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Hepatoprotective Therapy for Disease and Diabetes

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Abstract

Our work is devoted to the treatment of non-alcoholic fatty liver disease as a complication in patients with complex cardiovascular pathology and type 2 diabetes mellitus. The data of the study of the effect of the drug Hepa-Merz® on the functional state of the liver, endothelium, rheological properties of blood, the state of capillary blood flow, markers of endotoxemia and clinical state in this category of patients are presented. The results obtained confirm the possibility of using the drug Hepa-Merz® for liver functional disorders in patients with cardiovascular diseases and complex type 2 diabetes mellitus.

KEY WORDS: diabetes mellitus, cardiovascular pathology, hepatoprotectors

Introduction

For many years, diseases of the cardiovascular system have been leading in the ranking of the main causes of mortality in the population. According to experts, one of the important reasons for the discrepancy between the expected effectiveness of modern methods of therapy and real results is the lack of adherence to the principles of optimal therapy when choosing treatment regimens. Optimal drug therapy involves the appointment of a combination of drugs that allows you to achieve the maximum positive result with a minimum risk of side effects and complications. With a desire to achieve this efficacy, it is limited to the appointment of standard treatment regimens without taking into account

the individual characteristics of interaction, metabolism, bioavailability, speed and completeness of neutralization and elimination of drugs. At the same time, it is these factors, especially in conditions of comorbid pathology, that have a decisive influence on both the effectiveness and safety of the prescribed therapy.

The main body that regulates the state of pharmacokinetics and pharmacodynamics of drugs and determines the nature of drug-drug interactions is the liver. In the liver, among other things, the metabolism of almost all major classes of drugs that are included in the standards of treatment of cardiovascular pathology occurs: antiplatelet drugs and anticoagulants, beta-blockers, a significant number of ACE inhibitors and blockers of angiotensin II receptors, calcium channel antagonists.

In different countries, the treatment standards for these diseases differ, but are mostly similar to each other [1,2,3,4].

In turn, the pathogenesis of major diseases of the cardiovascular system is associated with changes in the structural and functional state of the liver. The highest risk of developing liver cirrhosis is in women over 45 years of age with metabolic syndrome, type 2 diabetes, arterial hypertension (AH) and signs of cytolysis syndrome during laboratory tests.

In connection with the foregoing, it is evident that therapeutically the event I in the treatment of coronary heart disease, type 2 diabetes, particularly complicated with hypertension should include correction of the functional state of the liver.

Modern approaches for prevention and treatment include: weight loss, restoration of insulin sensitivity (metformin), correction of lipid metabolism (statins) and the use of hepatoprotectors. If these items in most cases are counted by cardiologists and endocrinologists, district of hepatoprotective choice usually has difficulties.

It should be noted that today there is no generally accepted classification of hepatoprotectors. Several groups of hepatoprotectors are distinguished depending on the chemical structure and origin:

- herbal preparations;
- preparations of animal origin;
- preparations containing essential phospho-lipids (EPL);
- amino acids or their derivatives;
- antioxidant and vitamin-like vitaminsconnections;
- drugs of different groups [5].

Herbal products are most often used in clinical practice [6]. There is an opinion that any drug presented as a hepatoprotector is a priori effective and safe in the prevention and treatment of any disease. At the same time, practice shows that not all drugs of this class have convincing evidence of an improvement in the histological picture of the liver.

The aim of the study was to study the effect of Hepa-Merz® on the functional state of the liver, endothelium, rheological properties of blood, the state of capillary blood flow, markers of endotoxiosis, as well as the clinical state of patients with complex cardiovascular pathology, type 2 diabetes mellitus and chronic heart failure.



Material and methods

Study design intended to study the dynamics of the liver functional state of the endothelium, blood rheology, condition of capillary blood flow markers of endotoxemia prior to administration Hepa-Merz®, after the first (day per therapy) and fifth (the fifth day of therapy) infusions. The drug is in a single dose of 10 ml (1 ampoule). 45 patients aged 60-74 years (main age 68.4 ± 4.2 years) with a diagnosis of ischemic heart disease: stable exertional angina (main group) were examined.

