according to different studies.

Numerous epidemiological, prospective, retrospective, and specially-designed clinical studies found a strong association between the severity of renal dysfunction, measured by the reduction in glomerular filtration rate (GFR)/creatinine concentration of blood plasma), and the risk of total death and the emergence of various cardiovascular events, including myocardial infarction (MI), sudden death, cerebral ischemic stroke-onset heart failure (Berl and Henrich, 2006; Mielniczuk, Pfeffer, Lewis et al., 2008; National Recommendations of the All-Union Scientific Society of Cardiologists and the Russian Scientific Society of Nephrologists, 2008; Sarnak, Levey, Schoolwerth et al., 2003).

Similar to LVEF in CHF a decrease of glomerular filtration rate (GFR) and a level of creatinine are considered as independent signs of unfavorable prognosis. Mortality risk in GFR < 60 ml/min/1.73m2 was increasing 2.1 times, mortality risk of patients in reduced left ventricular systolic function (LVSF) if presence of renal insufficiency (RI) was increased 3.8 times, in normal systolic function - 2.9 times (Mukhin, Moiseev and Fomin, 2009; Nosadini and Tonolo, 2002). Hyper-enzymuria as marker characterizes dysfunction of glomerular and tubular apparatus in kidneys. The most broadly investigating enzymes of this group were the following: alanine aminotransferase (ALT), aspartate aminotransferase (AST), cholinesterase (ChE) and alkaline phosphatase (APh).

So, release of APh is related with damage of alkaline border and cytoplasmic membrane of tubular epithelium of proximal channels. Determination of APh in urine may be used for estimation of damage degree of surface structure of cytomembranes. Studying a state of glomerular filter is possible by determination of enzyme activity (ChE) in urine. Enzymes ALT and AST locate in cellular cytosol, cellular increase evidences deep disorders of cytoplasmic membranes of tubular epithelium with release of cytosol components into...
channels lumen (Mavlyanov, Akbarova and Khabilova, 2009; Nickolas, Barash and Devarajan, 2008).

Study was aimed at an early detection of subclinical disorders in renal function in patients with ischemic heart disease (IHD), post-infarction cardiosclerosis (PICS) complicated by II-III functional class (FC) of chronic heart failure (CHF) by determination of a level of enzymuria and glomerular filtration rate (GFR).

Materials and methods

Fifty-two patients with ischemic heart disease (IHD) with post-infarction cardiosclerosis were examined. The first group formed 27 patients with II FC CHF, the second one - 25 patients with III FC CHF. In the study were included patients aged 45-65. The control group was formed by 20 healthy persons. All the patients were underwent complex clinical examination, a level of serum creatinine, residual nitrogen and urine enzymes (alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (APh), cholinesterase (ChE) were determined by biochemical method on apparatus “Spectrophotometer CF-46” (Kamyshnikov, 2002). GFR was calculated by formula of Modification of Diet in Renal Disease (MDRD) study in ml/min/1.73 m2 (National Kidney Foundation, 2002).

Results and discussion

Our studies revealed that patients in the 1st group preserved normal indicators of GFR and residual nitrogen (RN) in blood serum: 91.2±2.5 8 ml/min and 30.5±2.71 mol/l, and patients of the 2nd group showed an insignificant decrease of GFR - 73.8±2.42 and increased normal indices of RN - 35.1±2.58 mol/l. At the same time, patients in the 1st and 2nd groups had GFR 17.4% and 35.1% reliably lower, and RN - 61.4% and 85.7% respectively reliably higher than indices in the control group (Fig. 1) that confirmed reduction of GFR and increase of residual nitrogen if increasing functional class of heart failure without clinical manifestations of renal dysfunction (Coca, Yalavarthy, Concato, and Parikh, 2008; Ix, Wassel, Stevens et al., 2011; Bricon, Leblanc, Benlakehal, Gay-Bellile, Erlich, and Boudaoud, 2005). Mean indices of GFR in the first and second groups corresponded to the 1st and 2nd stages of chronic renal disease.

![Figure 1. Indices of GFR (in ml/min/1.73 m²) and RN (mol/l) in patients CHF II and III FC](image-url)
Reliable (P <0.05) increase in a level of urine enzymes compared with control group was fixed in patients II FC CHF: ALT - 52.2%; AST - 39%; APh - 82.7%; ChE - 37.8% and was 3.85±0.17; 3.74±0.12; 1.48±0.13; 82.16±4.61 un/l. Level of ALT, AST, APh, ChE in urine of patients III FC CHF was respectively: 4.73±0.17; 4.11±0.12; 1.74±0.085; 91.21±3.67 un/l, and was also registered a reliable increase of ALT, AST, APh, ChE 87.0%, 52%, 114.8% and 53% respectively (P <0.01) as compared with control group (Table 1) that evidenced disorders in integrity of cytoplasmic membranes of tubular epithelium of renal channels and glomerular filter (Soni, Fahuan, Ronco, and Cruz, 2009). Reliable increase of level of urine enzymes established is an early sign of damage of tubule-epithelial apparatus of kidneys and it may be considered as reliable predictor of renal dysfunction in CHF patients.

### Table 1. Comparative Characteristic of Urine Enzyme Levels According to FC CHF (M+σ)

<table>
<thead>
<tr>
<th>Indices</th>
<th>Control (n = 20)</th>
<th>CHF II FC (n = 27)</th>
<th>CHF III FC (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT, un/l</td>
<td>2.53±0.071</td>
<td>3.85±0.17</td>
<td>4.73±0.17**</td>
</tr>
<tr>
<td>AST, un/l</td>
<td>2.69±0.085</td>
<td>3.74±0.12</td>
<td>4.11±0.12</td>
</tr>
<tr>
<td>APh, un/l</td>
<td>0.81±0.049</td>
<td>1.48±0.13</td>
<td>1.74±0.085</td>
</tr>
<tr>
<td>ChE, un/l</td>
<td>59.63±3.44</td>
<td>82.16±4.61*</td>
<td>91.21±3.67</td>
</tr>
</tbody>
</table>

Note: * - reliability P <0.05 to control group, ** - reliability P <0.01 to control group.

Analysis of the data obtained exhibited direct correlation dependence between an increase in a level of urine enzymes and that of residual nitrogen in blood serum and inverse correlation between glomerular filtration rate (GFR) and a level of residual nitrogen (RN) in blood serum, urine enzymes.

### Conclusion

Subclinical disorders of renal functions characterizing in reduction of GFR, an increase in a level of residual nitrogen and enzymuria noted to be in CHF patients by advancing of disease. Determination of urine enzymes level in CHF patients may be considered as diagnostic approach for an early diagnosis of renal dysfunction.

### References


