Development and optimization of pharmacotherapy for chronic heart failure with regards to kidney functional state

Abstract: the aim of the study was to estimate the effect of losartan on kidney function and renal blood flow in 78 patients with chronic heart failure (CHF) in the II–III functional class (FC). The treatment during 6 months with inclusion of losartan resulted in improvement of the parameters of kidney functional state with reliable increase in GFR and improvement of parameters of the renal blood flow.

Keywords: chronic heart failure, kidney dysfunction, glomerular filtration rate, renal hemodynamics.

Prognosis in the patients with chronic heart failure (CHF) is extremely unfavorable. In the patients with CHF functional class (FC) IV (NYHA) the mortality rate during half a year achieved 44%. In cases of mild form of CHF during 4 years after the establishment of diagnosis only a half of patients survive. In the recent studies devoted to kidney dysfunctions in CHF the significant increase in creatinin serum concentration and reduction of the glomerular filtration rate were noted in the majority of patients over the last years [1; 2]. The previous changes of the kidney functional state and renal hemodynamics have been studied insufficiently, and the methods, precise and accessible for clinical practice, allowing determination of early disturbances of the kidney functions in CHF have not been developed yet. The kidney nitrogen excretory function and the state of glomerular filtration have been poorly studied [3]. The state of renal hemodynamics and its prognostic role in this pathology has been also less studied. The association of the kidney dysfunction in the patients with CHF creates the crucial problems in relation to determination of the therapeutic strategy which in these two comorbid states should be combined. In this connection the performed investigation with purpose to develop and optimize the combined pharmacotherapy for CHF taking into account of their nephroprotective properties would be prospective and having scientific-practical value.

Purpose of research was to study the effect of losartan on the kidney functional state and renal blood flow in the patients with CHF in functional classes I–III CHF.

Material and Methods. This investigation included 65 males with ischemic heart disease (IHD) associated with FC I (19), FC II (24) and III (22) CHF (mean age 63.3 ± 5.8 years). Control group comprised of 10 healthy persons (mean age 42.3 ± 2.1 years).

The patients were randomized into groups in relation to FC CHF by classification of New-York Association of cardiologists on the basis of findings of the six-minute walk test (SWT) and by scale for evaluation of clinical state of the patients (SECS). The patients received additionally to the standard therapy (spi - ranolacton, beta-blockers, antiagregants) the lozartan, dose of lozartan titrated to 50–100 mg, a day (mean dose of this preparation was 66.3 ± 25.6 mg/day).

The kidney functional state was evaluated by the level of serum creatinin (Cr), GFR (by calculation there were determined GFR by formula MDRD (Modification of Diet in Renal Disease Study) in ml/min/1.73 m². The renal blood flow assessment was performed with use of the device of ultrasound examination SONOACEX6 (Korea) by color Doppler mapping as well as pulse-wave dopplerography and energy mapping with sector sensor 3.5 MHz. with scanning angle not more than 60°. The following parameters were used: peak blood flow systolic velocity (Vs characterizes amplitude of the systolic flow), blood flow maximum end-diastolic velocity (Vd characterizes blood flow velocity at the end of diastole), mean by time blood flow velocity (V mean is a result of mean values of all spectrum components of one or some cardiac cycles), Resistive index (RI characterizes the peripheral vascular resistance), pulse index (PI characterizes the state of peripheral resistance in the vascular bed). The velocity (Vs, Vd, Vmean) and parameters (RI, PI) were studied at the level of right and left renal artery, as well as of intraorgan (segment) arteries [4].

The statistic processing of the data obtained was performed with use of the package of electronic tables EXCEL 6.0 Windows-95. The parameters were described as mean arithmetic ± standard deviation (M ± SD), between group comparisons of quantitative values were made with use of criteria (t) Student. For evaluation of difference of mean values between two groups in not corresponding values with normal rule of the distribution there was used range criterion of Wilcockson. The analysis of the dependence of indications was performed with calculation of the coefficient of pair correlation of Pirson (r). The evaluation of the quantitative and qualitative indications was calculated by the coefficient of range correlation of Spirman (R). The criteria of reliability was p < 0.05.

Results and Discussion. The results of investigation show that in the patients with FC I, FC II and III CHF the initial parameters of Cr were 71.8 ± 25.35, 80.13 ± 18.52 and 85.0 ± 19.59 micromol/l, GFR by formula MDRD was 71.4 ± 11.2, 77.7 ± 21.87 and 70.57 ± 13 ml/min/1.73 m² respectively.