Randomly these patients were divided into two groups: the first group (15 patients) received conventional therapy, the second group (30 patients), according to the study design, standard therapy of full assignment original preperate L-ar – Nitin-L-aspartate the form of infusion at a dose of 10 ml 1 time per day. The examination was carried out one day after the first infusion and at the end of the course of treatment (after five infusions).

Selection into groups was carried out on the basis of anamnesis and clinical, instrumental and laboratory examinations (ECG, EchoCG, blood and urine tests). Clinical examination of patients was carried out in accordance with accepted diagnostic standards. The functional state of the endothelium sc e NIWA by laser Doppler flowmetry (LDF) for dual laser Doppler flowmetry [7].

The aggregation activity of venous blood platelets was studied using a two-channel laser analyzer of platelet aggregation. The level of spontaneous and induced platelet aggregation was assessed.

The rheological properties of blood were investigated using a rotational viscometer at shear rates of 10 s^{-1} , 20 s^{-1} , 50 s^{-1} , 100 s^{-1} , 200 s^{-1} with the calculation of the erythrocyte deformability index (IDE) and the erythrocyte aggregation index (IAE).

The state of microcirculation of the bulbar conjunctiva was studied using a Zeiss television slit lamp (Germany). Images were recorded using applied computer programs.

The indicators of the microcirculation system obtained by morphometric analysis were also analyzed. P was calculated vascular conjunctival index, extravascular conjunctival index and intravascular conjunctival index, as well as the general conjunctival index, which is equal to the sum of the scores of all indices.

Results

According to the results obtained, the first infusion of Hepa-Merz® led to a significant decrease in the level of liver enzymes. And although a pronounced cytolysis syndrome is not typical for cardiovascular pathology and the level of these indicators in the examination group slightly exceeded the standard indicators, the data presented can be regarded as a positive effect of the drug on the functional state of hepatocytes, a decrease in congestion in the biliary tract. Also, against the background of therapy with Hepa-Merz®, the level of fibrinogen, total cholesterol and triglycerides was significantly reduced. See Table 1, which confirms the

high hepatoprotective and anti-inflammatory efficacy of the drug. An increase in the volumetric blood flow rate of the skin at the peak of the creation of reactive hyperemia, which manifests itself from the first infusion and reaches clinically significant values while taking the drug, indicates an improvement in the vasomotor function of the endothelium and confirms the presence of the endothelioprotective effect of the drug Hepa-Merz®. See Table 2.

Discussion

The indicated changes in the state of hemovascular homeostasis indicators, associated with the restoration of the balance of the molecular components of the plasma, the fluid properties of the membranes of the blood corpuscles and the protective properties of the endothelium, became a prerequisite for an increase in the perfusion blood flow of organs and tissues, assessed by the microcirculation index and capillaroscopy data. The level of microcirculation index before treatment was poor, and after – was better. The improvement of capillary blood flow during therapy with the original L-ornithine-L-aspartate is also evidenced by the results of capillaroscopy of the bulbar conjunctiva and the nail bed, according to which, with the introduction of the drug, there was an increase in the velocity and homogenization of blood flow, a significant decrease in stagnation in the capillaries. The improvement in hemorheological parameters led to a decrease in the intravascular conjunctival index [7,8].

Given that systemic capillary tropical failure is the leading cause of death in patients with severe heart failure observed during therapy with the drug Hepa-Merz® increase in the microcirculation, indicating an increase in the number of erythrocytes, passing per unit time through a unit of fabric, it confirms the possibility of gaining metabolic processes in tissues, not only due to the participation of drug components in metabolic cycles, but also due to an increase in oxygen delivery to ischemic organs and tissues.

As it is known, the main mechanism of cell death in chronic hypoxia and intoxication is apoptosis. It is obvious that improving blood supply while reducing the level of endogenous intoxication and toxic effects of free radicals creates conditions for improving the viability of body tissues, which is manifesting a decrease in the activity of cell apoptosis. During therapy with Hepa-Merz®, a significant decrease in spontaneous and induced apoptosis of mononuclear cells, as well as the apoptosis index, which characterizes the potential cell viability, was observed. It is possible that the latter is evidence of the potential for a positive effect of the drug on the life expectancy of this category of patients [8,9].

