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Influence of Glutargin on Functional State of the Liver in Patients with Chronic Heart Failure

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Abstract. 104 patients (60 males and 54 females) with stage II-III arterial hypertension (AH) and chronic heart failure (CHF) were examined to study the effects of complex treatment with glutargin on the functional state of the liver in patients with CHF. Among patients there were 45 patients with stage IIA CHF NYHA FC III and 59 patients with stage IIB CHF NYHA FC IV. All the patients were divided depending on treatment: Group IA included 33 patients with AH complicated by stage IIA CHF; Group IIA included 12 patients with AH and stage IIB CHF who received basic therapy. Groups IA and IIA were the comparison groups. Group IB consisted of 39 patients with AH and stage IIA CHF, and Group IIB consisted of 20 patients with AH and stage IIB CHF, who, in addition to basic therapy, received arginine glutamate. The control group included 20 practically healthy persons. Standard clinical, ultrasound and biochemical investigations were performed. The results revealed that the inclusion of glutargin in treatment of patients with AH and CHF improves overall liver function reducing the degree of cytolytic and cholestatic syndromes and improving detoxification and protein-synthesizing functions of hepatocytes.

Keywords: chronic heart failure; liver function; treatment

Problem statement and analysis of the recent research

Chronic heart failure (CHF) remains a relevant medical and social problem worldwide, including Ukraine. According to national registers and epidemiological studies in European countries the prevalence of CHF among the adult population ranges from 1.5 to 5.5% and increases with age reaching 10-15% in people with an older age (over 70 years). The prognosis of symptomatic CHF is very important as about half of people who develop CHF die within 4 years and among patients with severe CHF the mortality rate within a year reaches 50% [1, 3]. Treatment of CHF remains a relevant problem both in Ukraine and worldwide [1, 4]. Impaired functioning of renin-angiotensin-aldosterone and sympathoadrenal systems being the leading ones in the development of CHF does not explain its progression on the background of basic therapy. The results of the recent research have revealed that in various cardiovascular diseases, including hypertension, atherosclerosis, heart failure secondary to activation of free radical oxidation some changes in the configuration of eNOS occur causing changes in activity and bioavailability of the enzyme [5, 6]. The conversion of glutamine and NO synthesis are impaired [2]. Preservation of liver function in patients with CHF is of great clinical importance in the inactivation of aldosterone as 85% of this hormone is metabolized in the liver and in case of liver failure it is accumulated in the plasma increasing by 3-4 times when metabolized [1]. However, therapeutic schemes considering the functional state of the liver in complex treatment of patients with CHF are still insufficiently developed.

The objective of the research was to study the influence of complex treatment using glutargin on the functional state of the liver in patients with chronic heart failure.

Materials and methods

104 patients (60 males, 54 females) with stage II-III arterial hypertension (AH) and CHF were examined at the age of (67.1±7.2) years with mean disease duration of (7.1±4.4) years. There were 45 patients with stage IIA CHF NYHA FC III and 59 patients with stage IIB CHF NYHA FC IV.

All the patients were divided depending on treatment: Group IA included 33 patients with AH complicated by stage IIA CHF who received basic therapy. Group IIA included 12 patients with AH and stage IIB CHF who received basic therapy. Groups IA and IIA were the comparison groups.

Group IB consisted of 39 patients with AH and stage IIA CHF who in addition to basic therapy received arginine glutamate (registration number UA/4022/04/01, Pharmaceutical Company Zdorovie Ltd, Ukraine). Group IIB consisted of 20 patients with AH and stage IIB CHF, who in addition to basic therapy received arginine glutamate. Intravenous infusion of 10 ml of a 40% solution of arginine glutamate diluted in 200 ml of a 0.9% solution of sodium chloride was administered for 5 days with further taking of medication orally at a dose of 0.5 g three times per day for 20 days on the background of basic therapy. The control group included 20 practically healthy persons.

Standard clinical, ultrasound and biochemical investigations were performed. Activities of lactate dehydrogenase (LDH), alkaline phosphatase (AP), gamma-glutamyl transpeptidase (GGTP), cholinesterase, blood levels of total cholesterol, triglycerides were determined using the method of the bichromatic spectrophotometry and biochemical analyzer Stat Fax 1904 plus (Germany) with standard sets. The intensity of the cytolysis syndrome was evaluated by the activities of alanine transaminase (ALT), aspartate aminotransferase (AST) including the determination of the AST/ALT ratio, LDH, GGTP, blood levels of bilirubin. Protein-synthesizing function of the liver was evaluated by the levels of protein, prothrombin, fibrinogen, and cholinesterase activity. The obtained results were statistically processed using IBM PC Pentium-200 and statistical software package Statistica 7 for Windows (StatSoft, the USA).

Results and discussion

The analysis of the research revealed that the use of glutargin in complex treatment of patients with arterial hypertension and CHF reduced clinical and biochemical manifestations of the disease. General physical and mental state became worse in 54 (91.53%) patients, it did not change in 5 (8.475) patients. In the comparison group general physical and mental state improved in 7 (15.56%) patients and became worse in 3 (6.67%) patients.

The inclusion of glutargin in complex treatment of patients with CHF resulted in normalization of liver size in 10 (16.95%) patients with stage IIA CHF and reduction in hepatomegaly by (2.19±0.88) cm in 41 (69.49%) patients ($p<0.05$), which according to the ultrasound results was accompanied by a decrease in the area of echolucency. In the comparison group the reduction in liver size was not significant.

Positive clinical dynamics under the influence of glutargin was accompanied by the improvement of biochemical parameters of the functional state of the liver (Table 1).

