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EFFECTS OF ARMADIN ON HEPATIC TRANSAMINASES IN RATS WITH ACUTE GENERALIZED PERITONITIS ON THE BACKGROUND OF DIABETES MELLITUS

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Abstract

The article discusses the issues about the effect of the Armadin on the hepatic transaminase in rats with acute generalized peritonitis on the background of diabetes mellitus. The experiment was performed on 48 white male adult rats, which were divided into two groups. The experimental group – animals with simulated acute generalized peritonitis against the background of streptozotocin-induced diabetes with the drug "Armadin" (ethylmethylhydroxypyridine succinate) application (n=24). The control group – animals with simulated acute generalized peritonitis against the background of streptozotocin-induced diabetes without pharmacocorrection (n = 24). Diabetes mellitus was simulated by a single intraperitoneal injection of streptozotocin at the dose of 60 mg/kg. Acute generalized peritonitis was induced with 10% faecal suspension in a dose of 0.5 ml per 100 g of animal weight in the abdominal cavity of laboratory animals by puncture method. Every day for 6 days, rats of experimental group received the drug "Armadin" at the doses of 100 mg/kg. We found a probable decrease in aminotransferase activity on day 3 of the study in rats of the

experimental group after administration of Armadin. Thus, ALT activity decreased by 26.7%, and AST activity – by 25.9% compared to the control group. On the 7th day of the study, the activity of ALT in the blood of rats of the experimental group decreased to 0.50 ± 0.03 mmol/l, which was 49.5% lower than the control group of rats in this period of the experiment. Similar changes are observed in the study of AST activity, where, accordingly, it decreased by 48 % relative to control. The positive effect of the drug "Armadin" on the body of rats, with AGP on the background of STZ-induced diabetes, is manifested by the restoration of the functional state of the liver.

Key words: acute generalized peritonitis; streptozotocin-induced diabetes; hepatic transaminase activities; liver; "Armadin".

Despite the introduction of the new methods of diagnosis and treatment, wide range of antimicrobial drugs, the mortality of patients with acute generalized peritonitis (AGP) remains high at 15.5 % to 37.8 % [1, 2, 3]. The analysis of the structural distribution of concomitant pathology in patients with acute peritonitis showed the presence of a significant proportion of diabetes mellitus, which correlates from 7.9% to 16.7% [4, 5, 6, 7]. Among the causes of mortality in peritonitis, complicated by multiple organ failure, one of the leading places is occupied by acute liver failure due to severe endotoxicosis. The leak of transaminase enzymes is characteristic reflects cellular and mitochondrial injury. The question of finding an effective pharmacocorrection of metabolic changes in combined pathology in order to reduce complications and mortality remains relevant.

The aim of this study was to estimate the plasma activity levels of hepatic transaminases in rats with experimental AGP against the background of streptozotocin (STZ)-induced diabetes under the condition the drug "Armadin".

Material and methods. The experiment was performed on 48 white male adult rats, which were divided into two groups. The experimental group – animals with simulated AGP against the background of STZ-induced diabetes with the drug "Armadin" (ethylmethylhydroxypyridine succinate) application (n=24). The control group – animals with simulated AGP against the background of STZ-induced diabetes without pharmacocorrection (n = 24).

Rats had free access to food and water while living conditions included constant ambient temperature (23±1 °C and 50±5 % humidity) and a 12-h light-dark cycle. The animals were cared for in accordance the Law of Ukraine No3447-IV "On the protection of

animals from cruel treatment" and in accordance with the EU Directive of 10/10/2010 on the protection of vertebrates animals used for experimental and other scientific purposes.

The animals were injected with a single dose of STZ (60 mg/kg body weight) intraperitoneally dissolved in 0.1 M citrate buffer (pH 4.5) after an overnight fast [8]. After the administration of STZ, the animals were given 1% sucrose solution to prevent hypoglycemia. On the 14th day after administration of STZ, animals were initiated acute peritonitis. In the experiment there was developed a model of peritonitis based on the introduction of 10% fecal suspension in the dosage of 0,5 ml per 100 g of the animal's weight into the abdominal cavity of rats by puncture [9]. The fecal suspension was prepared by mixing isotonic solution and the contents of the cecum of 3 intact animals, then it was filtered twice through a double layer of gauze and injected by puncture no later than 20 min after preparation. 24 animals of the main group received intraperitoneal injections of “Armadin” solution for injections, (50 mg/ml, Lekhim-Kharkiv, Ukraine) at the dosage of 100 mg/kg of body weight 1 time a day for 1, 2, 3, 4, 5, 6 day after introduction of fecal suspension.