This conclusion is supported by the improvement in the clinical condition of the examined patients. The results of this study indicate the advisability of including the drug Hepa-Merz® in the therapy of patients with complex cardiovascular pathology and type 2 diabetes mellitus.

The results obtained confirm the possibility of influence of the preparation Hepa-Merz® on the functional disorders of the liver in patients with complexes c hydrochloric cardiovascular disease and type 2 diabetes.



Taking into account the fact that the clinical effect of Hepa-Merz® begins to manifest itself from the first infusion, patients with cardiovascular pathology can be prescribed a short course of the drug in a daily dose of 10 ml 1 time per day for five days of therapy with further transfer to the granular form original L-ornithine-L-aspartate.

Conclusion

The following can be considered valuable conclusions of this work. Already the first infusion of Hepa-Merz® leads to a significant decrease in the level of liver enzymes; During therapy with Hepa-Merz®, the level of fibrinogen, CRP, total cholesterol and triglycerides is significantly reduced, which confirms the high hepatoprotective and anti-inflammatory efficacy of the drug; The level of endogenous intoxication with the use of the minimum therapeutic dose of Hepa-Merz® decreases by 12%, which indicates a decrease in tissue hypoxia and an improvement in the functional state of hepatocytes; Against the background of therapy with Hepa-Merz®, a significant decrease in spontaneous and induced apoptosis of mononuclear cells, as well as the apoptosis index, which characterizes the potential viability of cells, up to 30% is observed.

Note

Our research is purely scientific. The data cannot be interpreted as marketing or post-marketing.

Table 1. The level of markers characterizing the functional state of the liver in the examination group during therapy with original L-ornithine-L-aspartate.
(*= $p < 0.05$)

Parameters	Group (n = 30)			Group (n = 15)	
	Before	Day 1	After 5 days	Before	After 5 days
Fibrinogen	5.1 ± 0.7	4.5 ± 0.3	$3.5 \pm 0.2 *$	4.5 ± 0.3	4.0 ± 0.3
Total cholesterol	4.8 ± 0.3	4.46 ± 0.30	$3.92 \pm 0.20 *$	4.66 ± 0.30	4.44 ± 0.40
Triglyceride	3.2 ± 0.1	2.7 ± 0.2	$2.2 \pm 0.2 *$	3.21 ± 0.30	3.2 ± 0.2

Table 2. The vascular markers in the examination group during therapy with original L-ornithine-L-aspartate. (*= $p < 0.05$)

Index	Main group		Comparison group	
	Before starting treatment	On the fifth day of therapy	Before starting treatment	On the fifth day of therapy
Vascular conjunctival index	10.53 \pm 0.20	9.03 \pm 0.20 *	11.03 \pm 0.30	10.78 \pm 0.20
Extravascular conjunctival index	1.00 \pm 0.01	1.10 \pm 0.01 *	1.10 \pm 0.01	1.10 \pm 0.01
Intravascular conjunctival index	3.71 \pm 0.10	1.71 \pm 0.20 *	3.82 \pm 0.10	3.79 \pm 0.10
General conjunctival index	15.43 \pm 0.50	12.27 \pm 0.22 *	15.11 \pm 0.50	15.21 \pm 0.40
Arteriole diameter, μm	10.04 \pm 0.20	11.57 \pm 0.10 *	9.7 \pm 0.3	10.5 \pm 0.5
Venule diameter, μm	29.3 \pm 0.4	27.6 \pm 0.5 *	29.3 \pm 0.4	28.9 \pm 0.2
Arterioloventricular coefficient	0.41 \pm 0.01	0.44 \pm 0.01 *	0.42 \pm 0.01	0.42 \pm 0.01
The number of functioning capillaries in 1 mm ²	8.0 \pm 0.1	8.0 \pm 0.2	8.0 \pm 0.1	8.0 \pm 0.1

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