Table 1

Dynamics of parameters of functional state of the liver in patients with arterial hypertension and chronic heart failure under the influence of complex treatment with inclusion of glutargin, (M±m)

Parameter	Healthy persons, (n=20)	Basic therapy and glutargin Group IB (n=39)		Basic therapy and glutargin Group IIB (n=20)	
		before treatment	after treatment	before treatment	after treatment
Bilirubin, mcmol/l	12.08±0.92	24.84±2.35*	14.76±2.69*»·	30.14±2.65*	16.35±1.29*•
AST, mmol/l•hour	0.35±0.03	0.65±0.05*	0.39±0.05*·	0.79±0.07*	0.42±0.03•
ALT, mmol/l•hour	0.33±0.03	0.61±0.05*	0.37±0.05*·	0.72±0.06*	0.39±0.03•
LDH, mmol/l•hour	2.01±0.17	2.98±0.22*	2.25±0.28*·	3.33±0.23*	2.39±0.08*•
GGTP, mmol/l•hour	2.25±0.17	3.13±0.27*	2.38±0.30*·	3.55± 0.27*	2.47±0.20•
AP, mmol/l•hour	1.16±0.08	1.99±0.18*	1.24±0.15*·	2.20±0.17*	1.30±0.12*•
Thymol test, units	2.64±0.19	4.11±0.35*	3.70±0.37*·	4.07±0.35*	3.75±0.31*•
Cholinesterase, mmol/l	307.02±17.68	272.7±20.79*	285.2±25.33*·	243.68±20.61*	277.71± 23.86•
Total protein, g/l	75.38±2.6	70.96±5.24	74.11±15.97	65.48±5.10	72.25±3.81

Notes:

* – the probability of difference compared to healthy people, $p<0.05$;

• – the probability of difference before and after treatment, $p<0.05$.

In particular, after the course of treatment there was observed a reduction of cytolysis syndrome that was accompanied by decreased activities of ALT, AST, LDH and GGTP by 2.0, 2.0, 1.29 and 1.47 times, respectively ($p<0.05$) which was not observed in the comparison group (Table 2).

Table 2

Dynamics of parameters of functional state of the liver in patients with arterial hypertension and chronic heart failure under the influence of basic therapy, (M±m)

Indicator	Healthy persons n=20	Basic therapy, Group IA, n=33		Basic therapy, Group IIA, n=12	
		before treatment	after treatment	before treatment	after treatment
Bilirubin, mcmol/l	12.08±0.92	23.94±1.76*	20.85±1.72*·	30.13±2.55*	22.82±1.3*•
AST, mmol/l•hour	0.35±0.03	0.64±0.06*	0.59±0.06*·	0.78±0.05*	0.73±0.03*
ALT, mmol/l•hour	0.33±0.03	0.58±0.05*	0.55±0.05*·	0.71±0.05*	0.68±0.03*
LDH, mmol/l•hour	2.01±0.17	2.89±0.21*	2.68±0.28*·	3.34±0.24*	3.14±0.08*
GGTP, mmol/l•hour	2.25±0.17	3.20±0.30*	2.97±0.28*·	3.57± 0.28*	3.33±0.20*
AP, mmol/l•hour	1.16±0.08	1.87±0.19*	1.66±0.14*·	2.28±0.18*	2.06±0.12*
Thymol test, units	2.64±0.19	3.21±0.36*	2.97±0.37*·	4.03±0.35*	3.25±0.31*
Cholinesterase, mmol/l	307.02± 17.68	280.70± 21.89*	285.70± 25.33*·	241.69± 20.62*	248.1± 23.76*
Total protein, g/l	75.38±2.6	71.95±5.25	73.12±15.87	67.48±5.10	70.24±3.82

Notes:

* – the probability of difference compared to healthy people, $p<0.05$;

• – the probability of difference before and after treatment, $p<0.05$.

In our opinion, it can be explained by the peculiarities of the composition of glutargin and its pharmacodynamic properties.

When analyzing clinical effectiveness of using glutargin when treating patients with stage IIA-IIB CHF it was revealed that the intensity of the cytolysis syndrome changed as follows: in patients of Group IB AST activity reduced by 40.00% and in patients of Group IIB it reduced by 46.84% ($p<0.05$); ALT activity reduced by 39.34% and 45.83%, respectively ($p<0.05$); LDH activity reduced by 24.50% and 28.23%, respectively ($p<0.05$); GGTP activity reduced by 23.96% and 30.42%, respectively ($p<0.05$). It indicated the effectiveness of treatment with glutargin directed towards reducing the cytolysis syndrome.

The improvement of the detoxification function of the liver under the influence of therapy with inclusion of glutargin was observed in patients of both Group IB and Group IIB as indicated by thymol reduction by 9.98% in patients of Group IB ($p<0.05$) and by 7.86% in patients of Group II ($p<0.05$). The improvement of protein-synthesizing function of hepatocytes as indicated by increased activity of cholinesterase by 4.61% in patients of Group IB ($p<0.05$) and 13.97% in patients of Group IIB ($p<0.05$) was observed.

There was a reduction in biochemical manifestations of the cholestasis syndrome as indicated by decreased activity of alkaline phosphatase by 37.69% in patients of Group IB ($p<0.05$) and 40.91% in patients of Group IIB ($p<0.05$). Thus, it was revealed that treatment with inclusion of glutargin improved the functional state of the liver in patients with stage IIA CHF NYHA FC III as well as in patients with stage IIB CHF NYHA FC IV.

Conclusions

The inclusion of glutargin in complex treatment of patients with AH and CHF improves overall liver function reducing the cytolysis and cholestasis syndromes and improving detoxification and protein-synthesizing functions of hepatocytes.

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