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Реферати

МОРФОЛОГІЧНІ ОСОБЛИВОСТІ ДОКСОРУБІЦИН-ІНДУКОВАНИХ УРАЖЕНЬ ПЕЧІНКИ НА ТЛІ НЕАЛКОГОЛЬНОГО СТЕАТОГЕПАТИТУ

Маслова Г.С., Скрипник І.М., Єрошенко Г.А.

В роботі досліджено гістологічні особливості антрациклін-індукованих уражень печінки на тлі неалкогольного стеатогепатиту. В результаті проведеного дослідження встановлено, що у тварин з експериментальним неалкогольним стеатогепатитом у часточках печінки визначено помірно виражену жирову дистрофію печінки зі слабо вираженою осередковою білковою дистрофією гепатоцитів. В групі тварин з антрациклін-індукованим ураженням печінки встановлений помірний перипортальний некроз гепатоцитів на тлі слабко вираженої дрібнокрапельної жирової дистрофії. Виражений тотальний (центролобулярний і перипортальний) підгострий некроз печінки на тлі помірно вираженої жирової дистрофії виявлений у тварин з антрациклін-індукованим ураженням печінки на тлі експериментального неалкогольного стеатогепатиту.

Ключові слова: неалкогольний стеатогепатит, антрациклін-індуковані ураження печінки, щурі.

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МОРФОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ДОКСОРУБИЦИН-ИНДУЦИРОВАННОГО ПОРАЖЕНИЯ ПЕЧЕНИ НА ФОНЕ НЕАЛКОГОЛЬНОГО СТЕАТОГЕПАТИТА

Маслова Г.С., Скрипник И.М., Ерошенко А.

В работе исследованы гистологические особенности антрациклин-индуцированных поражений печени на фоне неалкогольного стеатогепатита. В результате проведенного исследования установлено, что у животных с экспериментальным неалкогольным стеатогепатитом в дольках печени выявлено умеренно выраженную жировую дистрофию печени со слабо выраженной очаговой белковой дистрофией гепатоцитов. В группе животных с антрациклин-индуцированным поражением печени установлен умеренный перипортальный некроз гепатоцитов на фоне слабо выраженной мелкокапельной жировой дистрофии. Выраженный тотальный (центролобулярный и перипортальный) подострый некроз печени на фоне умеренно выраженной жировой дистрофии обнаружен у животных с антрациклин-индуцированным поражением печени на фоне экспериментального неалкогольного стеатогепатита.

Ключевые слова: неалкогольный стеатогепатит, антрациклин-индуцированные поражения печени, крысы.

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REACTION OF HEMOMICROCIRCULATORY BED OF RAT LIVER AND CHANGES IN THE FUNCTIONAL STATE OF THE NITRIC OXIDE CYCLE UNDER THE CONDITIONS OF MODELING ALCOHOLIC HEPATITIS

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The purpose of the work was to study the changes in the hemomicrocirculatory bed of the liver and the role of the NO-ergic system in their development under the conditions of modeling alcoholic hepatitis. At the early stages of modeling alcoholic hepatitis, the thickness of the vascular wall of the central vein, interlobular artery and lobular arterioles increases, while the thickness of the vascular wall of the interlobular vein, the lobular venule and the sublobular vein decreases. These changes are associated with dysregulatory changes in the nitric oxide cycle in rat liver. Dysregulatory changes are manifested by an increase in the activity of inducible and constitutive isoforms of NO synthases against the background of decreased activity of arginases in the absence of statistically significant changes in the activity of nitrate and nitrite reductases in the liver of rats with simulated alcoholic hepatitis.

Key words: liver, alcoholic hepatitis, nitric oxide cycle, rats.

The work is a fragment of the research project "Peculiarities of pathological changes development in digestive system organs and development of their correction methods", state registration No. 0120U100502.

Alcohol consumption is the seventh leading risk factor for various diseases, injuries and death. In 6.8% of deaths among men and 2.2% among women, the cause is alcohol abuse. The total cost of eliminating the social consequences of alcohol consumption makes more than 1% of the gross national product for high- and middle-income countries, much higher than the budget for health care [5].

Alcohol consumption is a major cause of liver disease, and alcoholic hepatitis is a major chronic alcohol-related disease. Worldwide, per capita alcohol consumption is strongly correlated with mortality from liver cirrhosis [5]. It is estimated that alcohol abuse is the causative factor in 60 types of diseases and injuries and the simultaneous cause of at least in 200 other ones [8].

Despite the significant importance of the problem and the large number of publications devoted to the study of alcoholic hepatitis, the molecular mechanisms of alcoholic liver disease remain poorly understood. The role of nitric oxide (NO) in inflammation of the liver remains ambiguous because NO is reported to have both pro-inflammatory and anti-inflammatory properties [4]. The amount of NO, time and place of its synthesis are important factors of its biological impact. Among the nitric oxide-producing enzymes, the inducible isoform of NO synthase has a wide range of effects. New evidences emerge and lead to conclusion that the inducible isoform of NO synthase plays a key role in the initiation and development of liver tumors, which are a frequent complication of alcoholic hepatitis [2].

The development of alcoholic hepatitis is inextricably linked with the response of the liver hemomicrocirculatory bed. Vascular tone, capillary permeability directly depend on the NO-ergic system of the liver. Therefore, the study of changes in the NO-ergic system in the model of alcoholic hepatitis and its impact on the resistant, metabolic and capacitive links of the liver hemomicrocirculatory bed is a topical issue today.

The purpose of the work was to study the changes in the hemomicrocirculatory bed of the liver and the role of the NO-ergic system in their development under the conditions of modeling alcoholic hepatitis.

Materials and methods. The experiments were performed on 30 white adult Wistar male rats weighing 180-220 g. Animals were divided into 2 groups: group I – the control (n = 6); group II - animals with simulated alcoholic hepatitis (n = 24). We simulated alcoholic hepatitis by the method of forced intermittent alcoholism for 5 days, with repetition after two days by intraperitoneal administration of 16.5% ethanol solution in 5% glucose solution, at the rate of 4 ml / kg body weight [7]. The control group included animals that were subjected to similar manipulations throughout the study, but injected saline. Conditions for keeping animals in the vivarium were standard. Removal of animals from the experiment occurred on days 1, 3, 5 and 7 by taking blood from the right ventricle of the heart under thiopental anesthesia. Serum and liver were studied. During the experiments, the recommendations of the “European Convention for the protection of vertebrate animals used for experimental and other scientific purposes” were followed (Strasbourg, 1986). Experiments were conducted in accordance with the “General Principles of Animal Experiments” approved by the First National Congress of Bioethics, and the requirements of the "Procedure for conducting scientific experiments, experiments on animals" (2012).

In the serum of rats we determined the activity of γ-glutaminyltranspeptidase (γ-GTP) using a diagnostic kit, manufacturer NPP “Philisit-Diagnostics”.

The activity of inducible and constitutive isoforms of NO synthase [8], nitrite nitrate reductases and arginases was determined in rat liver homogenate [1].

Total NO-synthase (gNOS) activity was assessed by nitrite growth after incubation of 10% liver homogenate [1]. To determine the activity of constitutive NOS (cNOS) to the first aliquot was added 0.1 ml of 1% solution of aminoguanidine hydrochloride, extending the incubation time to 60 min [8]. The activity of inducible NOS (iNOS) was calculated by the formula: iNOS= gNOS-cNOS [8].

Nitrate-nitrite reductase activity was evaluated by reducing the concentration of nitrites and nitrates after incubation of 10% liver homogenate [1]. Arginase activity was determined by the increase of L-ornithine in 10% rat liver homogenate after incubation in phosphate buffer solution in the presence of excess L-arginine [1].

For morphometric studies, the liver was fixed in 10% neutral formalin, poured into paraffin blocks, from which semi-thin sections were prepared, which were stained with hematoxylin and eosin. Morphometric examination and microphotography were performed using a microscope Biorex-3 BM-500T with digital microphoto nozzle DCM 900 with programs adapted for research data. We determined the thickness of the vascular wall (by subtracting from the value of the outer diameter of the inner diameter of the vascular wall) of central vein, interlobular arteries and veins, arterioles and venules of hepatic lobes and sublobular vein.

Statistical processing of the results of biochemical studies was performed using pairwise comparison using the nonparametric Mann-Whitney method. Processing of the results of the morphometric study was performed using one-way analysis of variance by the method of Kruskal-Wallis with the subsequent use of pairwise comparison according to the exact Mann-Whitney test and taking into account the correction for the multiplicity of comparisons according to Bonferroni. All statistical calculations were performed in Microsoft office Excel and its extension Real Statistics 2019. The difference was considered statistically significant if $p<0.05$. Data in tables represented as mean ± standard error of mean (M±m).

Results of the study and their discussion. Biochemical analysis of serum in rats, with simulated alcoholic hepatitis, showed an increase in the activity of γ-GTP on the 3rd and 5th day of the experiment,

by 2.06 and 1.7 times respectively, compared to the control (p <0.05) and by 2.06 times on day 3 compared to the activity of γ-GTP on day 1 of the experiment (p <0.05) (tab. 1). On day 7 of the experiment, the activity of γ-GTP in the serum of rats decreased by 1.56 times compared with the activity of γ-GTP on day 5 of the experiment (p <0.05).

Table 1

Activity of γ-glutaminyltranspeptidase in the serum of rats with experimental alcoholic hepatitis, M±m

Parameters	Groups of animals				
	Control	1st day	3rd day	5th day	7th day
Activity of γ-glutaminyl-transpeptidase, μcat / l	0.67±0.04	0.67±0.05	1.38±0.16*^	1.14±0.09*	0.73±0.07^

* - p<0.05 compared to the control group of rats; ^ - p<0.05 compared to the previous term of the experiment.

The activity of cNOS in the liver of rats, with simulated alcoholic hepatitis, on the 3rd, 5th and 7th day of the experiment was increased by 1.93, 1.15 and 1.67 times, respectively, compared to the control (p <0.05) (tab. 2). On the 5th day of the experiment, the activity of cNOS in the liver of rats decreased by 1.68 times compared with the activity of cNOS on the 3rd day of the experiment (p <0.05). On the 7th day of the experiment, the activity of cNOS in the liver of rats increased by 1.45 times compared to the activity of cNOS on the 5th day of the experiment (p<0.05).

Table 2

Biochemical parameters in the liver of rats with experimental alcoholic hepatitis, M±m

Parameters, μmol / min per g of protein	Groups of animals				
	Control	1st day	3rd day	5th day	7th day
Activity of constitutive NO synthases	0.027±0.0003	0.052±0.007	0.052±0.004*	0.031±0.001*^	0.045±0.001*^
Inducible NO-synthase activity	0.16±0.02	1.07±0.15*	0.72±0.07*	0.14±0.02^	0.85±0.05*^
Nitrite reductase activity	3.11±0.51	3.4±0.42	2.54±0.48	1.23±0.13*	4.98±0.62^
Nitrate reductase activity	3.71±0.81	3.76±0.59	4.52±0.69	1.32±0.2*^	6.07±1.36^
Arginase activity	1.8±0.1	1.69±0.53	0.22±0.01*	0.18±0.01*	0.53±0.01*^

* - p<0.05 compared to the control group of rats; ^ - p<0.05 compared to the previous term of the experiment.

The activity of iNOS in the liver of rats simulated alcoholic hepatitis on days 1, 3 and 7 of the experiment increased by 6.69, 4.5 and 5.31 times, respectively, compared to the control (p<0.05). On day 5 of the experiment, the activity of iNOS in the liver of rats decreased by 5.14 times compared to the activity of iNOS on day 3 of the experiment (p<0.05). On the 7th day of the experiment, the activity of iNOS in the liver of rats increased by 6.07 times compared to the activity of iNOS on the 5th day of the experiment (p<0.05).

The activity of nitrite reductases in the liver of rats, which simulated alcoholic hepatitis, on the 5th day of the experiment was reduced by 2.53 times compared to the control (p<0.05). On the 7th day of the experiment, the activity of nitrite reductases in the liver of rats increased by 4.04 times compared to the activity of nitrite reductases on the 5th day of the experiment (p<0.05).

The activity of nitrate reductases in the liver of rats, which simulated alcoholic hepatitis, on the 5th day of the experiment was reduced by 3.42 times compared to the activity of nitrate reductases on the 3rd day of the experiment (p<0.05).

The activity of arginases in the liver of rats, which simulated alcoholic hepatitis, on the 3rd, 5th and 7th day of the experiment was reduced by 8.18, 10 and 3.4 times, respectively, compared to the control (p<0.05). On the 7th day of the experiment, the activity of arginases in the liver of rats increased by 2.94 times compared to the activity of arginases on the 5th day of the experiment (p<0.05).

A morphometric study of the hemomicrocirculatory bed of the liver of rats, with simulated alcoholic hepatitis, revealed that the thickness of the vascular wall of the central vein of the rats' hepatic lobe increased by 1, 3 and 7 days of the experiment, respectively, by 2.19, 2.04 and 1.39 times compared to the control (p<0.05) (tab. 3). On the 5th day of the experiment, the thickness of the vascular wall of the central vein of the rats' hepatic lobe decreased by 1.76 times compared to the thickness of the vascular wall on the 3rd day (p<0.05).

The vascular wall thickness of the interlobular artery of the liver of rats, with simulated alcoholic hepatitis, increased on the 1st, 3rd and 5th days of the experiment by 1.28, 1.54 and 1.51 times respectively, compared to the control (p<0.05). On day 7 of the experiment, the vascular wall thickness of the interlobular artery of rats decreased by 1.59 times compared to the vascular wall thickness on day 5 (p<0.05).

The vascular wall thickness of the hepatic lobe arterioles in rats, which were simulated alcoholic hepatitis on the 3rd, 5th and 7th day of the experiment increased by 2.28, 2.54 and 2.54 times respectively, compared to the control (p<0.05). On day 3 of the experiment, the vascular wall thickness of the hepatic lobe arterioles of rats increased by 1.83 times compared to the vascular wall thickness on the 1st day (p<0.05).

Table 3

Morphometric parameters of the hemomicrocirculatory bed of rats with experimental alcoholic hepatitis, M±m

Parameters, μm	Groups of animals				
	Control	1st day	3rd day	5th day	7th day
Vascular wall thickness of the central vein	1.13±0.11	2.47±0.12*	2.3±0.15*	1.31±0.07^	1.57±0.09*
Vascular wall thickness of the interlobular artery	3.48±0.06	4.46±0.26*	5.37±0.06*	5.27±0.12*	3.32±0.12^
Vascular wall thickness of the lobular arteriole	0.69±0.06	0.86±0.05	1.57±0.15*^	1.75±0.1*	1.75±0.11*
Vascular wall thickness of the lobular venule	2.26±0.15	1.39±0.07*	1.04±0.08*	1.11±0.03*	1.08±0.07*
Vascular wall thickness of the intelobular vein	4.77±0.21	1.51±0.1*	1.79±0.07*	3.34±0.23*^	2.2±0.14*^
Vascular wall thickness of the sublobular vein	4.83±0.17	2.85±0.08*	2.71±0.35*^	2.12±0.09*	1.96±0.07*

* - p<0.05 compared to the control group of rats; ^ - p<0.05 compared to the previous term of the experiment.

The vascular wall thickness of the hepatic lobe venules of rats, with simulated alcoholic hepatitis, decreased on the 1st, 3rd, 5th and 7th day of the experiment by 1.63, 2.17, 2.04 and 2.09 times respectively, compared to the control (p<0.05).

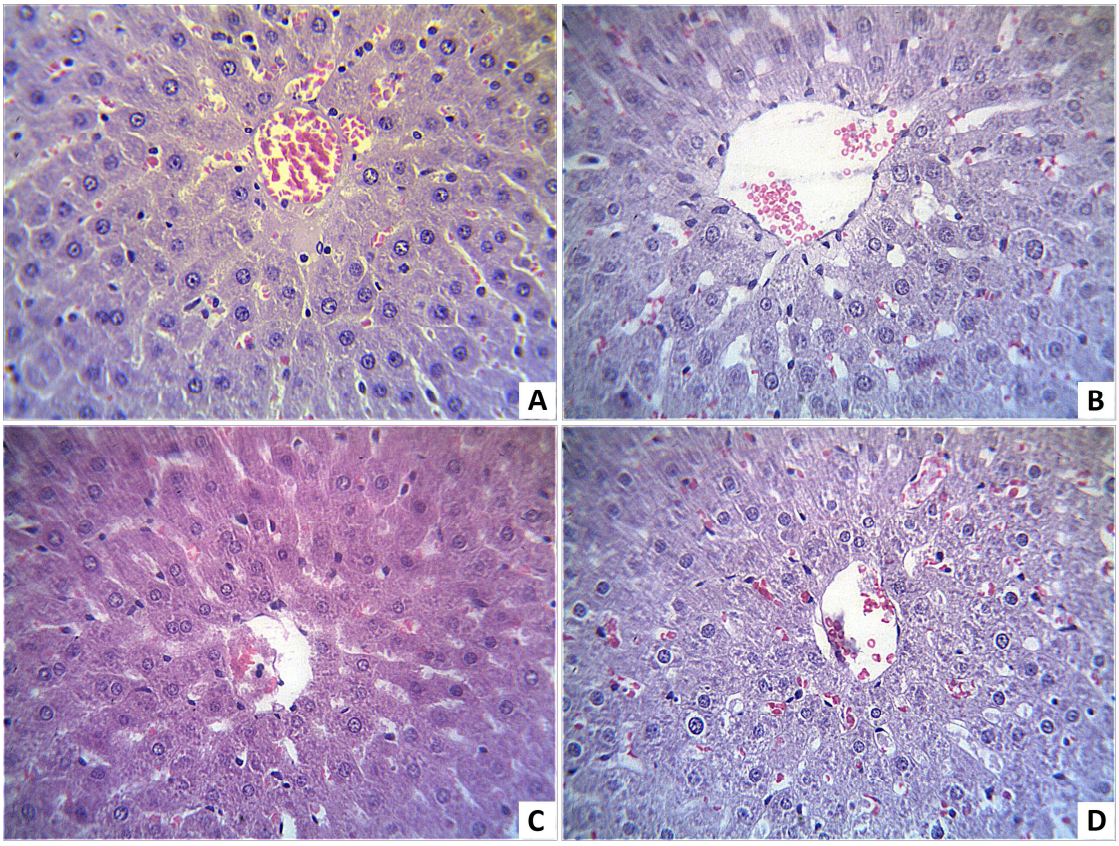
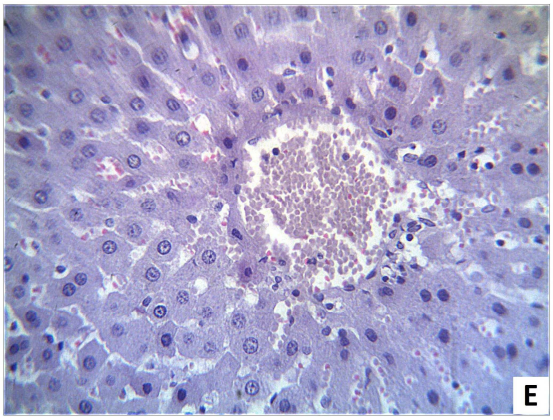


Fig. 1. Central vein of rat liver under conditions of alcoholic hepatitis simulation. Magnification: Lens x 40, Eyepiece x 10. A – control group of animals; B – 1st day of experiment; C – 3rd day of experiment; D – 5th day of experiment; E – 7th day of experiment.



The vascular wall thickness of the liver interlobular vein of rats with simulated alcoholic hepatitis, decreased on the 1st, 3rd, 5th and 7th day of the experiment by 3.16, 2.66, 1.43 and 2.17 times respectively, compared to the control (p<0.05). On the 5th day of the experiment, the vascular wall thickness of the rats' interlobular vein increased by 1.87 times compared to the vascular wall thickness on the 3rd day (p<0.05). On the 7th day of the experiment, the vascular wall thickness of the rats' interlobular vein decreased by 1.52 times compared to the vascular wall thickness on the 5th day (p<0.05).

The vascular wall thickness of the liver sublobular vein in rats with simulated alcoholic hepatitis, decreased on the 1st, 3rd, 5th and 7th day of the experiment by 1.69, 1.78, 2.28 and 1.22 times respectively, compared to the control (p<0.05).

On the first day of modeling, alcoholic hepatitis destruction of hepatocytes does not occur, because γ-GTP activity is within the levels of the control group of animals. An increase in the vascular wall thickness of the central vein and the interlobular artery can be considered signs of damage to these vessels (fig. 1B). A decrease in the vascular wall thickness of the lobular venule and the interlobular and sublobular vein may occur in response to a pressure decrease in the capacitive link of the hemomicrocirculatory bed of the rats' liver (fig. 2B). A possible reason for the described changes on the first day of the experiment is the action of nitric oxide, produced by inducible NO synthase.

On the third day of modeling alcoholic hepatitis, we observed a cytolysis of hepatocytes as evidenced by the increase in the activity of γ-GTP in the blood serum of rats. The dynamics of changes in the vascular walls thickness of the studied vessels on the third day remains the same as on the first day (fig. 1C, 2C). The role of constitutive isoforms of NO-synthase in the increased production of nitric oxide in the rats' liver with simulated alcoholic hepatitis. Competition between NO synthases and arginases for the substrate increases and leads to a decrease in the activity of arginases in the rats' liver with simulated alcoholic hepatitis. A possible reason for the decrease in the activity of arginases in the rats' liver may also be alcohol-dependent change in the polarization of Kupffer cells by M1 phenotype through activation of NF-κB transcription factor [2].

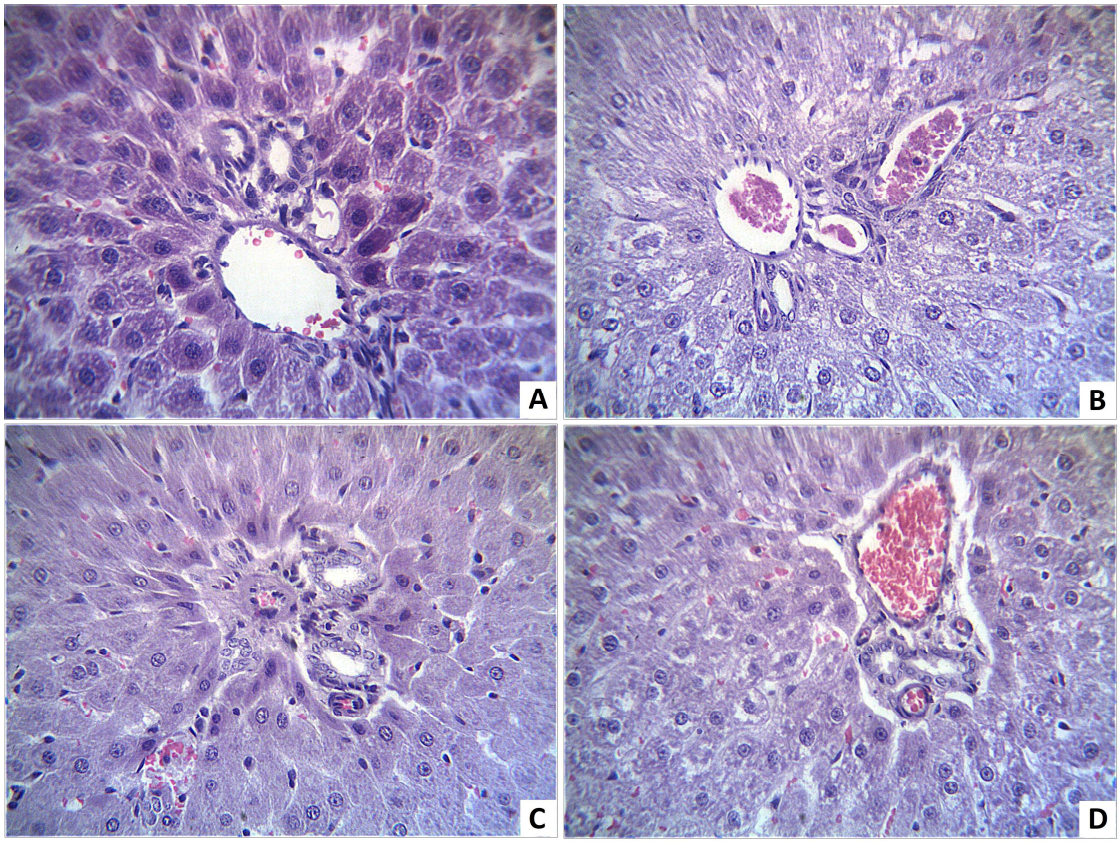
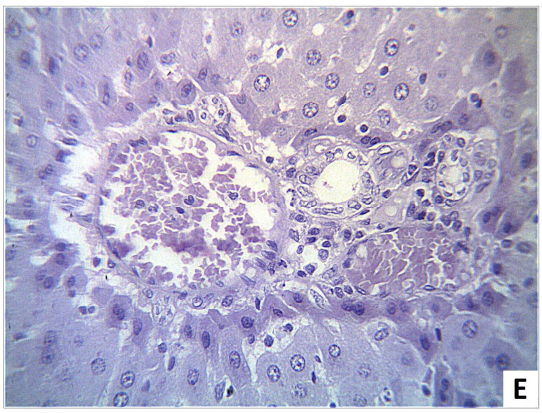


Fig. 2. Liver triad of rats under the conditions of modeling alcoholic hepatitis. Hematoxylin and eosin staining. Magnification: x 400. A – control group of animals; B – 1st day of experiment; C – 3rd day of experiment; D – 5th day of experiment; E – 7th day of experiment.



On the fifth day of modeling alcoholic hepatitis, the activity of γ-GTP in the blood serum of the rats' liver with simulated alcoholic hepatitis, remains at a high level. The vascular wall thickness of the central vein decreases, and that of the interlobular vein increases compared to the previous term of the experiment (fig. 1D, 2D). Production of nitric oxide in the rats' liver on the 5th day of modeling alcoholic hepatitis is reduced from all studied isoforms of NO synthase, as evidenced by the decrease in the activity of iNOS and cNOS to the level of the control group animals. Nitrate-nitrite reductive mechanism of nitric oxide production in the rats' liver with simulated alcoholic hepatitis, also reduces its activity. Thus, in the rat liver on the 5th day of modeling alcoholic hepatitis there occurs a dysregulation of nitric oxide production, confirmed by a decrease in the activity of arginases, NO synthases and nitrate-nitrite reductases. A possible

cause of this phenomenon may be a deficiency of the reaction substrate for arginases and the deposition of nitric oxide, which was synthesized in large quantities at the previous stages of the experiment, in the form of nitrosothiols.

On the seventh day of modeling alcoholic hepatitis, the activity of γ-GTP in the blood serum of rats is reduced compared to the previous period of the experiment. The vascular wall thickness of the interlobular arteries and veins in the rats' liver decreases compared to the previous period of the experiment (fig. 1E, 2E). Production of nitric oxide in the liver of rats with simulated alcoholic hepatitis is increased by NO synthases and nitrite reductases. Arginases also increase their activity. These changes may be associated with an increase in the amount of substrate for NO synthases and arginases functioning in the rat liver, which is associated with the activation of autophagy. Autophagy, caused by alcohol, leads to increased protein catabolism. Short-term alcohol consumption increases the autophagy of mitochondria and damaged proteins, while activity of proteosomal protein degradation and lysosome formation decreases [3]. Prolonged alcohol consumption, on the other hand, reduces autophagy [3].

An important role in alcoholic liver damage is played by the macrophage link of the immune system. It is proved that the destruction of Kupffer cells by gadolinium chloride leads to a decrease in the intensity of inflammation in the conditions of alcoholic hepatitis [4]. There is a hypothesis that the transition of liver macrophages to the proinflammatory M1 phenotype during alcohol consumption is associated with damage to the intestinal mucosal barrier by ethanol when taken orally [5]. Damage to the intestinal mucosal barrier leads to increased entry of bacterial lipopolysaccharides into the liver, which provokes polarization of liver macrophages by M1 phenotype through Toll-like receptors type 4 [6].

However, the relevance of this hypothesis in our experimental model is questionable. This is due to the fact that our experimental model of alcoholic hepatitis involves intraperitoneal administration of ethanol in the experiment. Therefore, ethanol-dependent damage to the intestinal mucosa during this period is debatable. Studying the activity of marker enzymes of macrophage polarization (iNOS, arginase) we can indirectly claim the predominance of M1 polarization on the 3rd and 7th day of modeling alcoholic hepatitis in rats. On the first day of the experiment, the activity of iNOS increases, which may indicate the beginning of changes in the polarization of liver macrophages. On the fifth day of alcoholic hepatitis simulation, despite the fact that the activity of iNOS decreases to values in the control group of animals, it can be argued that rat liver macrophages are mostly in M1 state, because the activity of arginases is significantly reduced.

Taking into account the changes in marker enzymes of macrophage polarization (iNOS and arginase) and the features of the experimental model, we can note that the change in macrophage polarization is more associated with alcohol-dependent damage to hepatocytes than with alcohol-dependent damage to the intestinal mucosa.

Conclusion

An the early stages of modeling alcoholic hepatitis, the vascular wall thickness of the central vein, interlobular artery and lobular arterioles increases, while the vascular wall thickness of the interlobular vein, the lobular venule and the sublobular vein decreases. These changes are associated with disregulatory changes in the nitric oxide cycle in rat liver.

Disregulatory changes are manifested by an increase in the activity of inducible and constitutive isoforms of NO synthases against the background of the decreased activity of arginases in the absence of statistically significant changes in the activity of nitrate and nitrite reductases in the liver of rats with simulated alcoholic hepatitis.

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Реферати

РЕАКЦІЯ ГЕМОМІКРОЦИРКУЛЯТОРНОГО РУСЛА ПЕЧІНКИ ТА ЗМІНИ В ФУНКЦІОНАЛЬНОМУ СТАНІ ЦИКЛУ ОКСИДУ АЗОТУ ЗА УМОВ МОДЕЛЮВАННЯ АЛКОГОЛЬНОГО ГЕПАТИТУ

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Метою роботи було вивчити зміни гемомікроциркуляторного русла печінки та роль NO-ергічної системи в їх розвитку за умов моделювання алкогольного гепатиту. На ранніх термінах моделювання алкогольного гепатиту товщина судинної стінки центральної вени та міжчасточкової артерії і часточкової артеріоли збільшується, а товщина судинної стінки міжчасточкової вени та часточкової венули і підчасточкової вени зменшується, що пов'язано з дизрегуляторними змінами в циклі оксиду азоту в печінці щурів. Дизрегуляторні зміни полягають у збільшенні активності індуцибельної та конститутивних ізоформ NO-синтаз на фоні зниження активності аргіназ за відсутності статистично значущих змін в активності нітрат- та нітритредуктаз в печінці щурів, яким моделювали алкогольний гепатит.

Ключові слова: печінка, алкогольний гепатит, цикл оксиду азоту, щури.

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РЕАКЦИЯ ГЕМОМИКРОЦИРКУЛЯТОРНОГО РУСЛА ПЕЧЕНИ И ИЗМЕНЕНИЯ В ФУНКЦИОНАЛЬНОМ СОСТОЯНИИ ЦИКЛА ОКСИДА АЗОТА ПРИ УСЛОВИИ МОДЕЛИРОВАНИЯ АЛКОГОЛЬНОГО ГЕПАТИТА

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Целью работы было изучить изменения гемомикроциркуляторного русла печени и роль NO-эргической системы в их развитии в условиях моделирования алкогольного гепатита. На ранних сроках моделирования алкогольного гепатита толщина сосудистой стенки центральной вены и междольковой артерии и внутридольковой артериолы увеличивается, а толщина сосудистой стенки междольковой вены, внутридольковой венулы и поддольковой вены уменьшается, что связано с дисрегуляторными изменениями в цикле оксида азота печени крыс. Дисрегуляторные изменения заключаются в увеличении активности индуцибельной и конститутивных изоформ NO-синтазы на фоне снижения активности аргиназы при отсутствии статистически значимых изменений в активности нитрат- и нитритредуктаз в печени крыс, которым моделировали алкогольный гепатит.

Ключевые слова: печень, алкогольный гепатит, цикл оксида азота, крысы.

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INFLUENCE OF PINEAL GLAND'S HYPOFUNCTION ON THE STRUCTURE OF VISCERAL ORGANS

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The purpose of this work was to study the morphological and functional changes in the pineal gland, heart, stomach, lungs and intestines of rats in the conditions of the pineal gland's hypofunction. The studies were carried out on 24 sexually mature male Wistar rats, which were kept in standard vivarium conditions with round-the-clock lighting for 30 days. As a result of the performed microscopic studies, it was found that the lack of melatonin is accompanied by erosive gastritis with atrophy of the glands, an increase in proliferative activity and in the number of pathological mitoses in the jejunum of rats, which may indicate the genesis of malignant tumors. Dystrophies, atrophy and hypertrophy of cardiomyocytes, foci of cardiomyocytes' lysis, circulatory impairment and inflammatory changes in lung tissues, which can be considered moderately expressed intestinal pneumonia, were revealed.

Key words: pineal gland, pinealocytes, hypofunction, cardiomyocytes, intestinal pneumonia, gastritis.

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Among the physiological characteristics of living organisms, the fundamental one is the rhythm of their activity, which manifests itself in the periodicity of many functions, circadian rhythms, and seasonality [5, 9]. The pineal gland is considered to be the central link that provides the body with information about changes in the light regime. The secretion product of the pineal gland is the hormone melatonin, which regulates the body's biorhythms, both directly affecting cells and by changing the secretion of other hormones and biologically active substances, which concentration varies depending on the time of day [7, 8]. Various