The euthanasia of the rats was performed under thiopental anesthesia on the 1st, 3rd and 7th days of modeling AGP accordinly to the reactive, toxic and terminal stages of the disease. In blood plasma activity was determined enzymes ALT, AST by Raitman-Frenkel method [10].

Statistical processing of the received data was performed on a personal computer using standard software packages of Microsoft Excel and with the help of the computer program Statistica for Windows version 6.0 (Stat Soft inc., USA). The results were presented as mean values (M) ± the error of the mean (m) and were tested by one-way ANOVA, followed by Fisher’s least significant difference procedure as a post-hoc test. A level of $P<0.05$ was considered significant.

Results. On 1 day in group of animals with Armadin there was an improvement in ALT and AST level compared with the control group: ALT decreased by 2.8 % and AST – by 2.7 %, respectively, but it was not statistically significant ($p>0,05$) (Table 1). On 3 day, the level of transaminases also decreased in animals with AGP on the background of STZ-induced diabetes with with the drug “Armadin” application compared with the group of animals without pharmacocorrection – the level of ALT decreased by 26.7 %, and the level of AST decreased by 25.9 % ($p<0.05$). On 7 day, we observed the most pronounced positive dynamics of transaminase levels in rats with AGP on the background of STZ-induced diabetes + “Armadin” compared with controls. Thus, the level of ALT in such animals decreased by 49.5 %, and the level of AST – by 47.9% ($p<0,05$).

Table 1

The activity of aminotransferases in the blood of rats with AGP on the background of STZ-induced diabetes with the drug "Armadin" application (M ± m, n = 24)

Indexes	Groups	Research time (days)		
		1 day	3 days	7 days
ALT, mmol/l	Control (animals with AGP on the background of STZ-induced diabetes)	0,74±0,04	0,90±0,02	0,99±0,04
	Experimental (animals with AGP on the background of STZ-induced diabetes + Armadin)	0,72±0,03 p >0,05	0,66±0,01 p <0,05	0,50±0,03 p <0,05
AST, mmol/l	Control (animals with AGP on the background of STZ-induced diabetes)	1,07±0,05	1,16±0,05	1,23±0,02
	Experimental (animals with AGP on the background of STZ-induced diabetes + Armadin)	1,04±0,05 p >0,05	0,86±0,04 p <0,05	0,64±0,04 p <0,05
Note: p – the probability of the difference between the indicators compared with the control group.				

The increase in the activity of aminotransferases in the blood of rats of the control group with AGP on the background of STZ-induced diabetes, may be due to the fact that under conditions of oxidative stress, biological cell membranes are damaged, resulting in aminotransferases leaking from hepatocytes.

We found a probable decrease in aminotransferase activity on day 3 of the study in rats of the experimental group after administration of Armadin. Thus, ALT activity decreased by 26.7%, and AST activity – by 25.9% compared to the control group.

On the 7th day of the study, the activity of ALT in the blood of rats of the experimental group decreased to 0.50 ± 0.03 mmol/l, which was 49.5% lower than the control group of rats in this period of the experiment. Similar changes are observed in the study of AST activity, where, accordingly, it decreased by 48 % relative to control.

Thus, changes in the activity of ALT and AST in the blood of rats of the experimental group, which used the drug "Armadin", indicate a stimulating effect of the experimental drug on the functional state of the liver.

Therefore, studies confirm the antioxidant properties of the drug "Armadin". It increases the activity of enzymatic and non-enzymatic parts of the body's antioxidant defense system, inhibits free radical processes and the formation of reactive oxygen species, thereby reducing oxidative stress in animals with AGP on the background of STZ-induced diabetes and further preventing toxic effects on the liver.

Conclusions:

1. In rats with AGP on the background of STZ-induced diabetes, the functional state of the liver is disturbed, which is characterized by increased permeability of biological membranes of cell membranes, which causes hyperenzymemia in the blood, in particular AST and ALT.

2. Increased activity of aminotransferases in the blood of rats with AGP on the background of STZ-induced diabetes indicates destructive processes in the liver, which causes an increase in the release of aminotransaminases from cellular organelles in the blood of rats of the experimental group.

3. The positive effect of the drug "Armadin" on the body of rats, with AGP on the background of STZ-induced diabetes, is manifested by the restoration of the functional state of the liver.

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