The GFR (MDRD) < 60 ml/min in the patients with FC I–III CHF was observed in 24% (16) patients. Analysis of data of renal hemodynamics showed that in all patients with FC I–III CHF at the level of right and left renal arteries there was noted increase in resistive index by 11.9% and 7% (p < 0.001 and p < 0.005) and pulse index — by 20% and 13.5% (p < 0.001 and p < 0.005), respectively, in comparison with control. The blood flow velocity during the diastole period at the level of right and left renal arteries was lower by 91.3% and 43.2% (p < 0.001 and p < 0.001), respectively in comparison with the control. The velocity parameters during systole period were...
lower by 45.6% and 40.5% (p < 0.001) at the level of right and left arteries, respectively in contrast to control parameters (Tab. 1). During lowering of the artery levels there was noted reduction of the velocity parameters at the level of right and left segment arteries in the systole by 38.4% and 30.7% (p < 0.001), in the diastole by 77.9% and 66.8% (p < 0.001), respectively in comparison with control. And at the level of right and left segment renal arteries there was noted increase in resistive index by 16.9% and 15.3% (p < 0.001) and pulse index — by 25.6% and 24.1% (p < 0.001 and p < 0.005), respectively in comparison with control.

### Table 1. – Characteristic of the parameters of renal hemodynamics (renal and segment arteries) in the patients with FC II–III CHF (M ± SD)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Renal right artery</th>
<th>Renal left artery</th>
<th>Segmental right artery</th>
<th>Segmental left artery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>CHF I–III FC</td>
<td>Control</td>
<td>CHF I–III FC</td>
</tr>
<tr>
<td>Vs cm/sec</td>
<td>59.7 ± 1.91</td>
<td>41.0 ± 5.03**</td>
<td>59.8 ± 1.91</td>
<td>42.47 ± 5.74**</td>
</tr>
<tr>
<td>RI</td>
<td>0.67 ± 0.016</td>
<td>0.749 ± 0.044**</td>
<td>0.71 ± 0.01</td>
<td>0.77 ± 0.056*</td>
</tr>
<tr>
<td>Vd cm/sec</td>
<td>19.7 ± 0.5</td>
<td>10.34 ± 2.45**</td>
<td>17.33 ± 0.87</td>
<td>9.85 ± 2.58*</td>
</tr>
<tr>
<td>Vmean, cm/sec</td>
<td>39.7 ± 0.89</td>
<td>25.67 ± 3.45**</td>
<td>35.5 ± 3.67</td>
<td>26.16 ± 3.67**</td>
</tr>
<tr>
<td>PI</td>
<td>1.0 ± 0.03</td>
<td>1.2 ± 0.11**</td>
<td>1.1 ± 0.02</td>
<td>1.25 ± 0.145**</td>
</tr>
</tbody>
</table>

Note: ** — reliability p < 0.001; * — p < 0.005 in relation to the control group.

We studied the kidney functional state in the patients with CHF, there was examined group of patients with CHF with minimum quantity of the additional factors having ability to result in kidney lesion. However even in spite on this fact in two third of the examined patients there was revealed reduction in GFR lower than 90, almost in 39% of patients — lower than 60 ml/min/1.73 m². In our opinion, this indicates that even “isolated” CHF can result in disturbance of the kidney functional state. These data are correlated to the results of that investigation in which there was performed strong selection of the patients [5; 6; 7].

The treatment during 6 months with inclusion of lozartan in the patients with FC I–III CHF led to the improvement of the parameters of the renal blood flow at the level of right and left renal artery, as well as segment renal arteries. During dynamics of treatment the patients with CHF at the level of right and left renal arteries there was noted tendency to reduction of the parameters of resistive index by 9.9% and 7% and pulse — by 15.5% and 13.5% (p < 0.05) index, at the time of decrease in indices of resistive and pulse parameters there was noted increase in velocity parameters during systole period by 9.9% and 11.9% and diastole by 13.5% and 11.5% (p < 0.05) in comparison with initial parameters. There was also found improvement of parameters of the renal blood flow at the level of segment arteries while not achieved of reliable values [8].

### Conclusions

In the patients with CHF during progressing disease there was noted subclinical disturbance of the kidney function characterized by decrease in GFR, worsening of the parameters of renal blood flow and they may be considered as predictors of the kidney dysfunctions in the patients with CHF.

In the patients with FC I–III CHF at the level of renal and segment renal arteries there noted additionally to the increase in parameters of resistive and pulse indices with reduction of velocity parameters during systole and diastole periods also increase in comparison with control parameters.

The treatment during 6 months with inclusion of lozartan resulted in improvement of the parameters of kidney functional state with reliable increase in GFR and improvement of parameters of the renal blood flow at the level of renal and segment renal arteries that characterizes nephroprotective effect of the therapy performed.

### References:


